Filed Pursuant to Rule 424(b)(3)
Registration No. 333-266184

PROPOSED MERGER
YOUR VOTE IS VERY IMPORTANT

To the Stockholders of Syros Pharmaceuticals, Inc. and Tyme Technologies, Inc.,

Syros Pharmaceuticals, Inc., a Delaware corporation, or Syros, and Tyme Technologies, Inc., a Delaware corporation, or Tyme, entered into an Agreement and Plan of Merger, or the Merger Agreement, on July 3, 2022, pursuant to which a direct, wholly owned subsidiary of Syros, Tack Acquisition Corp., or Merger Sub, will merge with and into Tyme, with Tyme surviving as a wholly owned subsidiary of Syros, which transaction is referred to herein as the merger. The surviving corporation following the merger is referred to herein as the combined company.

At the effective time of the merger, each share of Tyme common stock will be converted into the right to receive a number of shares of Syros common stock equal to the exchange ratio described in more detail in the section titled "*The Merger Agreement—Merger Consideration and Adjustment*" beginning on page 194 of the accompanying joint proxy statement/prospectus.

In connection with the merger, each outstanding and unexercised option to purchase shares of Tyme common stock granted to an individual who continues as a service provider to Tyme at the effective time will be assumed by Syros and converted into an option to purchase shares of Syros common stock, with necessary adjustments to reflect the exchange ratio. Each outstanding and unexercised option to purchase shares of Tyme common stock that is not assumed by Syros pursuant to the Merger Agreement will be terminated and no consideration will be delivered for such options to purchase shares. Also in connection with the merger, each outstanding and unexercised warrant to purchase shares of Tyme common stock (other than certain warrants that Tyme is required to repurchase in connection with the merger) will be assumed by Syros and converted into a warrant to purchase shares of Syros common stock, with necessary adjustments to reflect the exchange ratio.

Each share of Syros common stock and option to purchase Syros common stock or other equity award covering shares of Syros common stock that is issued and outstanding at the effective time of the merger will remain issued and outstanding and such shares and equity awards will be unaffected by the merger. Based upon the initially estimated exchange ratio, following the merger and giving effect to the issuance of Syros securities in a private placement financing to be conducted by Syros concurrently with the merger, or the PIPE Financing, (i) Syros securityholders immediately before the merger together with the investors in the PIPE Financing are expected to own approximately 63% of the aggregate number of outstanding shares of Syros common stock following the merger and (ii) Tyme securityholders immediately before the merger are expected to own approximately 37% of the aggregate number of outstanding shares of Syros common stock following the merger, subject to certain assumptions (including as to the amount of Tyme net cash at closing, which could be materially different). Assuming the exercise of all Syros pre-funded warrants, including the Pre-Funded PIPE Warrants and the Pre-Funded 2020 Warrants (as defined in the section titled "*Description of Syros Capital Stock*" beginning on page 422 of the accompanying joint proxy statement/prospectus), without giving effect to any beneficial ownership limitations applicable thereto, then (i) Syros securityholders immediately before the merger together with the investors in the PIPE Financing would own approximately 73% of the aggregate number of outstanding shares of Syros common stock following the merger and (ii) Tyme securityholders immediately before the merger would own approximately 27% of the aggregate number of outstanding shares of Syros common stock following the merger, subject to certain assumptions (including as to the amount of Tyme net cash at closing, which could be materially different). The foregoing percentages do not give effect to the exercise or conversion of outstanding stock options or warrants other than as set forth above.

Shares of Syros common stock are currently listed on The Nasdaq Global Select Market under the symbol "SYRS." Shares of Tyme common stock are currently listed on The Nasdaq Capital Market under the symbol "TYME." After completion of the merger, it is expected that the common stock of the combined company will

trade on The Nasdaq Global Select Market under the symbol "SYRS." On August 5, 2022, the last trading day before the date of the accompanying joint proxy statement/prospectus, the closing sale price of Syros common stock was $0.90 per share.

The closing of the merger is conditioned upon the satisfaction or waiver of the conditions to the closing of the merger as well as certain other conditions, including that the securities purchase agreement entered into between Syros and several institutional accredited investors, pursuant to which Syros agreed to issue and sell Syros securities in a private placement, shall remain in full force and effect, and all conditions precedent to the closing of such private placement shall have been completed or waived. The private placement is more fully described in the accompanying joint proxy statement/prospectus and in Syros' Current Report on Form 8-K filed with the U.S. Securities and Exchange Commission, or the SEC, on July 5, 2022.

Syros stockholders are cordially invited to attend the special meeting of Syros stockholders. Syros is holding its special meeting of stockholders, or the Syros special meeting, on September 15, 2022, at 10:00 A.M. Eastern Time, unless postponed or adjourned to a later date, in order to obtain the stockholder approvals necessary to complete the merger and related matters. The Syros special meeting will be held entirely online. Syros stockholders will be able to attend and participate in the Syros special meeting online by visiting meetnow.global/MYRZKZT where they will be able to listen to the meeting live, submit questions and vote. At the Syros special meeting, Syros will ask its stockholders to:

1. Approve, for purposes of Nasdaq Listing Rules 5635(a) and (d), the issuance of shares of Syros common stock pursuant to the terms of the Merger Agreement and the Securities Purchase Agreement.
2. Approve an amendment to the Syros restated certificate of incorporation to increase the number of authorized shares of Syros common stock from 200,000,000 shares to 700,000,000 shares.
3. Approve an amendment to the Syros restated certificate of incorporation to effect a reverse stock split of Syros common stock, by a ratio of not less than 1-for-5 and not more than 1-for-15, and a proportionate reduction in the number of authorized shares of Syros common stock, such ratio and the implementation and timing of the reverse stock split to be determined in the discretion of Syros' board of directors.
4. Approve the adoption of the Syros Pharmaceuticals, Inc. 2022 Equity Incentive Plan.
5. Consider and vote upon an adjournment of the Syros special meeting, if necessary, to solicit additional proxies if there are not sufficient votes in favor of Proposal Nos. 1, 2 and 3 or to ensure that any supplement or amendment to this joint proxy statement/prospectus is timely provided to holders of Syros common stock.

Tyme stockholders are cordially invited to attend the special meeting of Tyme stockholders. Tyme is holding its special meeting of stockholders, or the Tyme special meeting, on September 15, 2022, at 11:00 A.M. Eastern Time, unless postponed or adjourned to a later date, in order to obtain the stockholder approvals necessary to complete the merger and other matters. The Tyme special meeting will be held entirely online. Tyme stockholders will be able to attend and participate in the Tyme special meeting online by visiting https://www.cstproxy.com/tymeinc/2022, where they will be able to listen to the meeting live, submit questions and vote. At the Tyme special meeting, Tyme will ask its stockholders to:

1. Adopt the Merger Agreement, or the Tyme Merger Proposal.
2. Conduct an advisory, non-binding vote to approve merger-related executive compensation.
3. Approve an amendment to Tyme's amended and restated certificate of incorporation to effect a reverse stock split of Tyme common stock, by a ratio of not less than 1-for-15 and not more than 1-for-75, such ratio and the implementation and timing of the reverse stock split to be determined in the discretion of Tyme's board of directors.
4. Consider and vote upon an adjournment of the Tyme special meeting, if necessary, to solicit additional proxies if there are not sufficient votes in favor of Proposal Nos. 1, 2 and 3 or to ensure that any supplement or amendment to this joint proxy statement/prospectus is timely provided to holders of Tyme common stock.

As described in the accompanying joint proxy statement/prospectus, certain Syros stockholders who in the aggregate owned approximately 28% of the outstanding shares of Syros common stock as of June 30, 2022, and certain Tyme stockholders who in the aggregate owned approximately 31% of the outstanding shares of Tyme common stock as of June 30, 2022, are parties to voting agreements with Tyme or stockholder support agreements with Syros and Tyme, respectively, whereby such stockholders have effectively agreed to vote in favor of the approval of the transactions contemplated therein, including, with respect to Tyme stockholders, adoption of the Merger Agreement and approval of the merger and, with respect to Syros stockholders, the issuance of shares of Syros common stock pursuant to the terms of the Merger Agreement and the Securities Purchase Agreement, the increase in the number of authorized shares of Syros common stock to be effectuated prior to the effective time, and such other matters as may require approval of the Syros' stockholders pursuant to the Delaware General Corporation Law, or DGCL, with respect to the PIPE Financing, subject to the terms of the support agreements.

After careful consideration, each of the Syros and Tyme boards of directors have approved the Merger Agreement and have determined that it is advisable to consummate the merger. Syros' board of directors has approved the proposals described in the accompanying joint proxy statement/prospectus and recommends that its stockholders vote "FOR" the proposals described in the accompanying proxy statement/prospectus. Tyme's board of directors has approved the proposals described in the accompanying joint proxy statement/prospectus and recommends that its stockholders vote "FOR" the proposals described in the accompanying proxy statement/prospectus.

More information about Syros, Tyme, the Merger Agreement and transactions contemplated thereby and the foregoing proposals is contained in the accompanying joint proxy statement/prospectus. Syros and Tyme urge you to read the accompanying joint proxy statement/prospectus carefully and in its entirety. IN PARTICULAR, YOU SHOULD CAREFULLY CONSIDER THE MATTERS DISCUSSED UNDER "RISK FACTORS " BEGINNING ON PAGE 31 OF THE ACCOMPANYING JOINT PROXY STATEMENT/PROSPECTUS.

Syros and Tyme are excited about the opportunities the merger brings to Syros' and Tyme's stockholders and thank you for your consideration and continued support.

Sincerely,

Nancy Simonian, M.D.
Chief Executive Officer
Syros Pharmaceuticals, Inc.

Richard Cunningham
Chief Executive Officer
Tyme Technologies, Inc.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of the accompanying joint proxy statement/prospectus. Any representation to the contrary is a criminal offense.

The accompanying joint proxy statement/prospectus is dated August 8, 2022 and is first being mailed to stockholders on or about August 10, 2022.

SYROS PHARMACEUTICALS, INC.
35 CambridgePark Drive, 4th Floor
Cambridge, Massachusetts 02140
(617) 744-1340

NOTICE OF SPECIAL MEETING OF STOCKHOLDERS

To the stockholders of Syros Pharmaceuticals, Inc.:

NOTICE IS HEREBY GIVEN that a virtual special meeting of stockholders, or the Syros special meeting, will be held on September 15, 2022, at 10:00 A.M. Eastern Time, unless postponed or adjourned to a later date. The Syros special meeting will be held entirely online. You will be able to attend and participate in the Syros special meeting online by visiting meetnow.global/MYRZKZT where you will be able to listen to the meeting live, submit questions and vote.

The Syros special meeting will be held for the following purposes:

1. To approve, for purposes of Nasdaq Listing Rule 5635(a) and (d), the issuance of shares of common stock of Syros Pharmaceuticals, Inc., or Syros, to stockholders of Tyme Technologies, Inc., or Tyme, pursuant to the terms of the Agreement and Plan of Merger among Syros, Tyme and Tack Acquisition Corp., or Merger Sub, dated as of July 3, 2022, a copy of which is attached as *Annex A* to the accompanying joint proxy statement/prospectus, which is referred to in this Notice as the Merger Agreement, and to certain investors pursuant to the terms of the Securities Purchase Agreement, by and among Syros and the investors party thereto, dated as of July 3, 2022, a copy of which is attached as *Annex F* to the accompanying joint proxy statement/prospectus, which is referred to in this Notice as the Securities Purchase Agreement;

2. To approve an amendment to the Syros restated certificate of incorporation to increase the number of authorized shares of Syros common stock from 200,000,000 shares to 700,000,000 shares;

3. To approve an amendment to the Syros restated certificate of incorporation to effect a reverse stock split of Syros common stock, by a ratio of not less than 1-for-5 and not more than 1-for-15, and a proportionate reduction in the number of authorized shares of Syros common stock, such ratio and the implementation and timing of the reverse stock split to be determined in the discretion of Syros' board of directors;

4. To approve the adoption of the Syros Pharmaceuticals, Inc. 2022 Equity Incentive Plan; and

5. To consider and vote upon an adjournment of the Syros special meeting, if necessary, to solicit additional proxies if there are not sufficient votes in favor of Proposal Nos. 1, 2 and 3 or to ensure that any supplement or amendment to this joint proxy statement/prospectus is timely provided to holders of Syros common stock.

Record Date: Syros' board of directors has fixed August 8, 2022 as the record date for the determination of stockholders entitled to notice of, and to vote at, the Syros special meeting and any adjournment or postponement thereof. Only holders of record of shares of Syros common stock at the close of business on the record date are entitled to notice of, and to vote at, the Syros special meeting. At the close of business on the record date, Syros had 63,005,295 shares of common stock outstanding and entitled to vote.

Your vote is important. The affirmative vote of the holders of a majority of shares present in attendance or represented by proxy at the Syros special meeting and entitled to vote on the matter, assuming a quorum is present, is required for approval of Proposal Nos. 1, 4 and 5. The affirmative vote of the holders of a majority of the outstanding shares of Syros common stock entitled to vote at the Syros special meeting is required for approval of Proposal Nos. 2 and 3. Approval of Proposal No. 1, referred to as the Syros share issuance proposal, is a condition of the merger and approval of Proposal No. 2, referred to as the Syros share increase proposal, is necessary to complete the PIPE Financing, which is a condition to Tyme's obligation to complete the merger. Therefore, the merger cannot be consummated without the approval of Proposal No. 1 and, unless waived by Tyme, without the approval of Proposal No. 2.

Even if you plan to virtually attend the Syros special meeting, Syros requests that you sign and return the enclosed proxy or vote by mail or online to ensure that your shares will be represented at the Syros special meeting if you are unable to virtually attend. You may change or revoke your proxy at any time before it is voted at the Syros special meeting.

SYROS' BOARD OF DIRECTORS HAS DETERMINED AND BELIEVES THAT EACH OF THE PROPOSALS OUTLINED ABOVE IS FAIR TO, IN THE BEST INTERESTS OF, AND ADVISABLE TO SYROS AND ITS STOCKHOLDERS AND HAS APPROVED EACH SUCH PROPOSAL. SYROS' BOARD OF DIRECTORS RECOMMENDS THAT SYROS STOCKHOLDERS VOTE "FOR" EACH SUCH PROPOSAL.

Important Notice Regarding the Availability of Proxy Materials for the Stockholders' Meeting to Be Held on September 15, 2022 via the internet

The proxy statement/prospectus and annual report to stockholders are available at meetnow.global/MYRZKZT.

By Order of Syros' Board of Directors,

Nancy Simonian, M.D.
Chief Executive Officer
Cambridge, Massachusetts
August 8, 2022

Tyme Technologies, Inc.
1 Pluckemin Way, Suite 103
Bedminster, NJ 07921

Notice of Special Meeting of Stockholders

September 15, 2022 at 11:00 A.M. Eastern Time
To be conducted virtually live via the Internet at https://www.cstproxy.com/tymeinc/2022

The Tyme special meeting will be held for the following purposes:

1. To adopt the Merger Agreement, or the Tyme Merger Proposal;
2. To conduct an advisory, non-binding vote to approve merger-related executive compensation;
3. To approve an amendment to Tyme's amended and restated certificate of incorporation to effect a reverse stock split of Tyme common stock, by a ratio of not less than 1-for-15 and not more than 1-for-75, such ratio and the implementation and timing of the reverse stock split to be determined in the discretion of Tyme's board of directors;
4. To consider and vote upon an adjournment of the Tyme special meeting, if necessary, to solicit additional proxies if there are not sufficient votes in favor of Proposal Nos. 1, 2 and 3 or to ensure that any supplement or amendment to this joint proxy statement/prospectus is timely provided to holders of Tyme common stock.

You can vote at the Tyme special meeting or any adjournment thereof online or by mail if you were a Tyme stockholder of record at the close of business on August 8, 2022. You may revoke your proxy at any time before its exercise at the Tyme special meeting.

Tyme is holding the Tyme special meeting virtually live via the Internet; there is no physical location. The virtual Tyme special meeting will afford Tyme's stockholders the same rights and opportunities as an in-person meeting, allowing for active participation by all of Tyme's stockholders at no cost, regardless of their geographic location. You will be able to attend online by visiting https://www.cstproxy.com/tymeinc/2022. At the meeting date and the time described above and in this joint proxy statement/prospectus. You will need your 12-digit control number included on your voting instruction form or proxy card to enter https://www.cstproxy.com/tymeinc/2022. To merely listen to the meeting, if you are within the U.S. and Canada, please dial toll-free or if outside the U.S. and Canada, please dial (standard rates apply), and enter the passcode that will be posted at https://www.cstproxy.com/tymeinc/2022. If you hold your shares through a bank, broker or other nominee, you will need to take additional steps to participate in the meeting, as described in this joint proxy statement/prospectus.

The list of Tyme stockholders of record entitled to vote at the Tyme special meeting will be made available for viewing by stockholders for any relevant purpose during the Tyme special meeting and for ten days preceding the Tyme Stockholder Meeting by contacting Tyme at investorrelations@tymeinc.com. Tyme stockholders requesting access to the list will be asked to provide the 12-digit control number found on their proxy card or voting instruction form previously mailed or made available to Tyme stockholders entitled to vote at the Tyme special meeting.

By Order of the Board of Directors,

James Biehl
Chief Legal Officer and Corporate Secretary
Bedminster, NJ
August 8, 2022

Important Notice Regarding the Availability of Proxy Materials for the Tyme special meeting to be held on September 15, 2022 via the Internet at https://www.cstproxy.com/tymeinc/2022

This joint proxy statement/prospectus and Tyme's annual report on Form 10-K for the year ended March 31, 2022, as amended, are available at https://www.cstproxy.com/tymeinc/2022

REFERENCES TO ADDITIONAL INFORMATION

This joint proxy statement/prospectus incorporates important business and financial information about Syros Pharmaceuticals, Inc., which is referred to as Syros, and Tyme Technologies, Inc., which is referred to as Tyme, from other documents that Syros and Tyme have filed with the U.S. Securities and Exchange Commission, which is referred to as the SEC, and that are contained in or incorporated by reference into this joint proxy statement/prospectus. For a listing of documents incorporated by reference into this joint proxy statement/prospectus, please see the section entitled "*Where You Can Find More Information*" beginning on page 445 of this joint proxy statement/prospectus. This information is available for you free of charge to review through the SEC's website at www.sec.gov.

Any person may request a copy of this joint proxy statement/prospectus and any of the documents incorporated by reference into this joint proxy statement/prospectus or other information concerning Syros or Tyme, without charge, by written or telephonic request directed to the appropriate company or its proxy solicitor at the following contacts:

For Syros stockholders:

Syros Pharmaceuticals, Inc.
35 CambridgePark Drive, 4th Floor
Cambridge, Massachusetts 02140
(617) 744-1340
Attention: Corporate Secretary

For Tyme stockholders:

Tyme Technologies, Inc.
1 Pluckemin Way – Suite 103
Bedminster, New Jersey 07921
(212) 461-2315
Attention: Corporate Secretary

In order for you to receive timely delivery of the documents in advance of the special meeting of Syros stockholders to be held on September 15, 2022, which is referred to as the Syros special meeting, or the special meeting of Tyme stockholders to be held on September 15, 2022, which is referred to as the Tyme special meeting, as applicable, you must request the information no later than September 6, 2022.

The contents of the websites of the SEC, Syros, Tyme, or any other entity are not being incorporated into this joint proxy statement/prospectus. The information about how you can obtain certain documents that are incorporated by reference into this joint proxy statement/prospectus at these websites is being provided only for your convenience.

ABOUT THIS JOINT PROXY STATEMENT/PROSPECTUS

This document, which forms part of a registration statement on Form S-4 filed with the SEC by Syros, constitutes a prospectus of Syros under Section 5 of the Securities Act of 1933, as amended, which is referred to as the Securities Act, with respect to the shares of common stock of Syros to be issued to Tyme stockholders pursuant to the Agreement and Plan of Merger, dated as of July 3, 2022 (as it may be amended from time to time), by and among Syros, Tyme and Tack Acquisition Corp., which we refer to as Merger Sub, which is referred to as the Merger Agreement. This document also constitutes a joint proxy statement of Syros and Tyme under Section 14(a) of the Securities Exchange Act of 1934, as amended, which is referred to as the Exchange Act. It also constitutes a notice of meeting with respect to the Syros special meeting and a notice of meeting with respect to the Tyme special meeting.

Syros has supplied all information contained or incorporated by reference into this joint proxy statement/prospectus relating to Syros, and Tyme has supplied all such information relating to Tyme. Syros and Tyme have both contributed to the information related to the merger contained in this joint proxy statement/prospectus.

Syros and Tyme have not authorized anyone to provide you with information that is different from that contained in or incorporated by reference into this joint proxy statement/prospectus. Syros and Tyme take no responsibility for, and can provide no assurance as to the reliability of, any such other information. This joint proxy statement/prospectus is dated August 8, 2022, and you should not assume that the information contained in this joint proxy statement/prospectus is accurate as of any date other than such date unless otherwise specifically provided herein.

Further, you should not assume that the information incorporated by reference into this joint proxy statement/prospectus is accurate as of any date other than the date of the incorporated document. Neither the mailing of this joint proxy statement/prospectus to Syros stockholders or Tyme stockholders nor the issuance by Syros of shares of its common stock pursuant to the merger agreement will create any implication to the contrary.

This joint proxy statement/prospectus does not constitute an offer to sell, or a solicitation of an offer to buy, any securities, or the solicitation of a proxy, in any jurisdiction to or from any person to whom it is unlawful to make any such offer or solicitation in such jurisdiction.

All references in this joint proxy statement/prospectus to “Syros” refer to Syros Pharmaceuticals, Inc., a Delaware corporation. All references in this joint proxy statement/prospectus to “Tyme” refer to Tyme Technologies, Inc., a Delaware corporation. All references in this joint proxy statement/prospectus to “Merger Sub” refer to Tack Acquisition Corp., a Delaware corporation and wholly-owned subsidiary of Syros. All references in this joint proxy statement/prospectus to the “combined company” refer to Syros immediately following completion of the merger and the other transactions contemplated by the merger agreement. All references in this joint proxy statement/prospectus to “Syros common stock” refer to the common stock of Syros, par value $0.001 per share, and all references in this joint proxy statement/prospectus to “Tyme common stock” refer to the common stock of Tyme, par value $0.0001 per share.

TABLE OF CONTENTS

QUESTIONS AND ANSWERS ABOUT THE MERGER

Except where specifically noted, the following information and all other information contained in this joint proxy statement/prospectus does not give effect to the proposed reverse stock split of Syros common stock described in Syros Proposal No. 3 of this joint proxy statement/prospectus or the proposed reverse stock split of Tyme common stock described in Tyme Proposal No. 3 of this joint proxy statement/prospectus.

The following section provides answers to frequently asked questions about the merger. This section, however, provides only summary information. For a more complete response to these questions and for additional information, please refer to the cross-referenced sections.

Q: What is the merger?

A: Syros Pharmaceuticals, Inc., or Syros, and Tyme Technologies, Inc., or Tyme, have entered into an Agreement and Plan of Merger, or the Merger Agreement, dated as of July 3, 2022, a copy of which is attached as *Annex A* to this joint proxy statement/prospectus. The Merger Agreement contains the terms and conditions of the proposed business combination of Syros and Tyme. Pursuant to the Merger Agreement, Tack Acquisition Corp., or Merger Sub, a direct, wholly owned subsidiary of Syros, will merge with and into Tyme, with Tyme surviving as a wholly owned subsidiary of Syros. This transaction is referred to in this joint proxy statement/prospectus as the merger. After the completion of the merger, the combined company is expected to trade on The Nasdaq Global Select Market under the ticker symbol "SYRS" and will be led by Syros' existing management team and will remain focused on advancing Syros' pipeline of small molecule medicines for the treatment of cancer. Syros following the merger is referred to herein as the combined company.

At the effective time of the merger, each share of Tyme common stock will be converted into the right to receive a number of shares of Syros common stock equal to the exchange ratio described in more detail in the section titled "*The Merger Agreement—Merger Consideration*" beginning on page 203 of this joint proxy statement/prospectus.

In connection with the merger, each outstanding and unexercised option to purchase shares of Tyme common stock granted to an individual who continues as a service provider to Tyme at the effective time, following assumption by Syros at the effective time, will be eligible to be registered on a registration statement on Form S-8, will be assumed by Syros and will be converted into an option to purchase shares of Syros common stock, with necessary adjustments to reflect the exchange ratio. Each outstanding and unexercised option to purchase shares of Tyme common stock that is not assumed by Syros pursuant to the merger agreement will be terminated and no consideration will be delivered for such options to purchase shares. Also in connection with the merger, each outstanding and unexercised warrant to purchase shares of Tyme common stock (other than certain warrants that Tyme is required to repurchase in connection with the merger) will be assumed by Syros and converted into a warrant to purchase shares of Syros common stock, with necessary adjustments to reflect the exchange ratio.

Each share of Syros common stock and option to purchase Syros common stock that is issued and outstanding at the effective time of the merger will remain issued and outstanding and such shares will be unaffected by the merger. Based upon the initially estimated exchange ratio, following the merger and giving effect to the PIPE Financing, (i) Syros securityholders immediately before the merger together with the investors in the PIPE Financing are expected to own approximately 63% of the aggregate number of outstanding shares of Syros common stock following the merger and (ii) Tyme securityholders immediately before the merger are expected to own approximately 37% of the aggregate number of outstanding shares of Syros common stock following the merger, subject to certain assumptions (including as to the amount of Tyme net cash at closing, which could be materially different). Assuming the exercise of all Syros pre-funded warrants, including the Pre-Funded PIPE Warrants and the Pre-Funded 2020 Warrants, without

giving effect to any beneficial ownership limitations applicable thereto, then (i) Syros securityholders immediately before the merger together with the investors in the PIPE Financing would own approximately 73% of the aggregate number of outstanding shares of Syros common stock following the merger and (ii) Tyme securityholders immediately before the merger would own approximately 27% of the aggregate number of outstanding shares of Syros common stock following the merger, subject to certain assumptions (including as to the amount of Tyme net cash at closing, which could be materially different). The foregoing percentages do not give effect to the exercise or conversion of outstanding stock options or warrants other than as set forth above.

Q: Why are the two companies proposing to merge?

A: Syros and Tyme believe that the merger will result in a company with a strong leadership team and substantial capital resources to advance the combined company's robust pipeline, and will position the combined company to become a leader in redefining the standard of care for cancer patients. For a more complete description of the reasons for the merger, please see the sections titled "*The Merger—Syros Reasons for the Merger*" and "*The Merger—Tyme Reasons for the Merger*" beginning on pages 159 and 162, respectively, of this joint proxy statement/prospectus.

Q: Why am I receiving this joint proxy statement/prospectus?

A: You are receiving this joint proxy statement/prospectus because you have been identified as either a stockholder of Syros as of the record date entitled to vote at the Syros special meeting to approve the matters set forth herein, or as a stockholder of Tyme as of the record date entitled to vote at the Tyme special meeting to approve the matters set forth herein.

Q: What is the Syros PIPE Financing?

A: On July 3, 2022, immediately prior to the execution and delivery of the Merger Agreement, Syros entered into the Securities Purchase Agreement with certain accredited investors, pursuant to which the investors agreed to purchase (i) an aggregate of approximately 138.1 million shares of Syros common stock and/or pre-funded warrants to purchase shares of Syros common stock and (ii) accompanying warrants to purchase an aggregate of up to approximately 138.1 million additional shares of Syros common stock (or pre-funded warrants in lieu thereof), at a price per unit of $0.94 (or $0.9399 per unit comprising a pre-funded warrant and accompanying warrant). This private placement transaction is referred to as the PIPE Financing. The exercise price of the warrants is $1.034 per share, or if exercised for a pre-funded warrant in lieu thereof, $1.0339 per pre-funded warrant (representing the warrant exercise price of $1.034 per share minus the $0.0001 per share exercise price of each such pre-funded warrant). The warrants are exercisable at any time during the period beginning six months after the closing of the PIPE Financing and ending five years after such closing. The pre-funded warrants are exercisable at any time after their original issuance and will not expire. The expected gross proceeds from the PIPE Financing are approximately $130 million, before deducting estimated offering expenses and not including any proceeds that Syros may receive in connection with the exercise of the warrants. The closing of the PIPE Financing is conditioned upon the satisfaction or waiver of the conditions to the closing of the merger as well as certain other conditions.

Q: What proposal will be voted on at the Syros special meeting the approval of which is a condition to the closing of the merger?

A: Pursuant to the terms of the Merger Agreement, the following proposal must be approved by the requisite stockholder vote at the Syros special meeting in order for the merger to close:

- Proposal No. 1: To approve, for purposes of Nasdaq Listing Rules 5635(a) and (d), the issuance of shares of Syros common stock pursuant to the terms of the Merger Agreement and the Securities Purchase Agreement.

Proposal No. 1 is referred to herein as the Syros share issuance proposal. In addition to the requirement of obtaining Syros stockholder approval of the Syros share issuance proposal, each of the other closing conditions set forth in the Merger Agreement must be satisfied or waived. Completion of the PIPE Financing is one of the conditions to Tyme's obligations to consummate the merger, and the PIPE Financing can only be completed if Proposal No. 2 is also approved. For a more complete description of the closing conditions under the Merger Agreement, please see the section titled "*The Merger Agreement—Conditions to the Completion of the Merger*" beginning on page 215 of this joint proxy statement/prospectus.

The presence, by accessing online or being represented by proxy, at the Syros special meeting of the holders of a majority of the shares of Syros common stock outstanding and entitled to vote at the Syros special meeting is necessary to constitute a quorum at the meeting.

Q: What proposals are to be voted on at the Syros special meeting, other than the Syros share issuance proposal?

A: At the Syros special meeting, the holders of Syros common stock will also be asked to consider the following proposals:

- Proposal No. 2: To approve an amendment to the Syros restated certificate of incorporation to increase the number of authorized shares of Syros common stock from 200,000,000 to 700,000,000 shares.
- Proposal No. 3: To approve an amendment to the Syros restated certificate of incorporation to effect a reverse stock split of Syros common stock, by a ratio of not less than 1-for-5 and not more than 1-for-15, and a proportionate reduction in the number of authorized shares of Syros common stock, such ratio and the implementation and timing of the reverse stock split to be determined in the discretion of Syros' board of directors.
- Proposal No. 4. To approve the adoption of the Syros Pharmaceuticals, Inc. 2022 Equity Incentive Plan.
- Proposal No. 5: To consider and vote upon an adjournment of the Syros special meeting, if necessary, to solicit additional proxies if there are not sufficient votes in favor of Proposal Nos. 1, 2 and 3 or to ensure that any supplement or amendment to this joint proxy statement/prospectus is timely provided to holders of Syros common stock.

Such proposals, together with the Syros share issuance proposal and the Syros share increase proposal, are referred to collectively in this joint proxy statement/prospectus as the Syros proposals.

The approval of Syros Proposal Nos. 2, 3, 4 and 5 are not a condition to the merger. However, completion of the PIPE Financing is one of the conditions to Tyme's obligation to consummate the merger, and the PIPE Financing can only be completed if Proposal No. 2, which Syros refers to as the Syros share increase proposal, is also approved.

The presence, by accessing online or being represented by proxy, at the Syros special meeting of the holders of a majority of the shares of Syros common stock outstanding and entitled to vote at the Syros special meeting is necessary to constitute a quorum at the meeting for the purpose of approving the proposals.

Q: What stockholder votes are required to approve the proposals at the Syros special meeting?

A: The affirmative vote of a majority of the total votes cast by the holders of Syros common stock entitled to vote on the matter at the Syros special meeting is required for approval of Syros Proposal Nos. 1, 4 and 5. Abstentions and broker non-votes will have no effect on such proposals. The affirmative vote of the holders of a majority of the outstanding shares of Syros common stock entitled to vote at the Syros special meeting is required for approval of Syros Proposal Nos. 2 and 3. Abstentions and broker non-votes will have the same effect as "AGAINST" votes on such proposals.

Votes will be counted by the inspector of election appointed for the meeting, who will separately count "FOR" and "AGAINST" votes, abstentions and any broker non-votes. Abstentions and broker non-votes will be treated as shares present for the purpose of determining the presence of a quorum for the transaction of business at the special meeting.

As of June 30, 2022, the directors and certain executive officers of Syros owned or controlled approximately 8% of the outstanding shares of Syros common stock entitled to vote at the Syros special meeting. As of June 30, 2022, the Syros stockholders that are party to support agreements, including the directors and executive officers of Syros and certain other stockholders, owned an aggregate of 17,460,552 shares of Syros common stock representing approximately 28% of the outstanding shares of Syros common stock. Pursuant to the support agreements, these stockholders, including the directors and executive officers of Syros and certain other stockholders, have agreed to vote all shares of Syros common stock owned by them as of the record date in favor of Syros Proposal Nos. 1, 2, and 3, and against any competing Acquisition Proposal (as defined in the section of this proxy statement/prospectus entitled "*The Merger Agreement— Non-Solicitation*").

Q: As a Syros stockholder, how does Syros' board of directors recommend that I vote?

A: After careful consideration, Syros' board of directors unanimously recommends that Syros stockholders vote "FOR" all of the proposals.

Q: What proposal will be voted on at the Tyme special meeting the approval of which is a condition to the closing of the merger?

A: Pursuant to the terms of the Merger Agreement, the following proposal must be approved by the requisite stockholder vote at the Tyme special meeting in order for the merger to close:

- Proposal No. 1: To adopt the Merger Agreement.

Proposal No. 1 is referred to herein as the Tyme merger proposal. In addition to the requirement of obtaining Tyme stockholder approval of the Tyme merger proposal, each of the other closing conditions set forth in the Merger Agreement must be satisfied or waived. For a more complete description of the closing conditions under the Merger Agreement, please see the section titled "*The Merger Agreement—Conditions to the Completion of the Merger*" beginning on page 215 of this joint proxy statement/prospectus.

Q: What proposals are to be voted on at the Tyme special meeting, other than the Tyme merger proposal?

A: At the Tyme special meeting, the holders of Tyme common stock will also be asked to consider the following proposals:

- Proposal No. 2: To conduct an advisory,non-binding vote to approve merger-related executive compensation.
- Proposal No. 3: To approve an amendment to Tyme's amended and restated certificate of incorporation to effect a reverse stock split of Tyme common stock, by a ratio of not less than 1-for-15 and not more than 1-for-75, such ratio and the implementation and timing of the reverse stock split to be determined in the discretion of Tyme's board of directors.
- Proposal No. 4: To consider and vote upon an adjournment of the Tyme special meeting, if necessary, to solicit additional proxies if there are not sufficient votes in favor of Proposal Nos. 1, 2 and 3 or to ensure that any supplement or amendment to this joint proxy statement/prospectus is timely provided to holders of Tyme common stock.

The approval of Tyme Proposal Nos. 2, 3 and 4 are not a condition to the merger. Such proposals, together with the Tyme merger proposal, are referred to collectively in this joint proxy statement/prospectus as the Tyme proposals.

The presence, by accessing online or being represented by proxy, at the Tyme special meeting of the holders of at least one-third of the shares of Tyme common stock outstanding and entitled to vote at the Tyme special meeting is necessary to constitute a quorum at the meeting for the purpose of approving the proposals.

Q: What stockholder votes are required to approve the proposals at the Tyme special meeting?

A: The following table summarizes the vote threshold required for approval of each item of business to be transacted at the Tyme special meeting, provided that there is a quorum:

Proposal	Vote Required for Approval	Effect of Abstentions/ Withhold Votes (1)	Uninstructed Shares/ Effect of Broker Non-Votes (1)	Signed but Unmarked Proxy Cards (2)
1. Tyme Merger Proposal	Majority of outstanding shares of Tyme common stock	Same effect as a vote "Against"	Same effect as a vote "Against"	Voted "For"
2. Advisory Vote on Merger-related Executive Compensation	Majority of shares present at the Tyme special meeting or represented by proxy and entitled to vote thereon	Same effect as a vote "Against"	Not voted / no effect	Voted "For"
3. Amendment to Tyme's amended and restated certificate of incorporation to effect the Tyme Reverse Stock Split	Majority of outstanding shares of Tyme common stock	Same effect as a vote "Against"	Discretionary vote by broker	Voted "For"
4. Tyme Adjournment Proposal	Majority of shares present at the Tyme special meeting or represented by proxy and entitled to vote thereon	Same effect as a vote "Against"	Not voted / no effect	Voted "For"

(1) Abstentions and broker non-votes are included for purposes of determining whether a quorum is present, however, abstentions are considered "entitled to vote" whereas broker non-votes are not.

(2) If you sign and return your proxy card properly, but do not provide instructions on your proxy card as to how to vote your shares, your shares will be voted as shown in this column and in accordance with the judgment of the individuals named as proxies on the proxy card as to any other matter properly brought before the Tyme special meeting.

Votes will be counted by the inspector of election appointed for the meeting, who will separately count "FOR" and "AGAINST" votes, abstentions and any broker non-votes. Abstentions and broker non-votes will be treated as shares present for the purpose of determining the presence of a quorum for the transaction of business at the Tyme special meeting. Abstentions will be counted towards the vote totals for each proposal, and will have the same effect as "AGAINST" votes. Broker non-votes will have no effect on Tyme Proposal Nos. 2 and 4, but will have the same effect as an "AGAINST" vote on Tyme Proposal No. 1. Tyme Proposal No. 3 is a routine matter and therefore, a broker is entitled to vote shares held for a beneficial owner on Tyme Proposal No. 3 without instructions from the beneficial owner of those shares.

As of June 30, 2022, the directors (including Mr. Hoffman) and executive officers of Tyme beneficially owned approximately 11.8% of the outstanding shares of Tyme common stock entitled to vote at the Tyme special meeting. Tyme stockholders who held an aggregate of 53,428,292 shares (or approximately 31%) of the Tyme common stock outstanding as of June 30, 2022 have either agreed to vote all shares of Tyme common stock owned by them as of the record date in favor of Tyme Proposal No. 1 or are party to pre-existing voting agreements pursuant to which they have agreed to vote all shares of Tyme common stock either to a support agreement entered into in connection with the merger or voting agreements with Tyme to vote in accordance with the Tyme board of directors' recommendation with respect to any matter presented to Tyme's stockholders.

Q: As a Tyme stockholder, how does Tyme's board of directors recommend that I vote?

A: After careful consideration, Tyme's board of directors unanimously recommends that Tyme stockholders vote "FOR" all of the proposals.

Q: What will Tyme holders receive in the merger?

A: Tyme stockholders will receive shares of Syros common stock based upon the exchange ratio. The exchange ratio will be determined in accordance with the Merger Agreement based upon Tyme's net cash and the number of outstanding shares of Tyme common stock as of closing. Assuming Tyme net cash of approximately $62.3 million and no change to shares outstanding, the exchange ratio would be 0.4312 shares of Syros common stock for each share of Tyme common stock.

In connection with the merger, each outstanding and unexercised option to purchase shares of Tyme common stock granted to an individual who continues as a service provider to Tyme at the effective time, following assumption by Syros at the effective time, will be eligible to be registered on a registration statement on Form S-8, will be assumed by Syros and will be converted into an option to purchase shares of Syros common stock, with necessary adjustments to reflect the exchange ratio . Each outstanding and unexercised option to purchase shares of Tyme common stock that is not assumed by Syros pursuant to the Merger Agreement will be terminated and no consideration will be delivered for such options to purchase shares. Also in connection with the merger, each outstanding and unexercised warrant to purchase shares of Tyme common stock (other than certain warrants that Tyme is required to repurchase in connection with the merger) will be assumed by Syros and converted into a warrant to purchase shares of Syros common stock, with necessary adjustments to reflect the exchange ratio.

For a more complete description of what Tyme stockholders, optionholders and warrantholders will receive in the merger, please see the sections titled "*The Merger Agreement—Merger Consideration*" beginning on page 203 of this joint proxy statement/prospectus. For a description of the effect of the PIPE Financing on Syros' and Tyme's current securityholders, please see the section titled "*Agreements Related to the Merger—Securities Purchase Agreement and Registration Rights Agreements*" beginning on page 223 of this joint proxy statement/prospectus.

Q: What risks should I consider in deciding whether to vote in favor of the merger?

A: You should carefully review the section titled "*Risk Factors*" beginning on page 31 of this joint proxy statement/prospectus and the annexes attached hereto, which set forth certain risks and uncertainties related to the merger, risks and uncertainties to which the combined company's business will be subject, and risks and uncertainties to which each of Syros and Tyme, as independent companies, are subject.

Q: Where will the common stock of the combined company be publicly traded?

A: Syros will use its commercially reasonable efforts to cause the shares of Syros common stock following the merger to continue to be listed on Nasdaq.

Q: When do you expect the merger to be consummated?

A: Subject to the satisfaction or waiver of the closing conditions described under the section entitled "*The Merger Agreement—Conditions to the Completion of the Merger*" beginning on page 215 of this joint proxy statement/prospectus, including the adoption of the merger agreement by Tyme stockholders and the approval of the Syros share issuance proposal, the merger is expected to close in the second half of calendar year 2022 and promptly following the Syros and Tyme stockholder meetings. However, neither Syros nor Tyme can predict the actual date on which the merger will be completed, or if the merger will be completed at all, because completion of the merger is subject to conditions and factors outside the control of both companies.

Q: What happens if the merger is not completed?

A: If the Merger Agreement is not adopted by Tyme stockholders or if the merger is not completed for any other reason, Tyme stockholders will not receive any merger consideration for their shares of Tyme common stock in connection with the merger. Instead, Tyme will remain an independent public company and provided it is able to regain compliance with the Nasdaq Capital Market's continued listing standards, Tyme common stock will continue to be listed and traded on The Nasdaq Capital Market, Syros common stock will continue to be traded on The Nasdaq Global Select Market, and Syros will not complete the share issuance pursuant to the Merger Agreement and the Securities Purchase Agreement as contemplated by the Syros share issuance proposal. If the Merger Agreement is terminated under specified circumstances, either Syros or Tyme may be required to pay or cause to be paid to the other party a termination fee. See the section entitled "*The Merger Agreement—Termination Fees*" beginning on page 221 of this joint proxy statement/prospectus for a more detailed discussion of the termination fees.

Q: What do I need to do now?

A: You should read this joint proxy statement/prospectus carefully and in its entirety, including the annexes, and return your completed, signed and dated proxy card(s) by mail in the enclosed postage-paid envelope(s) or submit your voting instructions over the Internet, or by telephone, as soon as possible so that your shares will be voted in accordance with your instructions.

Your signed proxy card, telephonic proxy instructions, or internet proxy instructions must be received by September 14, 2022, 11:59 p.m. Eastern Time to be counted.

If you hold your shares in "street name" (as described below), you may provide your proxy instructions via telephone or the internet by following the instructions on your vote instruction form. Please provide your proxy instructions only once, unless you are revoking a previously delivered proxy instruction, and as soon as possible so that your shares can be voted at the Syros special meeting.

Q: What if I hold shares in both Syros and Tyme?

A: If you are both a Syros stockholder and a Tyme stockholder, you will receive two separate packages of proxy materials. A vote cast as a Syros stockholder will not count as a vote cast as a Tyme stockholder, and a vote cast as a Tyme stockholder will not count as a vote cast as a Syros stockholder. Therefore, please submit separate proxies for your shares of Syros common stock and your shares of Tyme common stock.

Q: How can I gain admission or vote my shares at my respective virtual meeting?

A: *Record Holders.* Shares held directly in your name as the stockholder of record of Syros or Tyme may be voted virtually at the Syros special meeting or the Tyme special meeting, as applicable. If you choose to vote your shares at the respective meeting, please follow the procedures described in the section entitled

"*The Special Meeting of Syros Stockholders*" beginning on page 139 of this joint proxy statement/prospectus, with respect to the Syros special meeting, and the section entitled "*The Special Meeting of Tyme Stockholders*" beginning on page 143 of this joint proxy statement/prospectus, with respect to the Tyme special meeting.

Shares in "street name." Shares held in "street name" may be voted virtually at the meeting by you only if you obtain a signed legal proxy from your bank, broker or other nominee giving you the right to vote the shares and follow the procedures to attend the meeting. If you choose to attend and vote your shares at the Syros special meeting or Tyme special meeting, as applicable, please follow the procedures described in the section entitled "*The Special Meeting of Syros Stockholders*" beginning on page 139 of this joint proxy statement/prospectus, with respect to the Syros special meeting, and the section entitled "*The Special Meeting of Tyme Stockholders*" beginning on page 143 of this joint proxy statement/prospectus, with respect to the Tyme special meeting.

Even if you plan to attend the Syros special meeting or the Tyme special meeting, as applicable, Syros and Tyme recommend that you submit a proxy to vote your shares in advance as described below so that your vote will be counted if you later decide not to or become unable to attend the respective meeting.

Additional information on attending the meetings can be found in the section entitled "*The Special Meeting of Syros Stockholders*" beginning on page 139 of this joint proxy statement/prospectus and in the section entitled "*The Special Meeting of Tyme Stockholders*" beginning on page 143 of this joint proxy statement/prospectus.

Q: How can I vote my shares without attending my respective meeting?

A: Whether you hold your shares directly as the stockholder of record of Syros or Tyme or beneficially in "street name," you may direct your vote by proxy without virtually attending the Syros special meeting or the Tyme special meeting, as applicable. You can vote by proxy over the Internet or by mail. Please note that if you hold shares beneficially in "street name," you should follow the voting instructions provided by your bank, broker or other nominee.

Additional information on attending the meetings can be found in the section entitled "*The Special Meeting of Syros Stockholders*" beginning on page 139 of this joint proxy statement/prospectus and in the section entitled "*The Special Meeting of Tyme Stockholders*" beginning on page 143 of this joint proxy statement/prospectus.

Q: What is the difference between holding shares as a stockholder of record and as a beneficial owner of shares held in "street name?"

A: If your shares of common stock of Syros are registered directly in your name with Computershare Trust Company, N.A., Syros' transfer agent, or if your shares of common stock of Tyme are registered directly in your name with Continental Stock and Transfer and Trust Company, Tyme's transfer agent, you are considered the stockholder of record with respect to those shares. As the stockholder of record, you have the right to vote, or to grant a proxy for your vote, directly to Syros or Tyme, as applicable, or to a third party to vote, at the respective meeting.

If your shares of common stock in Syros or Tyme are held by a bank, broker or other nominee, you are considered the beneficial owner of shares held in "street name," and your bank, broker or other nominee is considered the stockholder of record with respect to those shares. Your bank, broker or other nominee will provide you, as the beneficial owner, a package describing the procedure for voting your shares. You should follow the instructions provided by them to vote your shares. You are invited to attend the Syros special meeting or the Tyme special meeting, as applicable; however, you may not vote these shares in person at the respective special meeting unless you obtain a signed legal proxy, executed in your favor, from your bank, broker or other nominee that holds your shares, giving you the right to vote the shares in person at the applicable meeting.

Q: If my shares of Syros common stock or Tyme common stock are held in "street name" by my bank, broker or other nominee, will my bank, broker or other nominee automatically vote those shares for me?

A: Absent discretionary authority, your bank, broker or other nominee will only be permitted to vote your shares of Syros common stock or Tyme common stock, as applicable, if you instruct your bank, broker or other nominee how to vote. You should follow the procedures provided by your bank, broker or other nominee regarding the voting of your shares. Under the rules of the New York Stock Exchange, banks, brokers and other nominees who hold shares of Syros common stock or Tyme common stock in "street name" for their customers have authority to vote on "routine" proposals when they have not received instructions from beneficial owners. However, banks, brokers and other nominees are prohibited from exercising their voting discretion with respect to non-routine matters. With respect to non-routine items for which you do not give your broker instructions, your shares will be treated as a broker non-vote.

At the Syros special meeting, it is anticipated that Syros Proposal Nos. 1, 2, 4 and 5 will be non-routine, and that Syros Proposal No. 3 will be routine. At the Tyme special meeting, it is anticipated that Tyme Proposal Nos. 1, 2 and 4 will be non-routine, and that Tyme Proposal No. 3 will be routine. To make sure that your vote is counted, you should instruct your broker to vote your shares, following the procedures provided by your broker.

Q: What should I do if I receive more than one set of voting materials for the same meeting?

A: If you hold shares of Syros common stock or Tyme common stock in "street name" and also directly in your name as a stockholder of record or otherwise, or if you hold shares of Syros common stock or Tyme common stock in more than one brokerage account, you may receive more than one set of voting materials relating to the same meeting.

Record Holders. For shares held directly, please complete, sign, date and return each proxy card (or submit a proxy to cast your vote over the Internet, or by telephone, as provided on each proxy card) or otherwise follow the voting instructions provided in this joint proxy statement/prospectus in order to ensure that all of your shares of Syros common stock or Tyme common stock are voted.

Shares in "street name." For shares held in "street name" through a bank, broker or other nominee, you should follow the procedures provided by your bank, broker or other nominee to vote your shares.

Q: If a stockholder gives a proxy, how are the shares of Syros common stock or Tyme common stock voted?

A: Regardless of the method by which you choose to vote, the individuals named on the enclosed proxy card will vote your shares of Syros common stock or Tyme common stock, as applicable, in the way that you indicate. When completing the Internet or telephone processes or the proxy card, you may specify whether your shares of Syros common stock or Tyme common stock, as applicable, should be voted for or against, or abstain from voting on, all, some or none of the specific items of business to come before the respective meetings.

Q: How will my shares of Syros common stock be voted if I return a blank proxy?

A: If you are a stockholder of record and you sign, date and return your proxy and do not indicate how you want your shares of Syros common stock to be voted, then your shares of Syros common stock will be voted "FOR" each of the Syros proposals.

Q: How will my shares of Tyme common stock be voted if I return a blank proxy?

A: If you are a stockholder of record and you sign, date and return your proxy and do not indicate how you want your shares of Tyme common stock to be voted, then your shares of Tyme common stock will be voted "FOR" each of the Tyme proposals.

Q: Can I change my vote after I have submitted my proxy?

A: Any stockholder of record giving a proxy has the right to revoke it before the proxy is voted at the applicable meeting by doing any of the following:

- subsequently submitting a new proxy (including by submitting a proxy via the Internet or telephone) that is received prior to the applicable meeting (which should be received by the deadline specified on the accompanying proxy card in order to ensure that your proxy is counted);
- giving written notice of your revocation to Syros' corporate secretary or Tyme's corporate secretary, as applicable; or
- voting in person at the applicable meeting.

Execution or revocation of a proxy will not in any way affect your right to attend the applicable meeting and vote in person. Attending the applicable meeting will not, by itself, revoke a proxy. Written notices of revocation and other communications with respect to the revocation of proxies should be addressed:

if you are a Syros stockholder, to:

Syros Pharmaceuticals, Inc.
Attn: Corporate Secretary
35 CambridgePark Drive, 4th Floor
Cambridge, Massachusetts 02140

if you are a Tyme stockholder, to:

Tyme Technologies, Inc.
Attn: Corporate Secretary
1 Pluckemin Way – Suite 103
Bedminster, New Jersey 07921

If your shares are held in the name of a bank, broker or other nominee and you previously provided voting instructions to your bank, broker or other nominee, you should follow the instructions provided by your bank, broker or other nominee to revoke or change your voting instructions.

Q: Where can I find the voting results of the meetings?

A: The preliminary voting results for each meeting will be announced at that meeting. In addition, within four business days after completion of its meeting, each of Syros and Tyme intends to file the final voting results of its respective meeting with the SEC on a Current Report on Form 8-K.

Q: If I do not favor the merger, what are my rights?

A: Neither Syros stockholders nor Tyme stockholders are entitled to appraisal rights under the Delaware General Corporation Law, or the DGCL. If they are not in favor of the merger, Syros stockholders may vote against the Syros share issuance proposal and Tyme stockholders may vote against the Tyme merger proposal, subject to any support or voting agreements. For more information, see the section entitled "*The Merger—Appraisal Rights and Dissenters' Rights*" beginning on page 202 of this joint proxy statement/prospectus. Information about how Syros stockholders may vote on the proposals being considered in connection with the merger can be found under the section entitled "*The Special Meeting of Syros Stockholders*" beginning on page 139 of this joint proxy statement/prospectus. Information about how Tyme stockholders may vote on the proposals being considered in connection with the merger can be found under the section entitled "*The Special Meeting of Tyme Stockholders*" beginning on page 143 of this joint proxy statement/prospectus.

Q: Who will solicit and pay the cost of soliciting proxies?

A: Syros has engaged Morrow Sodali to assist in the solicitation of proxies for the Syros special meeting. Syros estimates that it will pay Morrow Sodali a fee of approximately $15,000, plus reimbursement of reasonable expenses. Syros has agreed to indemnify Morrow Sodali against various liabilities and expenses that relate to or arise out of its solicitation of proxies (subject to certain exceptions). Tyme has engaged MacKenzie Partners, Inc., which is referred to as MacKenzie, to assist in the solicitation of proxies for the Tyme special meeting and to provide related advice and informational support, for a services fee of $18,500 plus the reimbursement of customary disbursements. Tyme has agreed to indemnify MacKenzie against various liabilities and expenses that relate to or arise out of its solicitation of proxies (subject to certain exceptions). Syros and Tyme also may be required to reimburse banks, brokers and other custodians, nominees and fiduciaries or their respective agents for their expenses in forwarding proxy materials to beneficial owners of Syros common stock and Tyme common stock, respectively. Syros' directors, officers and employees and Tyme's directors, officers and employees also may solicit proxies, by telephone, by mail, by electronic means or in person. They will not be paid any additional amounts for soliciting proxies.

Q: What are broker non-votes and do they count for determining a quorum?

A: Generally, broker non-votes occur when shares held by a broker in "street name" for a beneficial owner are not voted with respect to a particular proposal because the broker (i) has not received voting instructions from the beneficial owner or (ii) lacks discretionary voting power to vote those shares. A broker is entitled to vote shares held for a beneficial owner on routine matters without instructions from the beneficial owner of those shares. On the other hand, absent instructions from the beneficial owner of such shares, a broker is not entitled to vote shares held for a beneficial owner on non-routine matters.

Broker non-votes will be treated as shares present for the purpose of determining the presence of a quorum for the transaction of business at each of the Syros special meeting and Tyme special meeting.

Q: What are the material U.S. federal income tax consequences of the merger to the United States holders of Syros and Tyme common stock?

A: The merger generally will result in no tax consequences to United States holders of Syros common stock as such holders will continue to own their shares of Syros common stock and are not exchanging such shares in the merger.

The merger is intended to qualify as either a tax-free contribution pursuant to Section 351 of the Internal Revenue Code of 1986, as amended, or the Code, taken together with the PIPE Financing, or a "reorganization" within the meaning of Section 368(a) of the Code. Assuming the merger qualifies for the intended tax treatment, subject to the limitations and qualifications described in the section entitled "*The Merger—Material U.S. Federal Income Tax Consequences of the Merger*" beginning on page 198 of this joint proxy statement/prospectus, a U.S. Holder (as defined in such section) of Tyme common stock generally will not recognize any gain or loss for U.S. federal income tax purposes on the exchange of shares of Tyme common stock for shares of Syros common stock in the merger, except with respect to cash received by such U.S. Holder in lieu of a fractional share of Syros common stock. It is possible that, under certain circumstances, the merger will not satisfy the requirements to qualify as either a tax-free contribution pursuant to Section 351 of the Code or a "reorganization" within the meaning of Section 368(a) of the Code.

Please review the information in the section entitled "*The Merger—Material U.S. Federal Income Tax Consequences of the Merger*" beginning on page 198 of this joint proxy statement/prospectus for a more complete description of the material U.S. federal income tax consequences of the merger to U.S. Holders of Tyme common stock. The tax consequences of the merger to each U.S. Holder will depend on the holder's particular facts and circumstances. You should consult your tax advisors as to the specific tax consequences to you of the merger.

Q: Who can help answer my questions?

A: If you are a Syros stockholder or a Tyme stockholder and would like additional copies of this joint proxy statement/prospectus without charge or if you have questions about the merger, including the procedures for voting your shares, you should contact:

if you are a Syros stockholder:

Syros Pharmaceuticals, Inc.
Attn: Corporate Secretary
35 CambridgePark Drive, 4th Floor
Cambridge, Massachusetts 02140
(617) 744-1340

if you are a Tyme stockholder:

Tyme Technologies, Inc.
Attn: Corporate Secretary
1 Pluckemin Way – Suite 103
Bedminster, New Jersey 07921
(212) 461-2315
investorrelations@tymeinc.com

PROSPECTUS SUMMARY

This summary highlights selected information from this joint proxy statement/prospectus and may not contain all of the information that is important to you. To better understand the merger and the proposals being considered at the Syros special meeting and at the Tyme special meeting, you should read this entire joint proxy statement/prospectus carefully, including the Merger Agreement and the other annexes to which you are referred in this joint proxy statement/prospectus. For more information, please see the section titled "Where You Can Find More Information" beginning on page 445 of this joint proxy statement/prospectus. Except where specifically noted, the following information and all other information contained in this joint proxy statement/prospectus does not give effect to the proposed reverse stock split of Syros or to the proposed reverse stock split of Tyme described in this joint proxy statement/prospectus.

The Companies

Syros Pharmaceuticals, Inc.
35 CambridgePark Drive, 4th Floor
Cambridge, Massachusetts 02140
Telephone: (617) 744-1340

Syros is a biopharmaceutical company seeking to redefine the power of small molecules to control the expression of genes. Based on its unique ability to elucidate regulatory regions of the genome, Syros aims to develop medicines that provide a profound benefit for patients with diseases that have eluded other genomics-based approaches. Syros is currently focused on developing treatments for cancer and diseases resulting from mutations of a single gene, also known as monogenic diseases, and building a clinical stage pipeline of gene control medicines.

Its lead product candidates are:

- Tamibarotene, a selective retinoic acid receptor alpha agonist for which Syros is conducting SELECT-MDS-1, a Phase 3 clinical trial evaluating tamibarotene in combination with azacitidine in a genomically defined subset of patients with higher-risk myelodysplastic syndrome, or HR-MDS, and for which it is conducting SELECT-AML-1, a randomized Phase 2 clinical trial evaluating tamibarotene in combination with venetoclax and azacitidine in a genomically defined subset of newly diagnosed patients with acute myeloid leukemia, or AML, who are not suitable candidates for standard intensive chemotherapy;
- SY-2101, a novel oral form of arsenic trioxide, or ATO, which it is evaluating in a dose confirmation study, and which it plans to follow with a Phase 3 clinical trial, in patients with newly diagnosed low-risk acute promyelocytic leukemia, or APL; and
- SY-5609, a highly selective and potent oral inhibitor of cyclin-dependent kinase 7, or CDK7, which Syros is evaluating in combination with chemotherapy in pancreatic cancer patients in an expansion cohort of its existing Phase 1 clinical trial, and which is being evaluated in combination with atezolizumab, a PD-L1 inhibitor, in BRAF-mutant colorectal cancer in an arm of a Phase 1/1b clinical trial sponsored by F. Hoffmann-La Roche AG, or Roche, that is now open for enrollment.

Syros also has multiple preclinical and discovery programs in oncology, including programs targeting the inhibition of cyclin-dependent kinase 12, or CDK12, cyclin-dependent kinase 11, and the WRN gene. Syros expects that its next development candidate will be nominated from its CDK12 program in the third quarter of 2022. Syros is seeking partnerships for its oncology discovery programs, including CDK12.

In December 2019, Syros entered into a collaboration with Global Blood Therapeutics, Inc., or GBT, to discover, develop and commercialize novel therapies for sickle cell disease and beta thalassemia. Syros also uses its gene

control platform in collaboration with third parties to identify and validate targets in diseases beyond its current areas of focus. To this end, Syros has entered into a target discovery, research collaboration and option agreement with Incyte Corporation, or Incyte, in January 2018, under which Syros uses its platform to identify novel therapeutic targets with a focus on myeloproliferative neoplasms. Syros expects to continue to execute on these existing collaborations with Incyte and GBT, for which its research efforts are fully funded externally.

Tyme Technologies, Inc.
1 Pluckemin Way – Suite 103
Bedminster, New Jersey 07921
Telephone: (212) 461-2315

Tyme is an emerging biotechnology company developing cancer metabolism-based therapies, or CMBTs, that are intended to be effective across a broad range of solid tumors and hematologic cancers, while also maintaining patients' quality of life through relatively low toxicity profiles. Unlike targeted therapies that attempt to regulate specific mutations within cancer, Tyme's therapeutic approach is designed to take advantage of a cancer cell's innate metabolic requirements to cause cancer cell death. Tyme has been focused on developing its novel compound, SM-88, as well as further evaluating its preclinical pipeline of novel CMBT™ programs, including TYME-18, and TYME-19 as a potential therapeutic for SARS CoV-2 diseases.

- SM-88 is CMBT that is chemically altered to be non-functional for fundamental tumor cell processes, including protein synthesis, which Tyme has initially investigated for oral administration. Scientific literature has highlighted that cancer cells can have a significantly higher consumption of certain amino acids compared to healthy cells, and these amino acids are required for cancer cell growth and function. Tyme believes that SM-88, its proprietary modified dysfunctional tyrosine is selectively consumed by cancer cells, and interrupts various cell functions, including protein synthesis, autophagy, and other cellular defenses, that ultimately leads to an oxidative stress-related apoptosis or cell death. Tyme also believes this selective cancer uptake of non-essential amino acids is supported by the current safety profile for SM-88, that has shown minimal observed drug-related SAEs.
- TYME-18 is a CMBT™ compound that is delivered intratumorally. TYME-18 leverages a member of the bile acid family to create a potential treatment for inoperable tumors. Preliminary observations of the local administration of TYME-18, a combination of a proprietary surfactant system and natural sulfonic acid, suggested its potential as an important regulator of energy metabolism that may impede the ability of tumors to increase in size, which, in addition to its lytic functionality, could prove useful in difficult-to-treat cancers. Tyme is assessing development priorities to determine if additional advancement of this program is warranted at this time.
- TYME-19 is an oral synthetic member of the bile acid family. Tyme also uses bile acids in its anti-cancer drug candidate, TYME-18. Because of its expertise in bile acids and their effects, Tyme was able to identify TYME-19 as a well-characterized bile acid with potential antiviral properties. Bile acids have primarily been used for liver disease; however, like all steroids, they are messenger molecules that modulate a number of diverse critical cellular processes. Bile acids can modulate lipid and glucose metabolism and can remediate dysregulated protein folding, with potentially therapeutic effects on cardiovascular, neurologic, immune, and other metabolic systems. Some agents in this class have also previously shown antiviral properties.

Tyme believes that early clinical results demonstrated by SM-88 in multiple advanced cancers, including breast, sarcomas, pancreatic, and prostate, reinforce the potential of its emerging CMBT™ pipeline.

Tack Acquisition Corp.
35 Cambridge Park Drive, 4th Floor
Cambridge, Massachusetts 02140
Telephone: (617) 744-1340

Tack Acquisition Corp., or Merger Sub, is a direct, wholly owned subsidiary of Syros and was formed solely for the purpose of carrying out the merger.

The Merger (see page 149)

If the merger is completed Merger Sub will merge with and into Tyme, with Tyme surviving the merger as a wholly owned subsidiary of Syros.

Subject to the terms and conditions of the Merger Agreement, at the closing of the merger, (a) each then outstanding share of Tyme common stock will be converted into the right to receive a number of shares of Syros common stock (subject to the payment of cash in lieu of fractional shares) calculated in accordance with the exchange ratio set forth in the Merger Agreement; (b) each outstanding and unexercised option to purchase shares of Tyme common stock granted to an individual who continues as a service provider to Tyme at the effective time will be assumed by Syros, subject to adjustment as set forth in the Merger Agreement; (c) each then outstanding Tyme stock option not assumed by Syros shall be terminated; (d) the warrant to purchase Tyme stock issued by Tyme on May 20, 2020 will be purchased by Tyme subject to the terms set forth in such warrant; and (e) all other warrants to purchase shares of Tyme common stock will be assumed by Syros, subject to adjustment as set forth in the Merger Agreement.

The exchange ratio was initially estimated to be 0.4312 shares of Syros common stock for each share of Tyme common stock, but the actual exchange ratio will depend on Tyme's net cash and the number of shares of Tyme common stock outstanding at the closing of the merger. Based upon the initially estimated exchange ratio, following the merger and giving effect to the PIPE Financing, (i) Syros securityholders immediately before the merger together with the investors in the PIPE Financing are expected to own approximately 63% of the aggregate number of outstanding shares of Syros common stock following the merger and (ii) Tyme securityholders immediately before the merger are expected to own approximately 37% of the aggregate number of outstanding shares of Syros common stock following the merger, subject to certain assumptions (including as to the amount of Tyme net cash at closing, which could be materially different). Assuming the exercise of all Syros pre-funded warrants, including the Pre-Funded PIPE Warrants and the Pre-Funded 2020 Warrants, without giving effect to any beneficial ownership limitations applicable thereto, then (i) Syros securityholders immediately before the merger together with the investors in the PIPE Financing would own approximately 73% of the aggregate number of outstanding shares of Syros common stock following the merger and (ii) Tyme securityholders immediately before the merger would own approximately 27% of the aggregate number of outstanding shares of Syros common stock following the merger, subject to certain assumptions (including as to the amount of Tyme net cash at closing, which could be materially different). The foregoing percentages do not give effect to the exercise or conversion of outstanding stock options or warrants other than as set forth above. The exchange ratio shall be adjusted equitably if, between the date of the Merger Agreement and the effective time of the merger, the outstanding shares of Syros common stock or Tyme common stock are changed into, or exchanged for, a different number of shares or a different class of stock.

Each share of Syros common stock issued and outstanding at the time of the merger will remain issued and outstanding, and such shares will be appropriately adjusted to reflect the proposed reverse stock split of Syros common stock, if Syros Proposal No. 3, or the Syros reverse stock split proposal, is approved and the Syros board of directors determines to effect the reverse stock split. In addition, each option to purchase shares of Syros common stock and each other equity award covering shares of Syros common stock that is outstanding immediately prior to the effective time of the merger, whether vested or unvested, will survive the closing and remain outstanding in accordance with its terms. The number of shares of Syros common stock underlying such equity awards, and any exercise prices for such equity awards will be appropriately adjusted to reflect the proposed reverse stock split of Syros common stock, if the Syros reverse stock split proposal is approved and the Syros board of directors determines to effect the reverse stock split.

For a more complete description of the merger and the exchange ratio please see the section titled "*The Merger Agreement*" in this joint proxy statement/prospectus.

The merger will be completed as promptly as practicable after all of the conditions to completion of the merger are satisfied or waived, including the adoption of the Merger Agreement by the Tyme stockholders and the approval by the Syros stockholders of the issuance of Syros common stock pursuant to the terms of the Merger Agreement and the Securities Purchase Agreement. Syros and Tyme are working to complete the merger as quickly as practicable. The merger is anticipated to close in the second half of 2022, promptly after each of the Syros special meeting and Tyme special meeting, which are each scheduled to be held on September 15, 2022. However, Syros and Tyme cannot predict the exact timing of the completion of the merger because it is subject to the satisfaction of various conditions.

Syros Reasons for the Merger (see page 159)

During the course of its evaluation of the Merger Agreement and the transactions contemplated by the Merger Agreement, Syros' board of directors held numerous meetings, consulted with Syros' senior management, legal counsel and financial advisor, and reviewed and assessed a significant amount of information. In reaching its decision to approve the Merger Agreement and the transactions contemplated by the Merger Agreement, Syros' board of directors considered a number of factors that it viewed as supporting its decision to approve the Merger Agreement, including:

- that the Syros board of directors and its financial advisors undertook a comprehensive and thorough process of reviewing and analyzing potential sources of capital to identify the opportunity that would, in the view of the Syros board of directors, create the most value for Syros stockholders;
- Syros' board of directors' belief, after initial fundraising discussions with prospective investors in a PIPE Financing and discussions with Syros' senior management, financial advisors and legal counsel, that it would be necessary to complete the merger, in combination with the PIPE Financing, to raise a sufficient quantum of capital to progress Syros' product candidates to significant value inflection points;
- the Syros board of directors' consideration of the expected cash balances of the combined company as of the closing of the merger resulting from the approximately $62.3 million of net cash expected to be held by Tyme upon completion of the merger together with the cash Syros currently holds and the $130 million of expected gross proceeds from the PIPE Financing;
- the Syros board of directors' belief that, as a result of arm's length negotiations with Tyme, Syros and its representatives negotiated the lowest exchange ratio to which Tyme was willing to agree, and that the other terms of the Merger Agreement, taken as a whole, include the most favorable terms to Syros in the aggregate to which Tyme was willing to agree;
- the Syros board of directors' view, following a review with Syros' management of Syros' and Tyme's current development and clinical trial plans, of the likelihood that the combined company, after giving effect to the amendment to Syros' debt facility, would possess sufficient cash resources at the closing of the merger to fund development of Syros' product candidates through upcoming value inflection points; and
- the Syros board of directors' view that the combined company will be led by an experienced senior management team from Syros, and a board of directors comprised of Syros' current board of directors, a board member nominated by Tyme and up to two board members nominated by investors in the PIPE Financing, effective as of the closing of the merger.

Tyme Reasons for the Merger (see page 162)

After numerous meetings and consideration and consultation with its senior management and its financial and legal advisors, the Tyme board of directors unanimously determined that the Merger Agreement, the merger and other transactions contemplated thereby are advisable and in the best interests of Tyme and its stockholders. The Tyme board of directors considered various reasons to reach its determination. For example:

- the financial condition and prospects of Tyme and the risks associated with continuing to operate Tyme on a stand-alone basis, particularly in light of the discontinuation of SM-88 in the Precision Promise trial in metastatic pancreatic cancer in January 2022 and internal estimates that Tyme could face substantial doubt in its ability to continue as a going concern by the end of 2024 without additional fundraising;
- Tyme's board of directors' belief, after a thorough review of strategic alternatives and discussions with Tyme's senior management, financial advisors and legal counsel, that the merger is more favorable to Tyme stockholders than the potential value that might have resulted from other strategic alternatives available to Tyme, including a liquidation of Tyme and the distribution of any available cash after wind down;
- Tyme's board of directors' belief that, as a result of arm's length negotiations with Syros, Tyme and its representatives negotiated the highest exchange ratio to which Syros was willing to agree, and that the other terms of the Merger Agreement, taken as a whole, include the most favorable terms to Tyme in the aggregate to which Syros was willing to agree;
- Tyme's board of directors' view, following a review with Tyme's management of Syros' current development and clinical trial plans, of the likelihood that the combined company would possess sufficient cash resources at the closing of the merger to fund development of Syros' product candidates through upcoming value inflection points;
- the ability of Tyme stockholders to participate in the growth and value creation of the combined company following the closing of the merger by virtue of their ownership of Syros common stock; and
- Tyme's board of directors' view that the combined company will be led by an experienced senior management team from Syros and a board of directors with representation from each of the current boards of directors of Tyme and Syros.

Opinion of Piper Sandler & Co. (see page 165)

On July 1, 2022, Piper Sandler & Co., or Piper Sandler, rendered its oral opinion to Syros' board of directors (which was subsequently confirmed in writing by delivery of Piper Sandler's written opinion, dated the same date) to the effect that, as of July 1, 2022, and based upon and subject to the various assumptions and limitations set forth therein, the exchange ratio as set forth in the Merger Agreement, or Exchange Ratio, pursuant to the Merger Agreement was fair to Syros from a financial point of view.

Piper Sandler's opinion was directed to Syros' board of directors, and only addressed the fairness, from a financial point of view, to Syros, of the Exchange Ratio pursuant to the Merger Agreement. The summary of Piper Sandler's opinion in this proxy statement is qualified in its entirety by reference to the full text of its written opinion, which is included as *Annex B* to this proxy statement and sets forth, among other things, the assumptions made, procedures followed, matters considered and limitations on the scope of the review undertaken by Piper Sandler in rendering its opinion. However, neither Piper Sandler's written opinion nor the summary of its opinion and the related analyses set forth in this proxy statement is intended to be, and they do not constitute, a recommendation to any stockholder of Syros as to how such stockholder should act or vote with respect to the merger or any other matter.

For more information, see *Annex B* to this proxy statement and the section of this proxy statement entitled "*The Merger—Opinion of Piper Sandler & Co*."

Opinion of Moelis & Company LLC (see page 176)

In connection with the merger, Tyme's board of directors received a written opinion, dated July 2, 2022, from Tyme's financial advisor, Moelis & Company LLC, referred to as Moelis, as to the fairness, from a financial point of view and as of the date of such opinion, to the holders of Tyme common stock of the Exchange Ratio provided in the merger pursuant to the Merger Agreement. **The full text of Moelis' written opinion dated July 2, 2022, which sets forth the assumptions made, procedures followed, matters considered and limitations on the review undertaken in connection with the opinion, is attached as *Annex C* to this joint proxy statement/prospectus and is incorporated herein by reference. Moelis' opinion was provided for the use and benefit of Tyme's board of directors (solely in its capacity as such) in its evaluation of the merger. Moelis' opinion is limited solely to the fairness, from a financial point of view, to the holders of Tyme common stock of the Exchange Ratio provided in the merger pursuant to the Merger Agreement, and does not address Tyme's underlying business decision to effect the merger or the relative merits of the merger as compared to any alternative business strategies or transactions that might be available with respect to Tyme. Moelis' opinion does not constitute a recommendation to any stockholder of Tyme as to how such stockholder should vote or act with respect to the merger or any other matter.**

The Special Meeting of Syros Stockholders (see page 139)

The Syros special meeting will be held virtually on September 15, 2022 at 10:00 A.M. Eastern Time. The purposes of the Syros special meeting are as follows:

1. To approve, for purposes of Nasdaq Listing Rules 5635(a) and (d), the issuance of shares of common stock of Syros Pharmaceuticals, Inc., or Syros, to stockholders of Tyme Technologies, Inc., or Tyme, pursuant to the terms of the Agreement and Plan of Merger among Syros, Tyme and Tack Acquisition Corp., or Merger Sub, dated as of July 3, 2022, a copy of which is attached as *Annex A* to the accompanying joint proxy statement/prospectus, which is referred to in this Notice as the Merger Agreement, and to certain investors pursuant to the terms of the Securities Purchase Agreement, by and among Syros and the investors party thereto, dated as of July 3, 2022, a copy of which is attached as *Annex F* to the accompanying joint proxy statement/prospectus, which is referred to in this Notice as the Securities Purchase Agreement;

2. To approve an amendment to the Syros restated certificate of incorporation to increase the number of authorized shares of Syros common stock from 200,000,000 shares to 700,000,000 shares;

3. To approve an amendment to the Syros restated certificate of incorporation to effect a reverse stock split of Syros common stock, by a ratio of not less than 1-for-5 and not more than 1-for-15, and a proportionate reduction in the number of authorized shares of Syros common stock, such ratio and the implementation and timing of the reverse stock split to be determined in the discretion of Syros' board of directors;

4. To approve the adoption of the Syros Pharmaceuticals, Inc. 2022 Equity Incentive Plan; and

5. To consider and vote upon an adjournment of the Syros special meeting, if necessary, to solicit additional proxies if there are not sufficient votes in favor of Proposal Nos. 1, 2 and 3 or to ensure that any supplement or amendment to this joint proxy statement/prospectus is timely provided to holders of Syros common stock.

The affirmative vote of the holders of a majority of shares present in attendance or represented by proxy at the Syros special meeting and entitled to vote on the matter, assuming a quorum is present, is required for approval

of Proposal Nos. 1, 4 and 5. The affirmative vote of the holders of a majority of the outstanding shares of Syros common stock entitled to vote at the Syros special meeting is required for approval of Proposal Nos. 2 and 3. Approval of Proposal No. 1, referred to as the Syros share issuance proposal, and Proposal No. 2, referred to as the Syros share increase proposal, is not a condition to the completion of the merger but is necessary to complete the PIPE Financing, which is a condition to Tyme's obligations to complete the merger. Therefore, the merger cannot be consummated without the approval of Proposal No. 1 and, unless waived by Tyme, Proposal No. 2.

Only holders of record of issued and outstanding shares of Syros common stock as of the close of business on August 8, 2022, the record date for the Syros special meeting, are entitled to notice of, and to vote at, the Syros special meeting. Syros stockholders may cast one vote for each share of Syros common stock that Syros stockholders held as of that record date.

The Special Meeting of Tyme Stockholders (see page 143)

The principal business of the Tyme special meeting will be:

1. To adopt the Merger Agreement;
2. To conduct an advisory, non-binding vote to approve merger-related executive compensation;
3. To approve an amendment to Tyme's amended and restated certificate of incorporation to effect a reverse stock split of Tyme common stock, by a ratio of not less than 1-for-15 and not more than 1-for-75, such ratio and the implementation and timing of the reverse stock split to be determined in the discretion of Tyme's board of directors;
4. To consider and vote upon an adjournment of the Tyme special meeting, if necessary, to solicit additional proxies if there are not sufficient votes in favor of Proposal Nos. 1, 2 and 3 or to ensure that any supplement or amendment to this joint proxy statement/prospectus is timely provided to holders of Tyme common stock.
5. To transact any other business as may properly come before the meeting or any adjournment or postponement thereof.

The affirmative vote of the holders of a majority of the outstanding shares of Tyme common stock is required to approve Tyme Proposal Nos. 1 and 3.

The affirmative vote of the holders of a majority of the shares present in attendance or represented by proxy at the Tyme special meeting and entitled to vote on the matter, assuming a quorum is present, is required to approve Proposal Nos. 2 and 4.

Background of the Merger (see page 149)

Merger Consideration (see page 203)

At the effective time of the merger, upon the terms and subject to the conditions set forth in the Merger Agreement, each outstanding share of Tyme common stock will be automatically converted solely into the right to receive a number of shares of Syros common stock equal to the exchange ratio described in more detail below.

Treatment of Tyme Equity Awards and Warrants (see page 204)

Under the terms of the Merger Agreement, each option to purchase shares of Tyme common stock that is granted to an individual who continues as a service provider to Tyme at the effective time and is outstanding and unexercised immediately prior to the effective time of the merger, whether or not vested, will be converted into a

number of options to purchase shares of Syros common stock to be determined by the exchange ratio. Each outstanding and unexercised option to purchase shares of Tyme common stock that is not assumed by Syros pursuant to the merger agreement will be terminated and no consideration will be delivered for such options. It is expected that holders of options to be terminated at the effective time of the merger will be given notice of a 30-day period prior to the effective time of the merger in which such holders will be able to exercise such options.

Also in connection with the merger, each warrant to purchase shares of Tyme common stock outstanding and unexercised as of the effective time (other than certain warrants that Tyme is required to repurchase in connection with the merger) will be converted into a warrant to purchase the number shares of Syros common stock to be determined by the exchange ratio.

Accordingly, from and after the effective time of the merger: (i) each outstanding Tyme stock option or warrant assumed by Syros may be exercised solely for shares of Syros common stock; (ii) the number of shares of Syros common stock subject to each outstanding Tyme stock option or warrant assumed by Syros will be determined by multiplying (A) the number of shares of Tyme common stock that were subject to such Tyme stock option or warrant, as in effect immediately prior to the effective time of the merger, by (B) the exchange ratio, and rounding the resulting number down to the nearest whole number of shares of Syros common stock; (iii) the per share exercise price of Syros common stock issuable upon exercise of each Tyme stock option or warrant assumed by Syros will be determined by dividing (A) the per share exercise price of Tyme common stock subject to such Tyme stock option or warrant, as in effect immediately prior to the effective time of the merger, by (B) the exchange ratio and rounding the resulting exercise price up to the nearest whole cent; and (iv) any restriction on the exercise, and any provision providing for the acceleration of vesting and/or exercisability, of any Tyme stock option or warrant assumed by Syros will continue in full force and effect and the term, exercisability, vesting schedule, acceleration rights and other provisions of such Tyme stock option or warrant will otherwise remain unchanged.

It is anticipated that Tyme's executive officers will enter into cooperation agreements with Tyme that will, among other things, extend the exercise period for each assumed Tyme option with an exercise price of less than $2.00 per share of Tyme common stock that such executive officer holds as of immediately following closing of the merger to the second anniversary of such executive officer's termination date, or, if earlier, until the earliest of (i) the second anniversary of the effective time, (ii) the original expiration date of such option, and (iii) any earlier termination or cashing out of options at Syros generally applicable to its option holders. See the subsection titled "*The Merger—Interests of Tyme Directors and Executive Officers in the Merger—Cooperation Agreements*" in this joint proxy statement/prospectus for further details related to the cooperation agreements.

However, to the extent provided under the terms of a Tyme stock option assumed by Syros in accordance with the terms of the Merger Agreement, such Tyme stock option shall, in accordance with its terms, be subject to further adjustment as appropriate to reflect any stock split, division or subdivision of shares, stock dividend, reverse stock split, consolidation of shares, reclassification, recapitalization or other similar transaction with respect to shares of Syros common stock subsequent to the effective time of the merger. In addition, the Syros board of directors or a committee thereof will succeed to the authority and responsibility of Tyme's board of directors or any committee thereof with respect to each Tyme option assumed by Syros in accordance with the terms of the Merger Agreement. Furthermore, in the case of each Tyme option assumed by Syros in accordance with the Merger Agreement that is subject to "double-trigger" accelerated vesting, for purposes of such double-trigger acceleration provisions a "Change of Control" (or term of similar import) of Tyme will refer to a "Change of Control" (or term of similar import) of Syros following the effective time of the merger.

Treatment of Syros Common Stock and Equity Awards (see page 204)

Each share of Syros common stock issued and outstanding at the time of the merger will remain issued and outstanding. In addition, each option to purchase shares of Syros common stock and each other equity award that covers shares of Syros common stock that is outstanding immediately prior to the effective time of the merger, whether vested or unvested, will survive the closing and remain outstanding in accordance with its terms. The number of shares of Syros common stock underlying such options and the exercise prices for such stock options, and each other equity award that covers Syros common stock, will be appropriately adjusted to reflect the proposed reverse stock split of Syros common stock, if the Syros reverse stock split proposal is approved and the Syros board of directors determines to effect the reverse stock split.

Conditions to the Completion of the Merger (see page 215)

To complete the merger, Syros stockholders must approve Syros Proposal No. 1, and, unless waived by Tyme, Syros Proposal No. 2, at the Syros special meeting and Tyme stockholders must approve the adoption of the Merger Agreement at the Tyme special meeting. Additionally, each of the other closing conditions set forth in the Merger Agreement must be satisfied or waived (including the closing of the PIPE Financing).

Non-Solicitation (see page 210)

The Merger Agreement contains "non-solicitation" provisions, pursuant to which, subject to specified exceptions, each of Syros and Tyme has agreed that neither it nor its subsidiaries will, and each of Syros and Tyme will use reasonable best efforts to cause its respective directors, officers, members, employees, agents, attorneys, consultants, contractors, accountants, financial advisors or other representatives not to, directly or indirectly:

- solicit, seek or initiate or knowingly take any action to facilitate or encourage any offers, inquiries or the making of any proposal or offer that constitutes, or could reasonably be expected to lead to, any Acquisition Proposal (as defined in the section of this proxy statement/prospectus entitled "*The Merger Agreement—Non-Solicitation*");
- enter into, continue or otherwise participate or engage in any discussions or negotiations regarding any Acquisition Proposal (as such term is defined in the Merger Agreement), or furnish to any person any non-public information or afford any person other than Syros or Tyme, as applicable, access to such party's property, books or records (except pursuant to a request by a governmental entity) in connection with any offers, inquiries or the making of any proposal or offer that constitutes, or could reasonably be expected to lead to, any Acquisition Proposal;
- take any action to make the provisions of any takeover statute inapplicable to any transactions contemplated by an Acquisition Proposal; or
- publicly propose to do any of the foregoing.

Board Recommendation Change (see page 212)

Subject to specified exceptions described in the Merger Agreement, Syros agreed that its board of directors may not take any of the following actions, each of which are referred to in this joint proxy statement/prospectus as a Syros board recommendation change:

- withhold, withdraw or modify, or publicly propose to withhold, withdraw or modify, the approval or recommendation of the Syros board of directors with respect to the Share Issuance or Syros Authorized Stock Increase (as such terms are defined in the Merger Agreement);

- fail to recommend against acceptance of a tender offer within ten business days after commencement; or
- publicly propose to adopt, approve or recommend any Acquisition Proposal.

Subject to specified exceptions described in the Merger Agreement, Tyme agreed that its board of directors may not take any of the following actions, each of which are referred to in this proxy statement/prospectus as a Tyme board recommendation change:

- withhold, withdraw or modify, or publicly propose to withhold, withdraw or modify, the approval or recommendation of Tyme's board of directors with respect to the merger;
- fail to recommend against acceptance of a tender offer within ten business days after commencement; or
- publicly propose to adopt, approve or recommend any Acquisition Proposal.

Termination of the Merger Agreement (see page 219)

Either Syros or Tyme may terminate the Merger Agreement under certain circumstances, which would prevent the merger from being consummated.

Termination Fees (see page 221)

If the Merger Agreement is terminated under specified circumstances, Syros will be required to pay Tyme a termination fee of $2.068 million. If the Merger Agreement is terminated under specified circumstances, Tyme will be required to pay Syros a termination fee of $2.443 million.

Support Agreements (see page 222)

In order to induce Syros to enter into the Merger Agreement, certain Tyme stockholders are parties to support agreements pursuant to which, among other things, each such Tyme stockholder has agreed, solely in his, her or its capacity as a Tyme stockholder, to vote all of his, her or its shares of Tyme common stock in favor of the adoption of the Merger Agreement. These Tyme stockholders also agreed to vote against any competing Acquisition Proposal with respect to Tyme.

As of June 30, 2022, the Tyme stockholders that are party to such a support agreement or another voting agreement with Tyme obligating them to vote in favor of the Tyme board of directors' recommendation on such matters owned an aggregate of 53,428,292 shares of Tyme common stock, representing approximately 31% of the outstanding shares of Tyme common stock. These stockholders include executive officers and directors of Tyme, as well as certain other stockholders owning a significant portion of the outstanding shares of Tyme common stock.

In addition, in order to induce Tyme to enter into the Merger Agreement, certain Syros stockholders have entered into support agreements pursuant to which, among other things, each such Syros stockholder has agreed, solely in his, her or its capacity as a Syros stockholder, to vote all of his, her or its shares of Syros common stock in favor of the Syros share issuance proposal, the increase in the number of authorized shares of Syros common stock to be effectuated prior to the effective time, and such other matters as may require approval of the Syros' stockholders pursuant to the Delaware General Corporation Law, or DGCL, with respect to the PIPE Financing, subject to the terms of the support agreements. These Syros stockholders also agreed to vote against any competing Acquisition Proposal with respect to Syros.

As of June 30, 2022, the Syros stockholders that are party to a support agreement owned an aggregate of 17,460,552 shares of Syros common stock representing approximately 28% of the outstanding shares of Syros common stock. These stockholders include executive officers and directors of Syros and certain other Syros stockholders holding a significant portion of the outstanding shares of Syros common stock.

Lock-Up Agreements (see page 223)

Certain of Syros' and Tyme's executive officers and directors have entered into lock-up agreements, pursuant to which such parties have agreed not to, except in limited circumstances, offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, or otherwise transfer or dispose of, any shares of Syros common stock until 90 days after the closing of the merger. The Syros stockholders who have executed lock-up agreements as of June 30, 2022, are expected to own, in the aggregate, approximately 6% of the shares of the combined company on a pro forma basis , and the Tyme stockholders who have executed lock-up agreements as of June 30, 2022, owned in the aggregate, less than 1% of the shares of the combined company on a pro forma basis. In addition, each of Syros and Tyme is obligated under the merger agreement to use commercially reasonable efforts prior to the closing of the merger to obtain a lock-up agreement from any person who will serve as a director or officer of the combined company following completion of the merger.

Securities Purchase Agreement and Registration Rights Agreements (see page 223)

Securities Purchase Agreement

Immediately prior to the execution and delivery of the Merger Agreement, Syros entered into the Securities Purchase Agreement with certain accredited investors, pursuant to which Syros agreed to issue and sell to the investors in the PIPE Financing an aggregate of 63,871,778 shares of Syros common stock and, in lieu of shares of Syros common stock to certain investors, pre-funded warrants to purchase an aggregate of 74,267,400 shares of Syros common stock, or the Pre-Funded PIPE Warrants, and, in each case, accompanying warrants, or the PIPE Warrants, to purchase an aggregate of up to 138,139,178 additional shares of Syros common stock (or Pre-Funded PIPE Warrants to purchase common stock in lieu thereof) at a price of $0.94 per share and accompanying PIPE Warrant (or $0.9399 per Pre-Funded PIPE Warrant and accompanying PIPE Warrant). The price per Pre-Funded PIPE Warrant and accompanying PIPE Warrant represents the price of $0.94 per share and accompanying PIPE Warrant to be sold in the PIPE Financing, minus the $0.0001 per share exercise price of each such Pre-Funded PIPE Warrant. The exercise price of the PIPE Warrants is $1.034 per share, or if exercised for a Pre-Funded PIPE Warrant in lieu thereof, $1.0339 per Pre-Funded PIPE Warrant (representing the PIPE Warrant exercise price of $1.034 per share minus the $0.0001 per share exercise price of each such Pre-Funded PIPE Warrant). The PIPE Warrants are exercisable beginning six months after the closing date of the PIPE Financing and prior to five years after the closing date of the PIPE Financing. The Pre-Funded PIPE Warrants are exercisable at any time after their original issuance and will not expire. The closing of the PIPE Financing is conditioned upon the satisfaction or waiver of the conditions to the closing of the merger as well as certain other conditions.

Registration Rights Agreement

Concurrently with the execution of the Securities Purchase Agreement, Syros entered into a registration rights agreement, or the Registration Rights Agreement, with the investors in the PIPE Financing, pursuant to which Syros agreed to register for resale the shares of Syros common stock and the issuance of the shares of Syros common stock underlying the PIPE Warrants and Pre-Funded PIPE Warrants held by the investors pursuant to a registration statement to be filed within 30 days of the closing of the PIPE Financing.

Affiliate Registration Rights Agreement

Concurrently with the execution of the Securities Purchase Agreement and the Registration Rights Agreement, Syros also entered into a registration rights agreement, or the Affiliate Registration Rights Agreement, with Baker Brothers Life Sciences, L.P. and 667, L.P., which are together referred to as the Baker Funds, pursuant to which the Baker Funds are entitled to certain resale registration rights with respect to shares of Syros common stock held by the Baker Funds. Under the Affiliate Registration Rights Agreement, following a request by the Baker Funds, Syros is obligated to file a resale registration statement on Form S-3, or other appropriate form, covering the shares of Syros common stock held by the Baker Funds. Syros has agreed to file such resale registration statement as promptly as reasonably practicable following such request, and in any event within sixty (60) days of such request, subject to specified exceptions, conditions and limitations.

Interests of Certain Directors, Officers and Affiliates of Syros (see page 186)

In considering the recommendation of the Syros board of directors with respect to issuing shares of Syros common stock in the merger and the other matters to be acted upon by the Syros stockholders at the Syros special meeting, Syros stockholders should be aware that Syros' directors and executive officers have interests in the merger that are different from, or in addition to, the interests of Syros' stockholders generally. Interests of the directors and executive officers may be different from or in addition to the interests of the stockholders for the following reasons, among others:

- Certain directors and executive officers of Syros and their affiliates have agreed to participate in the PIPE Financing.
- Syros' directors are expected to continue to serve on the board of directors of the combined company after the effective time of the merger, and will continue to be eligible to be compensated pursuant to the Syros non-employee director compensation policy.
- Syros' executive officers are expected to continue to serve in their respective positions as executive officers of the combined company.
- Under the Merger Agreement, Syros' directors and executive officers are entitled to continued indemnification, expense advancement and insurance coverage.

These interests are discussed in more detail in the section titled "*The Merger—Interests of Syros Directors and Executive Officers in the Merger*" beginning on page 186 of this joint proxy statement/prospectus. The members of Syros' board of directors were aware of and considered these interests, among other matters, in evaluating and negotiating the Merger Agreement, the merger, the Securities Purchase Agreement and the PIPE Financing and in recommending to the stockholders that the Syros proposals be approved.

Each of Syros' executive officers and each of Syros' directors has also entered into a support agreement and alock-up agreement in connection with the merger. For a more detailed discussion of the support agreements and lock-up agreements, please see the sections titled "*Agreements Related to the Merger—Support Agreements*" and "*Agreements Related to the Merger—Lock-Up Agreements*" beginning on pages 222 and 223, respectively, of this joint proxy statement/prospectus.

Interests of Certain Directors, Officers and Affiliates of Tyme (see page 188)

In considering the recommendation of Tyme's board of directors with respect to adoption of the Merger Agreement and the other matters to be acted upon by the Tyme stockholders at the Tyme special meeting, Tyme stockholders should be aware that Tyme's directors and executive officers have interests in the merger that are different from, or in addition to, the interests of Tyme's stockholders generally. Interests of the directors and

executive officers may be different from or in addition to the interests of the stockholders for the following reasons, among others:

- Upon a change of control of Tyme, certain executive officers of Tyme would be entitled to the payment of amounts equal to their respective target bonuses for the year ending March 31, 2023 pursuant to retention agreements and all outstanding option awards granted under the Tyme 2015 Incentive Plan would become fully vested and exercisable.
- All executive officers are expected to enter into cooperation agreements, which, among other things, would extend the exercise period of certain options being assumed by Syros for a period of up to two years after the effective time of the merger.
- Tyme will have the right to name one designee to serve on the board of directors of the combined company after the effective time of the merger, and such individual will become eligible to be compensated pursuant to the Syros non-employee director compensation policy.

These interests are discussed in more detail in the section titled "*The Merger—Interests of Tyme Directors and Executive Officers in the Merger*" beginning on page 188 of this joint proxy statement/prospectus. The members of Tyme's board of directors were aware of and considered these interests, among other matters, in evaluating and negotiating the Merger Agreement and the merger, and in recommending to the stockholders that the Tyme merger proposal be approved.

Each of Tyme's executive officers and each of Tyme's directors, other than Mr. Hoffman, has entered into a support agreement and a lock-up agreement in connection with the merger. Mr. Hoffman had previously entered into a voting agreement with Tyme, which obligates him to vote his shares in accordance with the recommendations of Tyme's board of directors. For a more detailed discussion of the support agreements and lock-up agreements, please see the sections titled "*Agreements Related to the Merger—Support Agreements*" and "*Agreements Related to the Merger—Lock-Up Agreements*" beginning on pages 222 and 223, respectively, of this joint proxy statement/prospectus.

Management Following the Merger (see page 370)

Effective as of the closing of the merger, the combined company's executive officers are expected to be members of the Syros executive management team prior to the merger, including:

- Nancy Simonian, M.D., President & Chief Executive Officer
- Conley Chee, Chief Commercial Officer
- Jason Haas, Chief Financial Officer
- Eric R. Olson, Ph.D., Chief Scientific Officer
- David A. Roth, M.D., Chief Medical Officer
- Kristin Stephens, Chief Development Officer

Prior to the effectiveness of the closing of the merger, Tyme shall designate one director to serve on the Syros board of directors. Such designee shall be subject to the approval of Syros' Nominating and Corporate Governance Committee, such approval not to be unreasonably withheld. In addition, investors in the PIPE Financing will have the right to designate up to two members of the board of directors of the combined company, subject to approval of Syros' board of directors.

Principal Stockholders of Syros (see page 432)

At the close of business on June 30, 2022, directors and executive officers of Syros beneficially owned and were entitled to vote less than 8% of the shares of Syros common stock outstanding. Each of Syros' directors and

executive officers have entered into a support agreement obligating them to vote their stock in favor of Syros Proposal Nos. 1, 2 and 3, and against any competing "Acquisition Proposal" (as defined in the Merger Agreement). The support agreements are discussed in more detail in the section titled "*Agreements Related to the Merger—Support Agreements*" beginning on page 222 of this proxy statement/prospectus.

Principal Stockholders of Tyme (see page 436)

As of June 30, 2022, the directors (including Mr. Hoffman) and executive officers of Tyme beneficially owned approximately 11.8% of the outstanding shares of Tyme common stock entitled to vote at the Tyme special meeting. As of June 30, 2022, the Tyme stockholders that have entered into support agreements in connection with the merger owned an aggregate of 10,356,880 shares of Tyme common stock representing approximately 6% of the outstanding shares of Tyme common stock. Pursuant to the support agreements, these stockholders have agreed to vote all shares of Tyme common stock owned by them as of the record date in favor of Tyme Proposal No. 1. In addition to these stockholders, Tyme's co-founders, Steve Hoffman and Michael Demurjian, who, as of June 30, 2022, owned approximately 25% of Tyme's outstanding common stock, have entered into voting agreements with Tyme to vote in accordance with the Tyme board of directors' recommendation with respect to any matter presented to Tyme's stockholders. The support agreements are discussed in more detail in the section titled "*Agreements Related to the Merger—Support Agreements*" beginning on page 222 of this proxy statement/prospectus.

Principal Stockholders of the Combined Company (see page 439)

Based upon the initially estimated exchange ratio, following the merger and giving effect to the PIPE Financing, (i) Syros securityholders immediately before the merger together with the investors in the PIPE Financing are expected to own approximately 63% of the aggregate number of outstanding shares of Syros common stock following the merger and (ii) Tyme securityholders immediately before the merger are expected to own approximately 37% of the aggregate number of outstanding shares of Syros common stock following the merger, subject to certain assumptions (including as to the amount of Tyme net cash at closing, which could be materially different). Assuming the exercise of all Syros pre-funded warrants, including the Pre-Funded PIPE Warrants and the Pre-Funded 2020 Warrants, without giving effect to any beneficial ownership limitations applicable thereto, then (i) Syros securityholders immediately before the merger together with the investors in the PIPE Financing would own approximately 73% of the aggregate number of outstanding shares of Syros common stock following the merger and (ii) Tyme securityholders immediately before the merger would own approximately 27% of the aggregate number of outstanding shares of Syros common stock following the merger, subject to certain assumptions (including as to the amount of Tyme net cash at closing, which could be materially different). The foregoing percentages do not give effect to the exercise or conversion of outstanding stock options or warrants other than as set forth above. The exchange ratio referenced above is an estimate only and the final exchange ratio will be determined pursuant to a formula described in more detail in the Merger Agreement and in this joint proxy statement/prospectus. The actual exchange ratio will depend on Tyme's net cash and the number of shares of Tyme common stock outstanding at the closing of the merger.

Material U.S. Federal Income Tax Consequences of the Merger (see page 198)

The merger is intended to qualify as either a tax-free contribution pursuant to Section 351 of the Code, taken together with the PIPE Financing, or a "reorganization" within the meaning of Section 368(a) of the Code. Assuming the merger qualifies for the intended tax treatment, subject to the limitations and qualifications described in the section entitled "*The Merger—Material U.S. Federal Income Tax Consequences of the Merger*" beginning on page 198 of this joint proxy statement/prospectus, a U.S. Holder (as defined in such section) of Tyme common stock generally will not recognize any gain or loss for U.S. federal income tax purposes on the exchange of shares of Tyme common stock for shares of Syros common stock in the merger, except with respect

to cash received by such U.S. Holder in lieu of a fractional share of Syros common stock. It is possible that, under certain circumstances, the merger will not satisfy the requirements to qualify as either a tax-free contribution pursuant to Section 351 of the Code or a "reorganization" within the meaning of Section 368(a) of the Code.

Please review the information in the section entitled "*The Merger—Material U.S. Federal Income Tax Consequences of the Merger*" beginning on page 198 of this joint proxy statement/prospectus for a more complete description of the material U.S. federal income tax consequences of the merger to U.S. Holders of Tyme common stock. The tax consequences of the merger to each U.S. Holder will depend on the holder's particular facts and circumstances. Please consult your tax advisors as to the specific tax consequences to you of the merger.

Risk Factors (see page 31)

Both Syros and Tyme are subject to various risks associated with their businesses and their industries. In addition, the merger, including the possibility that the merger may not be completed, poses a number of risks to each company and its respective securityholders, including the following risks:

- The exchange ratio will not be adjusted based on the market price of Syros common stock so the merger consideration at the closing may have a greater or lesser value than at the time the Merger Agreement was signed;
- Failure to complete the merger may result in Syros or Tyme paying a termination fee to the other party which could harm the common stock price and the future business and operations of each company;
- If the conditions to the merger are not satisfied or waived, the merger may not occur;
- The merger may be completed even though material adverse effects may result from the announcement of the merger, industry-wide changes and other causes;
- Some Syros and Tyme executive officers and directors have interests in the merger that are different from yours and that may influence them to support or approve the merger without regard to your interests;
- Syros' stockholders may not realize a benefit from the merger commensurate with the ownership dilution they will experience in connection with the merger; and
- If the merger is not completed, either company's stock price may fluctuate significantly.

These risks and other risks are discussed in greater detail under the section titled "*Risk Factors*" beginning on page 31 of this joint proxy statement/prospectus. Syros and Tyme both encourage you to read and consider all of these risks carefully.

Regulatory Approvals (see page 197)

Syros and Tyme are required to cooperate with each other and use (and to cause their respective subsidiaries to use) their commercially reasonable efforts to (i) take, or cause to be taken, all actions, and do, or cause to be done and to assist and cooperate with the other parties in doing, all things necessary, proper or advisable to consummate and make effective the contemplated transactions as promptly as practicable, (ii) as promptly as practicable, obtain from any governmental authority or any other third party any consents, licenses, permits, waivers, approvals, authorizations, or orders required to be obtained or made by Tyme or Syros or any of their subsidiaries in connection with the authorization, execution and delivery of the Merger Agreement and the consummation of the contemplated transactions, (iii) as promptly as practicable, make all necessary filings, and thereafter make any other required submissions, with respect to the Merger Agreement and the merger required under (A) the Securities Act of 1933, as amended, or the Securities Act, and the Securities Exchange Act of

1934, as amended, or the Exchange Act, and any other applicable federal or state securities laws, and (B) any other applicable law and (iv) execute or deliver any additional instruments necessary to consummate the transactions contemplated by, and to fully carry out the purposes of, the Merger Agreement.

Tyme and Syros shall reasonably cooperate with each other in connection with the making of all such filings. Tyme and Syros shall use their respective commercially reasonable efforts to furnish to each other all information required for any application or other filing to be made pursuant to the rules and regulations of any applicable law (including all information required to be included in this joint proxy statement/prospectus and the registration statement) in connection with the contemplated transactions.

Syros Nasdaq Listing; Delisting of Tyme Stock (see pages 202 and 214)

Syros anticipates that the common stock of the combined company will be listed on The Nasdaq Global Select Market following the closing of the merger under the trading symbol "SYRS."

If the merger is completed, Tyme common stock will be delisted from The Nasdaq Capital Market and deregistered under the Exchange Act, and Tyme will no longer be required to file periodic reports with the U.S. Securities and Exchange Commission, or the SEC, with respect to Tyme common stock.

Tyme has agreed to cooperate with Syros to take, or cause to be taken, all actions necessary to enable the delisting of the shares of Tyme common stock from The Nasdaq Capital Market and the deregistration of the shares of Tyme common stock under the Exchange Act after the effective time.

Anticipated Accounting Treatment (see page 202)

The merger is being accounted for as an in-substance recapitalization of Syros, as the assets and liabilities being acquired consist almost entirely of cash and cash equivalents and highly liquid assets. For more information on the accounting treatment see the section entitled "*The Merger—Anticipated Accounting Treatment"* beginning on page 202 of this joint proxy statement/prospectus.

Appraisal Rights and Dissenters' Rights (see page 202)

The holders of both Syros common stock and Tyme common stock are not entitled to appraisal rights in connection with the merger under the laws of the State of Delaware.

Comparison of the Rights of the Holders of Syros Stock and Tyme Stock (see page 425)

Both Syros and Tyme are incorporated under the laws of the State of Delaware and, accordingly, the rights of the stockholders of each are currently, and will continue to be, governed by the DGCL. If the merger is completed, Tyme stockholders will become Syros stockholders, and their rights will be governed by the DGCL, the second amended and restated bylaws of Syros, or the amended and restated bylaws, and the restated certificate of incorporation of Syros, as may be further amended by Syros Proposal Nos. 2 and 3 if approved by the Syros stockholders at the Syros special meeting. The rights of Syros stockholders contained in the restated certificate of incorporation and amended and restated bylaws of Syros differ from the rights of Tyme stockholders under the amended and restated certificate of incorporation and amended and restated bylaws of Tyme, as more fully described under the section titled "*Comparison of the Rights of Holders of Syros Stock and Tyme Stock*" beginning on page 425 of this joint proxy statement/prospectus.

Comparison of Syros and Tyme Market Prices and Implied Value of Merger Consideration

The following table sets forth the closing price per share of Syros common stock and of Tyme common stock as of July 1, 2022, the last trading day prior to the public announcement of the merger, and July 15, 2022, the most

recent practicable trading day prior to the date of this joint proxy statement/prospectus. The table also shows the implied value of the estimated merger consideration for each share of Tyme common stock as of the same two dates. This implied value was calculated by multiplying the closing price of a share of Syros common stock on the relevant date by an estimated exchange ratio of 0.4312, because the actual exchange ratio is not yet known. Syros common stock and Tyme common stock are listed on The Nasdaq Stock Market under the symbols "SYRS" and "TYME," respectively.

	Syros common stock	Tyme common stock	Implied per share value of merger consideration
July 1, 2022	$ 0.91	$ 0.27	$ 0.39
August 5, 2022	$ 0.90	$ 0.34	$ 0.39

The market prices of shares of Syros common stock and Tyme common stock have fluctuated since the date of the announcement of the merger and will continue to fluctuate from the date of this joint proxy statement/prospectus to the date the merger is completed, and the market price of shares of Syros common stock will continue to fluctuate after the completion of the merger. No assurance can be given concerning the market prices of Syros common stock or Tyme common stock before the completion of the merger or Syros common stock after the completion of the merger. Syros will issue a number of shares of Syros common stock in exchange for each share of Tyme common stock in accordance with an exchange ratio that will depend on Tyme's net cash and the number of shares of Tyme common stock outstanding at the closing of the merger. As a result, the implied value of the merger consideration to be received by Tyme stockholders will fluctuate based on any changes in the market price of Syros common stock prior to the completion of the merger, and any changes in Tyme's net cash and the number of shares of Tyme common stock outstanding at the closing of the merger. Accordingly, such implied value of the per share merger consideration to be received by Tyme stockholders upon completion of the merger could be greater than, less than or the same as the implied value of the merger consideration on the date of this joint proxy statement/prospectus. Syros and Tyme urge you to obtain current market quotations for the shares of Syros common stock and Tyme common stock. Syros common stock and Tyme common stock are listed on The Nasdaq Stock Market under the symbols "SYRS" and "TYME," respectively. For more information, please see the section entitled "*Where You Can Find More Information*" beginning on page 445 of this joint proxy statement/prospectus.

Litigation Related to the Merger

In connection with the merger, on July 25, 2022, a complaint captioned Irwin v. Tyme Technologies, Inc., et al., Case No. 3:22-cv-04727 was filed in the United States District Court for the District of New Jersey against Tyme and the members of its board. The complaint generally alleges violations of Sections 14(a) and 20(a) of the Exchange Act in connection with the registration statement on Form S-4 of which this joint proxy statement/prospectus is a part. In particular, the complaint generally alleges that the registration statement contains materially misleading and incomplete information concerning: (i) certain conflicts of interest involving Tyme management and its board; (ii) the background and process leading up to the merger; (iii) Syros' and Tyme's financial projections; (iv) the description of the fairness opinion and financial analyses performed by Piper Sandler, which acted as Syros' financial advisor for the merger; and (v) financial analyses performed by Moelis, which acted as Tyme's financial advisor for the merger.

Syros and Tyme believe that the complaint is wholly without merit.

Each of Syros and Tyme has also received correspondence from law firms claiming to represent purported stockholders, either threatening litigation, requesting books and records concerning the Merger pursuant to Section 220 of the DGCL, or making other demands relating to the Merger including that additional disclosures be provided. Neither Syros nor Tyme can predict whether any of such demands or threats will result in litigation, whether additional demands or litigation may materialize, or the outcome of litigation relating to the merger. If additional similar complaints are filed or additional demands are received, absent new or materially different allegations, Syros and Tyme will not necessarily disclose them.

MARKET PRICE AND DIVIDEND INFORMATION

Syros Common Stock/Dividends

The closing price of Syros common stock on July 1, 2022, the last trading day prior to the public announcement of the merger, was $0.91 per share and the closing price of Syros common stock on August 8, 2022 was $0.98 per share, in each case as reported on The Nasdaq Global Select Market.

Syros has never declared or paid cash dividends on its capital stock and does not anticipate paying any cash dividends in the foreseeable future. Notwithstanding the foregoing, any determination for Syros to pay cash dividends subsequent to the completion or abandonment of the merger will be at the discretion of Syros' board of directors and will depend upon a number of factors, including its results of operations, financial condition, future prospects, contractual restrictions, restrictions imposed by applicable law and other factors Syros' board of directors deems relevant.

Tyme Common Stock/Dividends

The closing price of Tyme common stock on July 1, 2022, the last trading day prior to the public announcement of the merger, was $0.27 per share and the closing price of Tyme common stock on August 8, 2022 was $0.32 per share, in each case as reported on The Nasdaq Capital Market.

Tyme has never declared or paid cash dividends on its capital stock and does not anticipate paying any cash dividends in the foreseeable future if Tyme remains a standalone operating company. Notwithstanding the foregoing, any determination for Tyme to pay cash dividends following abandonment of the merger will be at the discretion of Tyme's board of directors and will depend upon a number of factors, including Tyme's results of operations, financial condition, future prospects, contractual restrictions, restrictions imposed by applicable law and other factors Tyme's board of directors deems relevant.

RISK FACTORS

The combined company will be faced with a market environment that cannot be predicted and that involves significant risks, many of which will be beyond its control. In addition to the other information contained in this joint proxy statement/prospectus, you should carefully consider the material risks described below before deciding how to vote your shares of Syros common stock. You should also read and consider the risks associated with each of the businesses of Syros and Tyme because these risks will also affect the combined company. The risks associated with the business of Syros can be found in Syros' Annual Report on Form 10-K for the fiscal year ended December 31, 2021 and the risks associated with the business of Tyme can be found in Tyme's Annual Report on Form 10-K for the fiscal year ended March 31, 2022, as amended, as such risks may be updated or supplemented in each company's subsequently filed Quarterly Reports on Form 10-Q or Current Reports on Form 8-K (excluding any information and exhibits furnished under Item 2.02 or 7.01 thereof), each of which are incorporated by reference into this joint proxy statement/prospectus. In addition, you are urged to carefully consider the following material risks relating to the merger, the business of the combined company, the business of Syros, and the business of Tyme.

Risks Related to the Merger

The exchange ratio will be determined in accordance with a formula and is not yet knowable. The actual exchange ratio could be materially different than currently anticipated.

At the effective time of the merger, outstanding shares of Tyme common stock will be converted into shares of Syros common stock at the exchange ratio. The exchange ratio was initially estimated to be 0.4312 shares of Syros common stock for each share of Tyme common stock, but the actual exchange ratio will depend on Tyme's net cash and the number of shares of Tyme common stock outstanding at the closing of the merger. These figures, particularly with respect to Tyme's net cash, may be materially different than the estimates used when initially estimating the exchange rate and may result in a materially different exchange rate. Based upon the initially estimated exchange ratio, following the merger and giving effect to the PIPE Financing, (i) Syros securityholders immediately before the merger together with the investors in the PIPE Financing are expected to own approximately 63% of the aggregate number of outstanding shares of Syros common stock following the merger and (ii) Tyme securityholders immediately before the merger are expected to own approximately 37% of the aggregate number of outstanding shares of Syros common stock following the merger, subject to certain assumptions (including as to the amount of Tyme net cash at closing, which could be materially different). Assuming the exercise of all Syros pre-funded warrants, including the Pre-Funded PIPE Warrants and the Pre-Funded 2020 Warrants, without giving effect to any beneficial ownership limitations applicable thereto, then (i) Syros securityholders immediately before the merger together with the investors in the PIPE Financing would own approximately 73% of the aggregate number of outstanding shares of Syros common stock following the merger and (ii) Tyme securityholders immediately before the merger would own approximately 27% of the aggregate number of outstanding shares of Syros common stock following the merger, subject to certain assumptions (including as to the amount of Tyme net cash at closing, which could be materially different). The foregoing percentages do not give effect to the exercise or conversion of outstanding stock options or warrants other than as set forth above.

The following table illustrates what the exchange ratio and the Tyme stockholders' resulting pro forma ownership of Syros could be at certain levels of Tyme's net cash. These examples assume: (i) Tyme has 172,206,894 shares of common stock outstanding immediately prior to the effective time and (ii) Syros has 126,860,798 shares of common stock outstanding immediately prior to the effective time, after giving effect to the PIPE Financing and assuming the exercise of all Syros pre-funded warrants, including the Pre-Funded PIPE Warrants and the Pre-Funded 2020 Warrants, without giving effect to any beneficial ownership limitations applicable thereto, but before the issuance of shares in the merger, and without giving effect to the exercise or conversion of outstanding stock options or warrants other than as set forth above:

	($ in millions)				
Tyme Net Cash	$ 50.0	$ 55.0	$ 62.3	$ 65.0	$ 70.0
Exchange Ratio	0.3552	0.3861	0.4312	0.4479	0.4788
Former Tyme Stockholders' Pro Forma Ownership	23.23%	24.75%	26.87%	27.62%	28.97%

The exchange ratio will not be adjusted based on the market price of Syros common stock so the merger consideration at the closing may have a greater or lesser value than at the time the Merger Agreement was signed.

Any changes in the market price of Syros stock before the completion of the merger will not affect the number of shares Tyme stockholders will be entitled to receive pursuant to the Merger Agreement. Therefore, if before the completion of the merger, the market price of Syros common stock increases from the market price on the date of the Merger Agreement, then Tyme stockholders could receive merger consideration with substantially more value for their shares of Tyme common stock than the parties had negotiated when they established the exchange ratio. Similarly, if before the completion of the merger the market price of Syros common stock declines from the market price on the date of the Merger Agreement, then Tyme stockholders could receive merger consideration with substantially lower value. The Merger Agreement does not include a price-based termination right.

Failure to complete the merger may result in either Syros or Tyme paying a termination fee to the other party, which could harm the common stock price of Syros and future business and operations of each company.

If the merger is not completed, Syros and Tyme are subject to the following risks:

- if the Merger Agreement is terminated under specified circumstances, Syros will be required to pay Tyme a termination fee of $2.068 million;
- if the Merger Agreement is terminated under specified circumstances, Tyme will be required to pay Syros a termination fee of $2.443 million;
- the price of Syros common stock and Tyme common stock may decline and could fluctuate significantly; and
- each of Syros and Tyme may be required to pay certain costs related to the merger, such as financial advisor, legal and accounting fees, whether or not the merger is consummated.

If the Merger Agreement is terminated and the board of directors of Syros or Tyme determines to seek another business combination, there can be no assurance that either Syros or Tyme will be able to find a partner with whom a business combination would yield greater benefits than the benefits to be provided under the Merger Agreement.

If the merger or the PIPE Financing is not consummated and Syros is unable to obtain sufficient additional capital from other sources, there may continue to be substantial doubt about Syros' ability to continue as a going concern.

As of and for the year ended December 31, 2021 and as of and for the three-months ended March 31, 2022, Syros' management concluded that there was substantial doubt about Syros' ability to continue as a going concern for a period of at least twelve months from the issuance date of the respective consolidated financial statements. If the merger or the PIPE Financing is not consummated, there may continue to be substantial doubt about Syros' ability to continue as a going concern. There is no assurance that Syros will consummate the merger or the PIPE Financing, and if Syros is unable to continue as a going concern, it may be forced to substantially reduce its planned clinical operations or liquidate its assets and the values it receives for its assets in liquidation or dissolution could be significantly lower than the values reflected in its financial statements.

If the merger is not consummated and Tyme is unable to identify and implement an alternative strategic option, Tyme may choose to close down its trials and cease operations.

On March 29, 2022, Tyme announced that the Tyme board of directors had decided to explore potential strategic options to enhance stockholder value and engaged outside financial and legal advisors to assist with that process, with the goal of ensuring that Tyme was exploring a range of options to maximize value for Tyme stockholders.

Following an extensive process of evaluating strategic alternatives, on July 3, 2022, Tyme entered into the Merger Agreement. Tyme is devoting a substantial amount of its time and resources to consummating the merger, however, there can be no assurance that such activities will result in the consummation of the merger or that the merger will deliver the anticipated benefits or enhance stockholder value. If the merger is not consummated, Tyme may be unable to identify and implement an alternative strategic option, in which case, Tyme may choose to close down its trials and cease operations.

If the conditions to the merger are not satisfied or waived, the merger may not occur.

The closing of the merger is subject to a number of conditions as set forth in the Merger Agreement that must be satisfied or waived, including, among others: (i) the approval of the adoption of the Merger Agreement by the Tyme stockholders, (ii) the approval of the issuance of shares of Syros common stock by the Syros stockholders, (iii) the receipt of certain authorizations, consents, orders or approvals in connection with the merger and the consummation of the other transactions contemplated by the Merger Agreement, (iv) the effectiveness of the registration statement on Form S-4 of which this joint proxy statement/prospectus is a part under the Securities Act, (v) the absence of any order, executive order, stay, decree, judgment or injunction or statute, rule or regulation in effect that has the effect of making the merger illegal or otherwise prohibiting consummation of the merger, (vi) the approval of the listing of the additional shares of Syros common stock on The Nasdaq Stock Market, (vii) Tyme having net cash that exceeds $50.0 million as of the closing date of the merger and (viii) unless waived by Tyme, the completion of the PIPE Financing with gross proceeds of at least $100.0 million. The closing of the merger is also dependent upon the accuracy of representations and warranties made by the parties to the merger agreement (subject to customary materiality qualifiers and other customary exceptions) and the performance in all material respects by the parties of obligations imposed under the merger agreement. For a more complete summary of the conditions that must be satisfied or waived prior to completion of the mergers, see the section entitled "*The Merger Agreement—Conditions to Completion of the Merger*" beginning on page 215 of this joint proxy statement/prospectus.

There can be no assurance as to whether or when the conditions to the closing of the merger will be satisfied or waived or as to whether or when the merger will be consummated. If the conditions are not satisfied or waived, the merger may not occur or the closing may be delayed, and Syros and Tyme each may lose some or all of the intended benefits of the merger.

If the sale of some or all of the PIPE Financing fails to close, Syros may not consummate the merger; if Syros fails to consummate the merger, the PIPE Financing may not close.

In connection with the merger, Tyme's obligation to close the merger is conditioned upon the PIPE Financing being completed substantially concurrently with the merger with gross proceeds to Syros of at least $100 million. The proceeds from the sale of securities of Syros in the PIPE Financing will be made available to the combined company at the closing of the merger for general corporate purposes. Syros has entered into a definitive Securities Purchase Agreement with accredited institutional investors, obligating such investors to purchase securities in the PIPE Financing for an aggregate purchase price of $130 million. However, if the sale of Syros securities in the PIPE Financing does not close by reason of the failure by some or all of the PIPE Financing investors to fund the purchase price for those securities, for example, Syros may not satisfy its obligation under the Merger Agreement to consummate the PIPE Financing with gross proceeds of at least $100 million to Syros substantially concurrently with the merger. In the event of any such failure to fund, if Tyme does not waive Syros' requirement to satisfy such condition, Syros may not be able to obtain additional funds to account for such shortfall with respect to the PIPE Financing or the consummation of the merger on terms favorable to Syros, or at all. Additionally, the obligation of investors to close the PIPE Financing is contingent upon the occurrence of all conditions precedent to the closing set forth in the Merger Agreement, for example, that Tyme's net cash shall exceed $50 million (subject to certain exceptions) at the closing date of the merger. In the event of any such failure to meet conditions precedent, including the failure of Tyme's net cash to exceed $50 million as described above, if the PIPE investors do not waive Syros' requirement to satisfy such condition, Syros may not be able to

obtain additional funds to account for such shortfall resulting from the failure to consummate the merger or close the PIPE Financing on terms favorable to Syros, or at all. Any such shortfall would also reduce the amount of funds that Syros has available for working capital of Syros.

The merger may be completed even though a material adverse effect may result from the announcement of the merger, industry-wide changes or other causes.

In general, neither Syros nor Tyme is obligated to complete the merger if there is a material adverse effect affecting the other party between July 3, 2022, the date of the Merger Agreement, and the closing of the merger. However, certain types of changes are excluded from the concept of a "material adverse effect." Such exclusions include but are not limited to changes in general economic or market conditions, industry wide changes, changes in the generally accepted accounting principles in the United States, or GAAP, changes in laws, rules or regulations of general applicability or interpretations thereof, natural disasters, pandemics (including the COVID-19 pandemic), outbreaks of hostilities or acts of terrorism, changes resulting from the announcement or pendency of the merger, and failures to meet internal guidance, budgets, plans or forecasts. Therefore, if any of these events were to occur impacting Syros or Tyme, the other party would still be obliged to consummate the closing of the merger. If any such adverse changes occur and Syros and Tyme consummate the closing of the merger, the stock price of the combined company may suffer. This in turn may reduce the value of the merger to the stockholders of Syros, Tyme or both. For a more complete discussion of what constitutes a material adverse effect on Syros or Tyme, see the section titled "*The Merger Agreement—Representations and Warranties*" beginning on page 205 of this joint proxy statement/prospectus.

If Syros and Tyme complete the merger, the combined company may need to raise additional capital by issuing equity securities or additional debt, which may cause significant dilution to the combined company's stockholders or restrict the combined company's operations.

On July 3, 2022, Syros entered into securities purchase agreements with certain accredited investors, pursuant to which the investors agreed to purchase (i) an aggregate of approximately 138.1 million shares of Syros common stock and/or pre-funded warrants to purchase shares of Syros common stock and (ii) accompanying warrants to purchase an aggregate of up to approximately 138.1 million additional shares of Syros common stock (or pre-funded warrants in lieu thereof), at a price per unit of $0.94 (or $0.9399 per unit comprising a pre-funded warrant and accompanying warrant), referred to as the PIPE Financing. The expected gross proceeds from the PIPE Financing are approximately $130 million, before deducting estimated offering expenses and not including any proceeds that Syros may receive in connection with the exercise of the warrants. The closing of the PIPE Financing is conditioned upon the satisfaction or waiver of the conditions to the closing of the merger as well as certain other conditions. The PIPE Financing is more fully described under the section titled "*Agreements Related to the Merger—Securities Purchase Agreement and Registration Rights Agreements*" beginning on page 223 of this joint proxy statement/prospectus.

Additional financing may not be available to the combined company when it is needed or may not be available on favorable terms. To the extent that the combined company raises additional capital by issuing equity securities, such financing will cause additional dilution to all securityholders of the combined company, including Syros' pre-merger securityholders and Tyme's former securityholders. It is also possible that the terms of any new equity securities may have preferences over the combined company's common stock. Any issuance of equity securities that causes a change in control, as defined in the Loan Agreement (as defined below), would require the consent of Oxford Finance LLC, which consent may be granted or withheld in its sole discretion. The Loan Agreement restricts the ability of the combined company to incur debt financing and to create liens to secure any such financing. As such, any debt financing and any lien created to secure such debt financing is likely to require the consent of Oxford, which consent may be granted or withheld in its sole discretion. Any debt financing the combined company enters into may involve covenants that restrict its operations. These restrictive covenants may include limitations on additional borrowing and specific restrictions on the use of the combined company's assets, as well as prohibitions on its ability to create liens, pay dividends, redeem its stock or make

investments, which limitations and prohibitions may be more restrictive than the existing covenants in the Loan Agreement applicable to the combined company.

Some Syros and Tyme directors and executive officers have interests in the merger that are different from yours and that may influence them to support or approve the merger without regard to your interests.

Directors and executive officers of Syros and Tyme may have interests in the merger that are different from, or in addition to, the interests of other Syros and Tyme stockholders generally. These interests with respect to Syros directors and executive officers may include, among others, that Syros' directors and executive officers are expected to continue to serve as directors and executive officers, respectively, of the combined company after the effective time of the merger; and that Syros' directors and executive officers are entitled to certain indemnification and liability insurance coverage pursuant to the terms of the Merger Agreement. Additionally, certain directors and executive officers of Syros and their affiliates have agreed to participate in the PIPE Financing. These interests with respect to Tyme directors and executive officers may include, among others, acceleration of stock option vesting; that certain stock options to purchase shares of Tyme common stock will be converted into and become options to purchase shares of Syros common stock; retention bonus payments; extension of exercisability periods of previously issued stock option grants; severance payments if employment is terminated in a qualifying termination in connection with the merger and rights to continued indemnification; expense advancement and insurance coverage. In addition to the current members of the Syros board of directors who are expected to continue to serve on the Syros board of directors, following the closing of the merger, Tyme will have the right to designate one member of the Syros board of directors and investors in the PIPE Financing will have the right to designate up to two members of the Syros board of directors, who will each be eligible to be compensated as a non-employee director of Syros pursuant to the Syros director compensation program.

The Syros and Tyme boards of directors were aware of and considered those interests, among other matters, in reaching their decisions to approve and adopt the Merger Agreement, approve the merger, and recommend the approval of the Merger Agreement and related matters to Syros and Tyme stockholders. These interests, among other factors, may have influenced the directors and executive officers of Syros and Tyme to support or approve the merger.

For more information regarding the interests of Syros and Tyme directors and executive officers in the merger, please see the sections titled "*The Merger —Interests of Syros Directors and Executive Officers in the Merger*" beginning on page 186 of this joint proxy statement/prospectus and "*The Merger— Interests of Tyme Directors and Executive Officers in the Merger*" beginning on page 188 of this joint proxy statement/prospectus.

Syros stockholders may not realize a benefit from the merger and PIPE Financing commensurate with the ownership dilution they will experience in connection with the merger and the PIPE Financing.

If the combined company is unable to realize the full benefits currently anticipated from the merger, Syros stockholders will have experienced substantial dilution of their ownership interests without receiving any commensurate benefit, or only receiving part of the commensurate benefit to the extent the combined company is able to realize only part of the benefits currently anticipated from the merger and the PIPE Financing.

If the merger is not completed, Syros' and Tyme's stock prices may fluctuate significantly.

The market prices of Syros common stock and Tyme common stock are subject to significant fluctuations. During the12-month period ended July 1, 2022, the closing sales price of Syros common stock on The Nasdaq Global Select Market ranged from a high of $5.55 on September 2, 2021 to a low of $0.6940 on May 25, 2022, and the closing sales price of Tyme common stock on The Nasdaq Capital Market ranged from a high of $1.38 on July 26, 2021 to a low of $0.2270 on May 11, 2022. Market prices for securities of pharmaceutical, biotechnology and other life science companies have historically been particularly volatile. Although Syros common stock will remain subject to such significant fluctuations even if the merger is completed, the market

prices of Syros common stock and Tyme common stock will likely be volatile based on whether stockholders and other investors believe that Syros and Tyme can complete the merger or otherwise raise additional capital to support Syros' and Tyme's respective operations if the merger is not consummated and another strategic or financial transaction cannot be identified, negotiated and consummated in a timely manner, if at all.

The volatility of the market price of Syros common stock and Tyme common stock may be exacerbated by low trading volume or other factors. Moreover, the stock markets in general have experienced substantial volatility that has often been unrelated to the operating performance of individual companies. These broad market fluctuations may also adversely affect the trading price of Syros common stock and Tyme common stock. In the past, following periods of volatility in the market price of a company's securities, stockholders have often instituted class action securities litigation against such companies.

Syros and Tyme securityholders will have a reduced ownership and voting interest in, and will exercise less influence over the management of, the combined company following the completion of the merger as compared to their current ownership and voting interests in the respective companies.

After the completion of the merger, the current stockholders of Syros and Tyme will own a smaller percentage of the combined company than their ownership of their respective companies prior to the merger. Based upon the initially estimated exchange ratio, following the merger and giving effect to the PIPE Financing, (i) Syros securityholders immediately before the merger together with the investors in the PIPE Financing are expected to own approximately 63% of the aggregate number of outstanding shares of Syros common stock following the merger and (ii) Tyme securityholders immediately before the merger are expected to own approximately 37% of the aggregate number of outstanding shares of Syros common stock following the merger, subject to certain assumptions (including as to the amount of Tyme net cash at closing, which could be materially different). Assuming the exercise of all Syros pre-funded warrants, including the Pre-Funded PIPE Warrants and the Pre-Funded 2020 Warrants, without giving effect to any beneficial ownership limitations applicable thereto, then (i) Syros securityholders immediately before the merger together with the investors in the PIPE Financing would own approximately 73% of the aggregate number of outstanding shares of Syros common stock following the merger and (ii) Tyme securityholders immediately before the merger would own approximately 27% of the aggregate number of outstanding shares of Syros common stock following the merger, subject to certain assumptions (including as to the amount of Tyme net cash at closing, which could be materially different). The foregoing percentages do not give effect to the exercise or conversion of outstanding stock options or warrants other than as set forth above. The executive officers of Syros are expected to continue to serve as the executive officers of the combined company following the completion of the merger.

During the pendency of the merger, Syros and Tyme may not be able to enter into a business combination with another party on more favorable terms because of restrictions in the Merger Agreement, which could adversely affect their respective business prospects.

Covenants in the Merger Agreement impede the ability of Syros and Tyme to make acquisitions during the pendency of the merger, subject to specified exceptions. As a result, if the merger is not completed, the parties may be at a disadvantage to their competitors during that period. In addition, while the Merger Agreement is in effect, each party is generally prohibited from soliciting, proposing, seeking or knowingly encouraging, facilitating or supporting any inquiries, indications of interest, proposals or offers that constitute or may reasonably be expected to lead to certain transactions involving a third party, including a merger, sale of assets or other business combination, subject to specified exceptions. Any such transactions could be favorable to such party's stockholders, but the parties may be unable to pursue them. For more information, see the section titled "*The Merger Agreement—Non-Solicitation*" beginning on page 210 of this joint proxy statement/prospectus.

Certain provisions of the Merger Agreement may discourage third parties from submitting competing proposals, including proposals that may be superior to the transactions contemplated by the Merger Agreement.

The terms of the Merger Agreement prohibit each of Syros and Tyme from soliciting competing proposals or cooperating with persons making unsolicited takeover proposals, except in limited circumstances as described in further detail in the section titled "*The Merger Agreement—Non-Solicitation*" beginning on page 210 of this joint proxy statement/prospectus. In addition, if the Merger Agreement is terminated under specified circumstances, Syros would be required to pay Tyme a termination fee of $2.068 million or Tyme would be required to pay Syros a termination fee of $2.443 million. These termination fees may discourage third parties from submitting competing proposals to Syros or Tyme or their respective stockholders, and may cause the Syros board of directors or the Tyme board of directors to be less inclined to recommend a competing proposal.

The financial analyses, estimates and forecasts presented herein and considered by Syros and Tyme in connection with the merger may not be realized.

The unaudited prospective financial information of Syros and Tyme presented herein and considered by Syros and Tyme in connection with the merger were not prepared with a view toward public disclosure, and such information and the estimated synergies were not prepared with a view toward compliance with published guidelines of the SEC or the guidelines established by the American Institute of Certified Public Accountants for preparation and presentation of prospective financial information. The estimates and assumptions underlying the unaudited prospective financial information and estimated synergies involve judgments with respect to, among other things, future economic, competitive, regulatory and financial market conditions, future tax rates and future business decisions which may not be realized and that are inherently subject to significant business, economic, competitive and regulatory uncertainties and contingencies, including, among others, risks and uncertainties described under the sections entitled "*Risk Factors*" and "*Cautionary Statement Concerning Forward-Looking Statements*," all of which are difficult to predict and many of which are beyond the control of Syros and/or Tyme. In addition, the unaudited prospective financial information and estimated synergies will be affected by Syros' or Tyme's, as applicable, ability to achieve strategic goals, objectives and targets over the applicable periods. As a result, there can be no assurance that the underlying assumptions will prove to be accurate or that the projected results or synergies will be realized, and actual results or synergies likely will differ, and may differ materially, from those reflected in the unaudited prospective financial information and the estimated synergies, whether or not the merger is completed, which could have an adverse effect on Syros' business, financial condition and result of operations.

The merger may not qualify as either a tax-free contribution pursuant to Section 351 of the Code, taken together with the PIPE Financing, or a "reorganization" within the meaning of Section 368(a) of the Code.

It is intended that the merger will qualify as either a tax-free contribution pursuant to Section 351 of the Code, taken together with the PIPE Financing, or a "reorganization" within the meaning of Section 368(a) of the Code. No ruling has been or will be requested from the IRS with respect to the tax consequences of the merger, and no opinion of counsel has been obtained or will be obtained regarding the treatment of the merger as a tax-free contribution or a tax-free reorganization. Furthermore, it is possible that, under certain circumstances, the merger will not satisfy the requirements to qualify as either a tax-free contribution pursuant to Section 351 of the Code or a "reorganization" within the meaning of Section 368(a) of the Code.

If the merger qualifies as neither a tax-free contribution pursuant to Section 351 of the Code nor a "reorganization" within the meaning of Section 368(a) of the Code, a U.S. Holder (as defined in the section entitled "*The Merger—Material U.S. Federal Income Tax Consequences of the Merger*" beginning on page 198 of this joint proxy statement/prospectus) of Tyme common stock generally would recognize gain or loss for U.S. federal income tax purposes with respect to the Tyme common stock surrendered in the merger in an amount equal to the difference between the fair market value, at the time of the merger, of the Syros common stock

received in the merger (plus any cash received in lieu of a fractional share) and such U.S. Holder's aggregate adjusted tax basis in the Tyme common stock surrendered therefor in the merger.

Please review the information in the section entitled "*The Merger—Material U.S. Federal Income Tax Consequences of the Merger*" beginning on page 198 of this joint proxy statement/prospectus for a more complete description of the material U.S. federal income tax consequences of the merger to U.S. Holders of Tyme common stock. The tax consequences to each such holder of the merger will depend on the holder's particular facts and circumstances. You should consult your tax advisors as to the specific tax consequences to you of the merger.

Risks Related to Syros

Risks Related to the COVID-19 Pandemic

Public health epidemics or outbreaks, including COVID-19, have had, and will continue to have, an adverse impact on Syros' business.

Public health crises such as pandemics, epidemics and outbreaks could adversely impact Syros' business. The novel strain of a virus named SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2), or coronavirus, which causes coronavirus disease 2019, or COVID-19, has caused an ongoing global pandemic that continues to evolve, and to date has led to the implementation of various responses, including government-imposed quarantines, travel restrictions and other public health safety measures, as well as reported adverse impacts on healthcare resources, facilities and providers around the world. COVID-19 has and may continue to impact Syros' operations and those of its third-party partners, and its ultimate impact will depend on future developments which are highly uncertain and cannot be predicted with confidence, including the scope, severity, duration and any recurrence of the COVID-19 pandemic, including through any new variant strains of the underlying virus, the actions taken to contain the pandemic or mitigate its impact, the direct and indirect economic effects of the pandemic and containment measures, the effectiveness of vaccination and booster vaccination campaigns, among others. The continued development and fluidity of the COVID-19 pandemic precludes any prediction as to its full impact on Syros' business.

Further, in response to the COVID-19 pandemic and in accordance with direction from state and local governmental authorities, Syros took, and have continued to take, both temporary and ongoing precautionary measures, intended to help minimize the risk of the virus to its employees and their families, such as restricting access to its facility to those individuals whose job responsibilities require or are significantly enhanced by on site presence during periods of significant transmission, limiting the number of people that can be present at its facility at any one time, restricting access to its facilities to those employees who are fully vaccinated, and implementing a number of additional health and safety protocols. Working arrangements for many of Syros' employees differ from the arrangements before the COVID-19 pandemic, and Syros expects a number of employees will continue to work in a remote capacity or a hybrid of in-person and remote work. Syros may face several challenges or disruptions during its return to the workplace transition, including re-integration challenges for its employees, and its hybrid of in-person and remote work option may negatively impact productivity, or disrupt, delay, or otherwise adversely impact its business.

Compliance with governmental measures imposed in response to COVID-19 has caused and will continue to cause Syros to incur additional costs. Any inability to comply with such measures could subject Syros to restrictions on its business activities, fines, and other penalties, any of which could adversely affect its business. If new restrictions were to prevent Syros' research and development personnel from accessing its laboratory space, its core research activities may be significantly limited or curtailed, possibly for an extended period of time. Sustained restrictions on Syros' ability to conduct research would have an adverse impact on its ability to perform under its collaboration agreements with GBT and Incyte, as well as delay the time in which Syros would be able to nominate new drug candidates for clinical development.

Syros believes that it has sufficient supply of clinical trial material to conduct its ongoing clinical trial activities, and Syros is implementing contingency plans to ensure that this continues to be the case. Syros is monitoring the

potential impact of surges of COVID-19 cases in jurisdictions where its contract manufacturing organization partners and clinical sites are located. Syros cannot provide assurance that the COVID-19 pandemic will not delay or otherwise adversely affect its clinical development, research, manufacturing and business operations activities, as well as its business generally, in the future, which could have a material adverse impact on its operations and financial condition and results. These factors include:

- the impact on Syros' clinical trial operations, including studystart-up activities, of any diversion of healthcare resources away from the conduct of its ongoing or planned clinical trials in order to focus on pandemic concerns, including the availability of necessary materials, the attention of physicians serving as its clinical trial investigators, access to hospitals serving as its clinical trial sites, and staffing shortages or other factors limiting the availability of hospital staff supporting the conduct of its clinical trials;
- the impact on Syros' clinical trials or its other development and regulatory objectives if Syros is unable to initiate sites or screen and enroll patients on the timelines that it originally anticipated, if Syros is unable to continue remote monitoring of clinical trial data or utilizing telehealth systems, local laboratory assessments and in-home nursing visits for enrolled patients, or if any patient enrolled in one of its clinical trials is unable to remain on study due to a positive COVID-19 diagnosis;
- potential interruptions in global shipping affecting the transport of clinical trial materials, such as investigational drug product, patient samples, and other supplies used in Syros' clinical trials;
- the impact of limitations on travel or working conditions that could interrupt key clinical trial activities, such as clinical trial site initiations and monitoring activities, travel by Syros' employees, contractors or patients to clinical trial sites, or the ability of employees at any of its contract manufacturers or contract research organizations, or CROs, to report to work, any of which could delay or adversely impact the conduct or progress of its clinical trials and other research and manufacturing activities;
- any future interruption of, or delays in receiving, supplies of clinical trial material from Syros' contract manufacturing organizations due to staffing shortages, production slowdowns or stoppages, raw material or other supply shortages, or stoppages or disruptions in delivery systems;
- availability of future capacity at Syros' contract manufacturers to produce sufficient drug substance and drug product to meet forecasted clinical trial demand if any of these manufacturers suffer staffing shortages or elect or are required to divert attention or resources to the manufacture of other pharmaceutical products;
- delays in ongoing laboratory experiments and operations if Syros is required to reduce the number of employees in its laboratories, or if the CROs Syros has retained to supplement its internal research efforts are unable to perform as anticipated, whether due to capacity constraints, staffing shortages, or otherwise; and
- business disruptions caused by potential workplace closures and an increased reliance on employees working from home, challenges in recruiting employees required to execute on Syros' research and development plans, cybersecurity and data accessibility issues, which may be adversely impacted by a remote work environment, and communication or transit disruptions, any of which could adversely impact its business operations and delay necessary interactions among its employees and between its company and the third parties upon which Syros relies.

These and other factors arising from theCOVID-19 pandemic could worsen in countries with higher infection rates and case counts or could return to countries where the pandemic has been partially contained, each of which could further adversely impact Syros' ability to conduct clinical trials and its business generally and could have a material adverse impact on its operations and financial condition and results. In addition, a recession, depression or other sustained adverse market event resulting from the COVID-19 pandemic could materially and adversely affect its business and the value of Syros common stock.

Risks Related to Syros' Financial Position and Need for Additional Capital

Syros has incurred significant losses since inception, expects to incur significant and increasing losses for at least the next several years, and may never achieve or maintain profitability.

Syros has incurred significant annual net operating losses in every year since its inception. Syros expects to continue to incur significant and increasing net operating losses for at least the next several years. Syros' net losses were $86.6 million, $84.0 million, and $75.4 million for the years ended December 31, 2021, 2020 and 2019, respectively. As of December 31, 2021, Syros had an accumulated deficit of $463.6 million. Syros has not generated any revenues from product sales, has not completed the development of any product candidate and may never have a product candidate approved for commercialization. Syros has financed its operations to date primarily through the sale of equity securities. Syros has devoted substantially all of its financial resources and efforts to research and development and general and administrative expense to support such research and development. Syros' net losses may fluctuate significantly from quarter to quarter and year to year. Net losses and negative cash flows have had, and will continue to have, an adverse effect on Syros' stockholders' equity and working capital.

Syros anticipates that its future funding requirements, both short-term and long-term, will depend on many factors and will increase substantially if and as it:

- continues its planned clinical development activities with respect to tamibarotene,SY-2101 and SY-5609;
- develops and seeks approval of companion diagnostic tests for use in identifying patients who may benefit from treatment with its products and product candidates;
- initiates and continues research, preclinical and clinical development efforts for its research and preclinical programs;
- further develops its gene control platform;
- seeks to identify and develop additional product candidates, which may involve entering into collaborations, licensing agreements or other arrangements;
- acquires or in-licenses other product candidates or technologies;
- seeks regulatory and marketing approvals for Syros' product candidates that successfully complete clinical trials, if any;
- establishes sales, marketing, distribution and other commercial infrastructure in the future to commercialize various products for which Syros may obtain marketing approval, if any;
- becomes obligated to make milestone payments upon the successful completion of specified development and commercialization activities;
- requires the manufacture of larger quantities of product candidates for clinical development and, potentially, commercialization;
- maintains, expands and protects its IP portfolio;
- hires and retains additional personnel and add operational, financial and management information systems, including personnel and systems to support its product development and commercialization efforts; and
- adds equipment and physical infrastructure to support its research and development programs.

Syros' ability to become and remain profitable depends on its ability to generate revenue. Syros does not expect to generate significant revenue unless and until Syros is, or any collaborator is, able to obtain marketing approval for, and successfully commercialize, one or more of Syros' product candidates. Successful commercialization

will require achievement of key milestones, including initiating and successfully completing clinical trials of its product candidates, obtaining marketing approval for these product candidates, manufacturing, marketing and selling products for which marketing approval has been obtained, satisfying any post-marketing requirements and obtaining reimbursement for Syros' products from private insurance or government payors. Because of the uncertainties and risks associated with these activities, Syros is unable to accurately predict the timing and amount of revenues, and if or when it might achieve profitability. Syros may never succeed in these activities and, even if it does, or any collaborators do, Syros may never generate revenues that are large enough for it to achieve profitability. If Syros does achieve profitability, it may not be able to sustain or increase profitability on a quarterly or annual basis. Syros' failure to become and remain profitable would decrease the value of its company and could impair its ability to raise capital, expand its business, maintain its research and development efforts, diversify its pipeline of product candidates or continue its operations and cause a decline in the value of its common stock.

Syros will need substantial additional funding to execute its operating plan and continue to operate as a going concern, and if Syros is unable to raise capital, Syros could be forced to delay, reduce or eliminate its product development programs or commercialization efforts.

Developing pharmaceutical products, including conducting preclinical studies and clinical trials, is a time consuming, expensive and uncertain process. Accordingly, Syros will need to obtain substantial additional funding in connection with its continuing operations. If Syros is unable to raise capital when needed or on attractive terms, Syros may be forced to delay, reduce or eliminate its research and development programs or any future commercialization efforts.

Syros believes that its cash, cash equivalents and marketable securities as of March 31, 2022 will enable it to fund its planned operating expense and capital expenditure requirements into the second quarter of 2023. These funds may not be sufficient to fund operations for at least the next twelve months from the date of issuance of Syros' condensed consolidated financial statements, which raises substantial doubt about Syros' ability to continue as a going concern. Syros' future viability beyond one year from the date of issuance of its condensed consolidated financial statements is dependent on its ability to raise additional capital to finance its operations. Syros' estimate as to how long Syros expect its existing cash, cash equivalents, and marketable securities to be able to continue to fund its operations is based on assumptions that may prove to be wrong, and Syros could use its available capital resources sooner than Syros currently expects. Further, changing circumstances, some of which may be beyond Syros' control, could cause Syros to consume capital significantly faster than it currently anticipates, and Syros may need to seek additional funds sooner than planned. In any event, Syros' existing cash, cash equivalents and marketable securities will not be sufficient to fund all of the efforts that Syros plans to undertake or to fund the completion of development of its product candidates or its other preclinical programs.

Following the closing of the merger, the PIPE Financing and the Loan Amendment (as defined below), the total cash balance of the combined company is expected to be approximately $240.0 million (after transaction expenses), which Syros believes will be sufficient to fund its planned operating expenses and capital expenditure requirements into 2025, allowing it to advance its late-stage clinical programs toward commercialization, including tamibarotene, currently being studied in the SELECT-MDS-1 trial and the randomized portion of the SELECT-AML-1 trial, and SY-2101, which it plans to advance into a Phase 3 trial for the treatment of APL in the second half of 2023.

Syros' future funding requirements will depend on many factors, including those discussed in the Risk Factors,*"Risks Related to Syros"* in this joint proxy statement/prospectus under "*Risks Related to Syros' Financial Position and Need for Additional Capital—Syros has incurred significant losses since inception, expects to incur significant and increasing losses for at least the next several years, and may never achieve or maintain profitability.*" Syros' future funding requirements may also depend on:

- whether a drug candidate will be nominated to enter into investigational new drug application-enabling studies under Syros' sickle cell disease collaboration with GBT, whether GBT will exercise its option

to exclusively license IP arising from the collaboration, whether and when any option exercise fees, milestone payments or royalties under the collaboration agreement with GBT will ever be paid, and whether Syros exercises its U.S. co-promotion option under the GBT agreement;

- whether Syros' target discovery collaboration with Incyte will yield any validated targets, whether Incyte will exercise any of its options to exclusively license IP directed to such targets, and whether and when any of the target validation fees, option exercise fees, milestone payments or royalties under the collaboration agreement with Incyte will ever be paid;
- the cost of precommercial activities related to our product candidates, including the costs of any physician education programs relating to selecting and treating genomically defined patient populations;
- the timing and amount of milestone and other payments due to licensors for patent and technology rights used in Syros' gene control platform or to TMRC Co. Ltd., or TMRC, associated with the development, manufacture and commercialization of tamibarotene;
- the timing and amount of milestone payments due to Orsenix, LLC, or Orsenix, associated with the development and commercialization of SY-2101; and
- the timing and amount of milestone payments due to QIAGEN Manchester Limited , or Qiagen, associated with the development and commercialization of a companion diagnostic test for use with tamibarotene.

Raising additional capital may cause dilution to Syros' stockholders, restrict its operations or require it to relinquish rights to its technologies or product candidates.

Syros expects its expenses to remain high in connection with its planned operations. To the extent that Syros raises additional capital through the sale of common stock, convertible securities or other equity securities, as Syros did through a public offering of its common stock in January 2021, the ownership interests of its existing stockholders may be substantially diluted, and the terms of these securities could include liquidation or other preferences and anti-dilution protections that could adversely affect its stockholders' rights. In addition, debt financing, such as Syros' term loan facility with Oxford that Syros entered into in February 2020 and amended in July 2022, has created fixed payment obligations and imposed restrictive covenants that limit its ability to take specific actions, such as incurring additional debt, making capital expenditures, creating liens, redeeming stock or declaring dividends, that could adversely impact its ability to conduct its business. In addition, securing financing could require a substantial amount of time and attention from Syros' management and may divert a disproportionate amount of their attention away from day-to-day activities, which may adversely affect its management's ability to oversee the development of its product candidates.

If Syros raises additional funds through collaborations or marketing, distribution or licensing arrangements with third parties, such as its collaboration agreement with GBT, Syros may have to relinquish valuable rights to its technologies, future revenue streams or product candidates or grant licenses on terms that may not be favorable to it. If Syros is unable to raise additional funds when needed, Syros may be required to delay, limit, reduce or terminate its product development or future commercialization efforts or grant rights to develop and market product candidates that Syros would otherwise prefer to develop and market itself. In this regard, Syros recently announced that it plans to determine the best course for further development of SY-5609 after assessing the safety and clinical activity data from the safety lead-in portion of the trial evaluating SY-5609 in combination with chemotherapy in relapsed/refractory metastatic pancreatic cancer patients that it expects to report in the second half of 2022. Further, Syros has announced that it is seeking partnerships for its oncology discovery programs, including its CDK12 program. In addition, Syros previously announced that it did not plan to pursue Phase 3 development of SY-2101 unless and until it secures additional capital. Syros believes that the total cash balance of the combined company following the closing of the merger, PIPE Financing and Loan Amendment will be sufficient to fund Syros' planned operating expenses and capital expenditure requirements into 2025, including the advancement of its late stage clinical assets, and has recently announced that, subject to the closing

of the merger, PIPE Financing and Loan Amendment, Syros now expects to initiate a Phase 3 clinical trial of SY-2101 in the second half of 2023. However, Syros cannot provide assurance that these transactions will be consummated, or that sufficient additional capital to support the further development of SY-5609 or its oncology discovery programs can be obtained, or will be obtained on favorable terms.

The terms of Syros' Loan and Security Agreement place restrictions on its operating and financial flexibility.

In February 2020, Syros entered into a Loan and Security Agreement with Oxford, which is secured by substantially all of its currently owned or later acquired personal property other than its IP (but including the right to payments and proceeds of IP), which is subject to a negative pledge. Syros refers to the Loan and Security Agreement with Oxford as the Loan Agreement. Syros borrowed $20.0 million upon execution of the Loan Agreement and borrowed an additional $20.0 million term loan advance in December 2020. One additional term loan advance of $20.0 million remains available under the Loan Agreement, subject to certain terms and conditions, including the achievement of certain milestones.

On July 3, 2022, Syros entered into an amendment to the Loan Agreement, or the Loan Amendment, pursuant to which Oxford, its capacity as lender and agent, has agreed to modify the Loan Agreement in order to, among other things, (i) consent to the entry into the Merger Agreement, and subject to certain conditions, the consummation of the merger, (ii) upon the consummation of the Merger and the PIPE Financing and the receipt of proceeds therefrom, and subject to the payment of certain fees, extend the interest only period from March 1, 2023 to March 1, 2024 and extend the maturity date from February 1, 2025 to February 1, 2026, and (iii) upon the achievement of certain milestones and subject to the payment of certain fees, further extend the interest only period to September 1, 2024 and maturity date to August 1, 2026.

The Loan Agreement, as amended by the Loan Amendment, contains representations and warranties, affirmative and negative covenants applicable to Syros and its subsidiaries and events of default, as more fully described in the Loan Agreement and Loan Amendment. In particular, the Loan Agreement also includes events of default, the occurrence and during the continuation of which provide Oxford, as collateral agent, with the right to exercise remedies against it and the collateral securing the loans under the Loan Agreement, including foreclosure against Syros' property securing the Loan Agreement, including its cash, potentially requiring it to renegotiate its agreement on terms less favorable to it, or to immediately cease operations.

Further, if Syros is liquidated, the lenders' right to repayment would be senior to the rights of the holders of its common stock to receive any proceeds from the liquidation. Oxford could declare a default upon the occurrence of any event that they interpret as a material adverse change as defined under the Loan Agreement, thereby requiring Syros to repay the loan immediately or to attempt to reverse the declaration of default through negotiation or litigation. Any declaration by Oxford of an event of default could significantly harm Syros' business and prospects and could cause the price of its common stock to decline.

Risks Related to the Discovery, Development and Commercialization of Product Candidates

Syros' approach to the discovery and development of product candidates based on its gene control platform is novel and unproven, and Syros does not know whether it will be able to develop any products of commercial value.

Syros is focused on discovering and developing medicines for the treatment of cancer and other diseases based upon its gene control platform. Syros is leveraging its platform to create a pipeline of gene control product candidates for genomically defined patients whose diseases have not been adequately addressed to date by other genomics approaches and to design and conduct efficient clinical trials with a higher likelihood of success. While Syros believes that applying its gene control platform to create medicines for genomically defined patient populations may potentially enable drug research and clinical development that is more efficient than conventional small molecule drug research and development, Syros' approach is both novel and unproven. The

cost and time needed to develop Syros' product candidates is therefore difficult to predict, and its efforts may not result in the discovery and development of commercially viable medicines. Syros may also be incorrect about the effects of its product candidates on the diseases of genomically defined patient populations, which may limit the utility of its approach or the perception of the utility of its approach. For example, Syros has not yet succeeded and may never succeed in demonstrating efficacy and safety for its current or any future product candidates in a pivotal clinical trial or in obtaining marketing approval thereafter. Furthermore, Syros' estimates of genomically defined patient populations available for study and treatment may be lower than expected, which could adversely affect its ability to conduct clinical trials and may also adversely affect the size of any market for medicines Syros may successfully commercialize.

Syros' gene control platform may fail to help it discover and develop additional potential product candidates.

A significant portion of the research that Syros is conducting involves identifying novel targets and points of intervention and developing new compounds using its gene control platform. The drug discovery that Syros is conducting using its gene control platform may not be successful in identifying compounds that have commercial value or therapeutic utility. Syros' gene control platform may initially show promise in identifying potential product candidates, yet still fail to yield viable product candidates for clinical development or commercialization. For example, insights that are obtained through the use of Syros' gene control platform may be generated independently through alternative approaches or be published by third parties, or competitors may develop alternative therapies that render its potential product candidates non-competitive or less attractive. Further, compounds created through Syros' gene control platform may not demonstrate efficacy, safety or tolerability, or potential product candidates may be shown to have harmful side effects or other characteristics that indicate that they are unlikely to receive marketing approval and achieve market acceptance.

Syros' research programs to identify new product candidates will require substantial technical, financial and human resources, and Syros may be unsuccessful in its efforts to identify new product candidates. If Syros is unable to identify suitable additional compounds for preclinical and clinical development, Syros' ability to develop product candidates and obtain product revenues in future periods could be compromised, which could result in significant harm to its financial position and adversely impact Syros' stock price.

In the near term, Syros is dependent on the success of tamibarotene, SY-2101 and SY-5609. If Syros is unable to initiate or complete the clinical development of, obtain marketing approval for or successfully commercialize tamibarotene, SY-2101 or SY-5609, either alone or with a collaborator, or if Syros experiences significant delays in doing so, its business could be substantially harmed.

Syros currently has no products approved for sale and are investing a significant portion of its efforts and financial resources in the development of tamibarotene, SY-2101 and SY-5609. Syros' ability to generate product revenue will depend heavily on the successful clinical development and eventual commercialization of its current and any future product candidates, such as tamibarotene, SY-2101 and SY-5609.

Syros, and any collaborators, are not permitted to commercialize, market, promote or sell any product candidate in the United States without obtaining marketing approval from the U.S. Food and Drug Administration, or the FDA. Foreign regulatory authorities, such as the European Medicines Agency, or the EMA, impose similar requirements in foreign jurisdictions. Before obtaining marketing approval from regulatory authorities for the sale of Syros' product candidates, Syros must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of its product candidates in humans.

Clinical trials of a new product candidate require the enrollment of a sufficient number of patients, including patients who are suffering from the disease the product candidate is intended to treat and who meet other eligibility criteria. Syros' anticipated time to data in its clinical trials and the quantity of data to be presented from these trials is and will continue to be subject to its continued ability to recruit eligible patients and the satisfaction by patients of other eligibility criteria for participation in the trial. In the case of tamibarotene, Syros'

time to data is also dependent on the prevalence of patients with the RARA, the gene that codes for RARα, biomarker and the impact of new product approvals in the AML and myelodysplastic syndrome, or MDS, fields. The rate of patient enrollment in the trial is difficult to predict. As a result, there can be no assurance that Syros will enroll or have data from its clinical trials when Syros anticipates.

Clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to outcome. Syros cannot guarantee that any clinical trials will be conducted as planned or completed on schedule, if at all. The clinical development of Syros' product candidates is susceptible to the risk of failure inherent at any stage of product development. Moreover, Syros, or any collaborators, may experience any of a number of possible unforeseen adverse events in connection with clinical trials, many of which are beyond Syros' control, including:

- Syros, or its collaborators, may fail to demonstrate efficacy in a clinical trial or across a broad population of patients;
- it is possible that, even if one or more of Syros' product candidates has a beneficial effect, that effect will not be detected during clinical evaluation as a result of one or more of a variety of factors, including the size, duration, design, measurements, conduct or analysis of its clinical trials. Conversely, as a result of the same factors, Syros' clinical trials may indicate an apparent positive effect of a product candidate that is greater than the actual positive effect, if any. For example, many compounds that initially showed promise in earlier stage testing have later been found to cause side effects that prevented further development of the compound;
- Syros' product candidates may have undesirable side effects or other unexpected characteristics or otherwise expose participants to unacceptable health risks, causing Syros, its collaborators or its investigators, regulators or institutional review boards, or IRBs, or the data safety monitoring board, or DSMB, for such trial to halt, delay, interrupt, suspend or terminate the trials or cause Syros, or any collaborators, to abandon development or limit development of that product candidate to certain uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective;
- if Syros' product candidates have undesirable side effects, it could result in a more restrictive label, or it could result in the delay or denial of marketing approval by the FDA or comparable foreign regulatory authorities;
- clinical trials of Syros' product candidates may produce negative or inconclusive results, and Syros, or its collaborators, may decide, or regulators may require Syros, to conduct additional clinical trials, including testing in more subjects, or abandon product development programs;
- regulators or IRBs may not authorize Syros, its collaborators or its investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- Syros or its collaborators may have delays in reaching or fail to reach agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites;
- the number of patients required for clinical trials of Syros' product candidates may be larger than Syros anticipates; enrollment in these clinical trials, which may be particularly challenging for some of the diseases Syros targets, may be slower than it anticipates; or participants may drop out of these clinical trials at a higher rate than Syros anticipates;
- third-party contractors used by Syros or its collaborators may fail to comply with regulatory requirements or meet their contractual obligations in a timely manner, or at all;
- significant preclinical study or clinical trial delays could shorten any periods during which Syros, or any collaborators, may have the exclusive right to commercialize Syros' product candidates or allow its competitors, or the competitors of any collaborators, to bring products to market before Syros, or any collaborators, do;

- the cost of clinical trials of Syros' product candidates may be greater than anticipated; and
- the supply or quality of Syros' product candidates or other materials necessary to conduct clinical trials of its product candidates may be insufficient or inadequate.

In addition, Syros is conducting its SELECT-MDS-1 clinical trial in foreign countries and may conduct other clinical trials outside the United States in the future. Syros does not have employees or significant operational capabilities located outside of the United States, and it relies on third parties, such as cCROs, to conduct its clinical trials in foreign countries. Conducting clinical trials in foreign countries presents additional risks that may delay completion of Syros' clinical trials. These risks include the failure of enrolled patients in foreign countries to adhere to clinical protocols as a result of differences in healthcare services or cultural customs, managing additional administrative burdens associated with foreign regulatory schemes, as well as political and economic risks relevant to such foreign countries.

Syros' failure to successfully begin and complete clinical trials of its product candidates, including tamibarotene,SY-2101 and SY-5609, and to demonstrate the efficacy and safety necessary to obtain regulatory approval to market any of its product candidates could result in additional costs to Syros, or any collaborators, would impair Syros' ability to generate revenue from product sales, regulatory and commercialization milestones and royalties and would significantly harm its business.

Adverse events or undesirable side effects caused by, or other unexpected properties of, product candidates that Syros develops may be identified during development and could delay or prevent their marketing approval or limit their use.

Because gene control techniques are relatively new, side effects from gene control approaches may be unpredictable. Tamibarotene has been observed to be associated with adverse events, such as mild or moderate dry skin, skin rash, headache and bone pain, as well as retinoic acid syndrome and elevated levels of cholesterol, lipids, liver function enzymes and white blood cells, which were severe in certain cases. Furthermore, retinoids such as tamibarotene may cause birth defects and therefore may carry a warning on their label. Other examples of retinoids, a class of chemical compounds that are related to vitamin A, include all trans retinoic acid (also known as ATRA), Retin-A, retinol (found in over-the-counter skin creams), isotretinoin and bexarotene. Additionally, SY-5609 has been observed to be associated with adverse events such as nausea, diarrhea, thrombocytopenia, fatigue and anemia. Furthermore, Syros has extremely limited experience administering SY-2101 to humans, so the safety profile it will demonstrate in human clinical trials remains uncertain.

Syros cannot predict at this time whether the combination of its product candidates with another product, or with any premedication administered to mitigate potential side effects, will be well tolerated by patients in clinical studies or that any unexpected adverse events or undesirable side effects will not occur. If any of its product candidates is associated with adverse events or undesirable side effects or has properties that are unexpected, Syros, or any collaborators, may need to abandon development or limit development of that product candidate to certain uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective.

Failure to successfully validate, develop and obtain regulatory approval for companion diagnostics could harm Syros' drug development strategy.

As one of the key elements of Syros' development strategy, Syros seeks to identify genomically defined subsets of patients within a disease category who may derive benefit from the product candidates Syros is developing. In collaboration with partners, Syros plans to develop companion diagnostics to help it to more accurately identify patients within a particular subset, both during Syros' clinical trials and in connection with the commercialization of its product candidates that Syros is developing or may in the future develop. Companion diagnostics are subject to regulation by the FDA and comparable foreign regulatory authorities as medical devices and require separate regulatory approval prior to commercialization. Syros does not develop companion diagnostics

internally and thus Syros will be dependent on the sustained cooperation and effort of one or more third-party collaborators in developing, obtaining approval for, and commercializing these companion diagnostics. Syros and its collaborators may encounter difficulties in developing and obtaining approval for the companion diagnostics, including issues relating to selectivity/specificity, analytical validation, reproducibility, or clinical validation. For example, if Syros is to succeed in obtaining regulatory approval for a companion diagnostic to identify genomically defined subsets of patients with AML or MDS using Syros' RARA biomarker, Syros will need to demonstrate to regulatory authorities that RARA biomarker selection is associated with a response to tamibarotene. In March 2022, Syros entered into a Master Collaboration Agreement and associated project work plan with Qiagen pursuant to which Qiagen will develop and commercialize a companion diagnostic for this biomarker. Any delay or failure by Syros, Qiagen, or any future collaborators to develop or obtain regulatory approval of the companion diagnostics could delay or prevent approval of Syros' product candidates. In addition, Qiagen or any future collaborators may encounter production difficulties that could constrain the supply of the companion diagnostics, and both they and Syros may have difficulties gaining acceptance of the use of the companion diagnostics in the clinical community. If such companion diagnostics fail to gain market acceptance, it would have an adverse effect on Syros' ability to derive revenues from sales, if any, of its products. In addition, Qiagen or any other companion diagnostic collaborator with whom Syros contracts may decide not to commercialize or to discontinue selling or manufacturing the companion diagnostic that Syros anticipates using in connection with development and commercialization of its product candidates, or its relationship with such collaborator may otherwise terminate. Syros may not be able to enter into arrangements with another provider to obtain supplies of an alternative diagnostic test for use in connection with the development and commercialization of its product candidates or do so on commercially reasonable terms, which could adversely affect and/or delay the development or commercialization of its product candidates.

If Syros, or any collaborators, experience delays or difficulties in the enrollment of patients in clinical trials, Syros' or their receipt of necessary regulatory approvals could be delayed or prevented.

Syros, or any collaborators, may not be able to initiate or continue clinical trials for its current product candidates or any future product candidates that it, or any collaborators, may develop if Syros, or they, are unable to locate and enroll a sufficient number of eligible patients to participate in clinical trials. Patient enrollment is a significant factor in the timing of clinical trials, and is affected by many factors, including the size and nature of the patient population, the severity of the disease under investigation, and the availability of approved or investigational therapeutics for the relevant disease, the proximity of patients to clinical sites, the eligibility criteria for and design of the trial, efforts to facilitate timely enrollment, competing clinical trials, clinicians' and patients' perceptions as to the potential advantages and risks of the drug being studied in relation to other available therapies, and actual or threatened public health emergencies and outbreaks of disease (including, for example, the COVID-19 pandemic). In addition, patients that enroll may subsequently be dropped from the clinical trial due to having misrepresented their eligibility to participate or due to non-compliance with clinical trial protocol, resulting in the need to increase the enrollment size for the clinical trial or extend the clinical trial's duration.

In particular, Syros intends to enrich certain of its clinical trials with patients most likely to respond to its gene control therapies. Genomically defined diseases may, however, have relatively low prevalence and it may be difficult for Syros or third parties with whom it collaborates to identify patients for its trials, which may lead to delays in enrollment for its trials. Syros intends to develop, or engage third parties such as Qiagen to develop, companion diagnostics for use in its clinical trials and for commercial use, but Syros or such third parties may not be successful in developing such companion diagnostics, furthering the difficulty in identifying genomically defined subsets of patients for its clinical trials. Moreover, in light of the recent approval of new products for the treatment of AML, there is substantial competition for patients to be enrolled in clinical trials for this disease. Syros' inability, or the inability of any collaborators, to enroll a sufficient number of patients for Syros', or their, clinical trials could result in significant delays or may require Syros or them to abandon one or more clinical trials altogether. Enrollment delays in Syros', or their, clinical trials may result in increased development costs for Syros' product candidates, delay or halt the development of and approval processes for Syros' product candidates and jeopardize its, or any collaborators', ability to commence sales of and generate revenues from

Syros' product candidates, which could cause the value of Syros' company to decline and limit its ability to obtain additional financing, if needed.

Results of preclinical studies and early clinical trials may not be predictive of results of future or late-stage clinical trials.

Syros cannot assure you that it will be able to replicate in human clinical trials the results it observed in earlier studies. Moreover, the outcome of preclinical studies and early clinical trials may not be predictive of the success of later or late-stage clinical trials, and interim results of clinical trials do not necessarily predict success in future clinical trials. Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials after achieving positive results in earlier development, and Syros could face similar setbacks.

In some instances, there can be significant variability in safety or efficacy results between different clinical trials of the same product candidate due to numerous factors, including changes in trial procedures set forth in protocols, differences in the size and type of the patient populations, changes in and adherence to the dosing regimen and other clinical trial protocols and the rate of dropout among clinical trial participants. If Syros fails to receive positive results in clinical trials of its product candidates, the development timeline and regulatory approval and commercialization prospects for its most advanced product candidates, and, correspondingly, its business and financial prospects would be negatively impacted.

Syros has never obtained marketing approval for a product candidate and it may be unable to obtain, or may be delayed in obtaining, marketing approval for its current product candidates or any future product candidates that Syros, or any collaborators, may develop.

Syros has never obtained marketing approval for a product candidate. It is possible that the FDA may refuse to accept for substantive review any new drug applications, or NDAs, that Syros submits for its product candidates or may conclude after review of Syros' data that its application is insufficient to obtain marketing approval of Syros' product candidates. If the FDA does not accept or approve Syros' NDAs for any of its product candidates, it may require that Syros conduct additional clinical trials, preclinical studies or manufacturing validation studies and submit that data before it will reconsider Syros' applications. Depending on the extent of these or any other FDA-required trials or studies, approval of any NDA or application that Syros submits may be delayed by several years, or may require Syros to expend more resources than Syros has available. It is also possible that additional trials or studies, if performed and completed, may not be considered sufficient by the FDA to approve Syros' NDAs. In addition, Syros' development programs contemplate the development of companion diagnostics by Syros' third-party collaborators, such as Qiagen. Companion diagnostics are subject to regulation as medical devices and must themselves be approved for marketing by the FDA or certain other foreign regulatory agencies before Syros may commercialize its product candidates.

Any delay in obtaining, or an inability to obtain, marketing approvals would prevent Syros from commercializing its product candidates or any companion diagnostics, generating revenues and achieving and sustaining profitability. If any of these outcomes occur, Syros may be forced to abandon its development efforts for its product candidates, which could significantly harm its business.

Even if any product candidates that Syros, or any collaborators, may develop receive marketing approval, Syros or others may later discover that the product is less effective than previously believed or causes undesirable side effects that were not previously identified, which could compromise Syros' ability, or that of any collaborators, to market the product.

Clinical trials of tamibarotene, SY-2101 or SY-5609 or any future product candidates that Syros, or any collaborators, may develop will be conducted in carefully defined subsets of patients who have agreed to enter into clinical trials. Consequently, it is possible that Syros' clinical trials, or those of any collaborators, may

indicate an apparent positive effect of a product candidate that is greater than the actual positive effect, if any, or alternatively fail to identify undesirable side effects. If, following approval of a product candidate, Syros, or others, discover that the product is less effective than previously believed or causes undesirable side effects that were not previously identified, Syros could be subject to the withdrawal of prior regulatory approvals and/or the imposition of additional regulatory requirements, restrictions on manufacturing, labelling and marketing, and product recalls. In addition, Syros, or any collaborators, could be sued and held liable for harm caused to patients and could become subject to fines, injunctions or the imposition of civil or criminal penalties. Any of these events could harm Syros' reputation, business and operations and could negatively impact its stock price.

Even if Syros' current product candidates, or any future product candidate that Syros, or any collaborators, may develop receives marketing approval, it may fail to achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success, in which case Syros may not generate significant revenues or become profitable.

Syros has never commercialized a product, and even if one of its product candidates is approved by the appropriate regulatory authorities for marketing and sale, it may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. Physicians are often reluctant to switch their patients from existing therapies even when new and potentially more effective or convenient treatments enter the market. Further, patients often acclimate to the therapy that they are currently taking and do not want to switch unless their physicians recommend switching products or they are required to switch therapies due to lack of reimbursement for existing therapies.

Efforts to educate the medical community and third-party payors on the benefits of Syros' product candidates may require significant resources and may not be successful. If any of Syros' product candidates is approved but does not achieve an adequate level of market acceptance, Syros may not generate significant revenues and it may not become profitable. The degree of market acceptance of Syros' product candidates, if approved for commercial sale, will depend on a number of factors, including the efficacy and safety of the product, the potential advantages of the product compared to competitive therapies, the prevalence and severity of any side effects, whether the product is designated under physician treatment guidelines as a first-, second- or third-line therapy, Syros' ability, or the ability of any collaborators, to offer the product for sale at competitive prices, the product's convenience and ease of administration compared to alternative treatments, the willingness of the target patient population to try, and of physicians to prescribe, the product, limitations or warnings, including distribution or use restrictions, contained in the product's approved labeling, the strength of sales, marketing and distribution support, changes in the standard of care for the targeted indications for the product; and the availability and amount of coverage and reimbursement from government payors, managed care plans and other third-party payors.

Syros may expend its limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

Because Syros has limited financial resources, it intends to focus on developing product candidates for specific indications that it identifies as most likely to succeed, in terms of both their potential for marketing approval and commercialization. As a result, Syros may forego or delay pursuit of opportunities with other product candidates or for other indications that may prove to have greater commercial potential. In this regard, Syros previously announced that it does not plan to pursue Phase 3 development of SY-2101 unless and until it secures additional capital, and has more recently announced that it expects to initiate a Phase 3 clinical trial of SY-2101 in the second half of 2023 upon consummation of the merger, the PIPE Financing and the Loan Amendment. In addition, Syros has elected to deprioritize its planned evaluation of SY-5609 in patients with hematologic malignancies, and plans to determine the best course for further development of SY-5609 after assessing the safety and clinical activity data from the safetylead-in portion of the trial evaluating SY-5609 in combination

with chemotherapy in relapsed/refractory metastatic pancreatic cancer patients that it expects to report in the second half of 2022.

Syros' resource allocation decisions may cause it to fail to capitalize on viable commercial products or profitable market opportunities. Syros' spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable product candidates. If Syros does not accurately evaluate the commercial potential or target market for a particular product candidate, it may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for Syros to retain sole development and commercialization rights to the product candidate.

If Syros is unable to establish sales, marketing and distribution capabilities or enter into sales, marketing and distribution arrangements with third parties, Syros may not be successful in commercializing any product candidates if approved.

Syros does not have a sales, marketing or distribution infrastructure and has no experience in the sale, marketing or distribution of pharmaceutical products. To achieve commercial success for any approved product, Syros must either develop a sales and marketing organization or outsource these functions to third parties. Syros plans to build focused capabilities to commercialize development programs for certain indications where it believes that the medical specialists for the indications are sufficiently concentrated to allow it to effectively promote the product with a targeted sales team. The development of sales, marketing and distribution capabilities will require substantial resources, will be time consuming and could delay any product launch. If the commercial launch of a product candidate for which Syros recruits a sales force and establish marketing and distribution capabilities is delayed or does not occur for any reason, it could have prematurely or unnecessarily incurred these commercialization costs. This may be costly, and Syros' investment could be lost if it cannot retain or reposition its sales and marketing personnel. In addition, Syros may not be able to hire or retain a sales force that is sufficient in size or has adequate expertise in the medical markets that it plans to target. If Syros is unable to establish or retain a sales force and marketing and distribution capabilities, its operating results may be adversely affected. If a potential partner has development or commercialization expertise that Syros believes is particularly relevant to one of its products, then Syros may seek to collaborate with that potential partner even if it believes it could otherwise develop and commercialize the product independently.

In certain indications, Syros plans to seek to enter into collaborations that it believes may contribute to its ability to advance development and ultimately commercialize its product candidates. Syros also intends to seek to enter into collaborations where it believes that realizing the full commercial value of its development programs will require access to broader geographic markets or the pursuit of broader patient populations or indications. As a result of entering into arrangements with third parties to perform sales, marketing and distribution services, Syros' product revenues or the profitability of these product revenues may be lower, perhaps substantially lower, than if it were to directly market and sell products in those markets. Furthermore, Syros may be unsuccessful in entering into the necessary arrangements with third parties or may be unable to do so on terms that are favorable to it. In addition, Syros may have little or no control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market Syros' products effectively.

If Syros does not establish sales, marketing and distribution capabilities, either on its own or in collaboration with third parties, Syros will not be successful in commercializing any of its product candidates that receive marketing approval.

Syros faces substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than it does.

Syros expects that it, and any collaborators, will face significant competition from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide with respect to any of

Syros' product candidates that Syros, or any collaborators, may seek to develop or commercialize in the future. Specifically, there are a number of large pharmaceutical and biotechnology companies that currently market and sell products or are pursuing the development of product candidates for the treatment of the key indications of Syros' most advanced programs.

For example, Syros is aware of several new drugs approved by the FDA since 2018 for the treatment of newly diagnosed AML or patient subsets within newly diagnosed AML (including ivosidenib, venetoclax, and glasdegib), and one new drug approved by the FDA in 2020 for the treatment of MDS or patient subsets within MDS (decitabine/cedazuridine). Tamibarotene may also face competition from other agents currently in clinical development for AML and MDS, including those in late-stage development from Gilead Sciences, Inc., Abbvie Inc., Roche Holding AG, Novartis AG, Astex Pharmaceuticals, Inc. and Pfizer Inc.

SY-2101 may face competition from Trisenox® or any of the generic forms of Trisenox, an intravenously administered, or IV, ATO product approved by the FDA for the treatment of APL, or APL. Syros is also aware of a traditional Chinese medicine (TCM)-based formulation of oral arsenic commercially available in China. In addition, Syros is aware of an oral formulation of ATO in clinical development by Phebra Pty Ltd, or Phebra, an Australian based specialty pharmaceutical group. Phebra has entered into an agreement with Medsenic SAS, a European biopharmaceutical company, for the investigation of their oral ATO compound for the treatment of autoimmune diseases. Syros is also aware of an oral formulation of ATO being studied in an academic setting in Hong Kong.

In addition, Syros is aware of selective CDK7 inhibitors being developed in early clinical trials by Carrick Therapeutics Ltd. and Exelixis, Inc., and three other selective CDK7 inhibitor programs that Syros believes are in preclinical development from Qurient Co. Ltd., Yungjin Pharma Co., Ltd., and The Translational Genomics Research Institute, and a collaboration between Exscientia Ltd. and GT Apeiron Therapeutics Ltd. focused on developing novel cyclin-dependent kinase, or CDK, inhibitors, including selective CDK7 inhibitors. SY -5609 may face competition from these CDK7 inhibitors. There is also significant competition from products with mechanisms other than CDK7 inhibition in pancreatic cancer and BRAF-mutant colorectal cancer, the disease areas where Syros is currently focusing its development of SY-5609. Syros' competitors may succeed in developing, acquiring or licensing technologies and products that are more effective, have fewer side effects or more tolerable side effects or are less costly than any product candidates that Syros is currently developing or that it may develop, which could render its product candidates obsolete and noncompetitive.

Syros' competitors may develop and commercialize products that are safer or more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that Syros, or any collaborators, may develop. For example, the evolving standard of care for the treatment of patients with AML and the response rates and duration of response seen with approved and investigational agents in this disease may result in a longer and more complex clinical development path for tamibarotene, which in turn will impact the potential return on investments in clinical trials of tamibarotene. Syros' competitors also may obtain FDA or other marketing approval for their products before Syros, or any collaborators, are able to obtain approval for Syros', which could result in Syros' competitors establishing a strong market position before Syros, or any collaborators, are able to enter the market.

Many of Syros' existing and potential future competitors have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining marketing approvals and marketing approved products than Syros does. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of Syros' competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with Syros in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, the development of Syros' product candidates.

Even if Syros, or any collaborators, are able to commercialize any product candidate that Syros, or they, develop, the product may become subject to unfavorable pricing regulations, third-party payor reimbursement practices or healthcare reform initiatives, any of which could harm Syros' business.

The commercial success of Syros' product candidates will depend substantially, both domestically and abroad, on the extent to which the costs of its product candidates will be paid by third-party payors, including government health care programs and private health insurers. If coverage is not available, or reimbursement is limited, Syros, or any collaborators, may not be able to successfully commercialize Syros' product candidates. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow Syros, or any collaborators, to establish or maintain pricing sufficient to realize a sufficient return on Syros' or their investments. In the United States, no uniform policy of coverage and reimbursement for products exists among third-party payors and coverage and reimbursement levels for products can differ significantly from payor to payor. As a result, the coverage determination process is often a time consuming and costly process that may require Syros to provide scientific and clinical support for the use of its products to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance.

There is significant uncertainty related to third-party payor coverage and reimbursement of newly approved drugs. Marketing approvals, pricing and reimbursement for new drug products vary widely from country to country. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, Syros, or any collaborators, might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay commercial launch of the product, possibly for lengthy time periods, which may negatively impact the revenues Syros is able to generate from the sale of the product in that country. Adverse pricing limitations may hinder Syros' ability or the ability of any collaborators to recoup Syros' or their investment in one or more product candidates, even if Syros' product candidates obtain marketing approval.

Patients who are provided medical treatment for their conditions generally rely on third-party payors to reimburse all or part of the costs associated with their treatment. Therefore, Syros' ability, and the ability of any collaborators, to successfully commercialize any of Syros' product candidates will depend in part on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from third-party payors. Third-party payors decide which medications they will cover and establish reimbursement levels. The healthcare industry is acutely focused on cost containment, both in the United States and elsewhere. Government authorities and other third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications, which could affect Syros' ability or that of any collaborators to sell Syros' product candidates profitably. These payors may not view Syros' products, if any, as cost-effective, and coverage and reimbursement may not be available to Syros' customers, or those of any collaborators, or may not be sufficient to allow Syros' products, if any, to be marketed on a competitive basis. Cost-control initiatives could cause Syros, or any collaborators, to decrease the price Syros, or they, might establish for products, which could result in lower than anticipated product revenues. If the prices for Syros' products, if any, decrease or if governmental and other third-party payors do not provide coverage or adequate reimbursement, Syros' prospects for revenue and profitability will suffer.

There may also be delays in obtaining coverage and reimbursement for newly approved drugs, and coverage may be more limited than the indications for which the drug is approved by the FDA or comparable foreign regulatory authorities. Moreover, eligibility for reimbursement does not imply that any drug will be paid for in all cases or at a rate that covers Syros' costs, including research, development, manufacture, sale and distribution. Reimbursement rates may vary, by way of example, according to the use of the product and the clinical setting in which it is used. Reimbursement rates may also be based on reimbursement levels already set for lower cost drugs or may be incorporated into existing payments for other services.

In addition, increasingly, third-party payors are requiring higher levels of evidence of the benefits and clinical outcomes of new technologies and are challenging the prices charged. Further, the net reimbursement for drug products may be subject to additional reductions if there are changes to laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. An inability to promptly obtain coverage and adequate payment rates from both government-funded and private payors for any of Syros' product candidates for which Syros, or any collaborator, obtain marketing approval could significantly harm Syros' operating results, Syros' ability to raise capital needed to commercialize products and Syros' overall financial condition.

Product liability lawsuits against Syros could divert its resources, cause it to incur substantial liabilities and limit commercialization of any products that Syros may develop.

Syros will face an inherent risk of product liability claims as a result of the clinical testing of its product candidates despite obtaining appropriate informed consents from its clinical trial participants. Syros will face an even greater risk if Syros or any collaborators commercially sell any product that Syros may or they may develop. For example, Syros may be sued if any product Syros develops allegedly causes injury or is found to be otherwise unsuitable during clinical testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability or a breach of warranties. Claims could also be asserted under state consumer protection acts. If Syros cannot successfully defend itself against product liability claims, Syros may incur substantial liabilities or be required to limit commercialization of its product candidates. Regardless of the merits or eventual outcome, liability claims may result in, among other consequences, decreased demand for Syros' product candidates or products that Syros may develop, injury to its reputation and significant negative media attention, withdrawal of clinical trial participants, significant costs to defend resulting litigation, substantial monetary awards to trial participants or patients, loss of revenue, reduced resources of Syros' management to pursue its business strategy, and the inability to commercialize any products that Syros may develop.

Although Syros maintains clinical trial liability insurance coverage in the amount of up to $10.0 million in the aggregate, this insurance may not fully cover potential liabilities that Syros may incur. The cost of any product liability litigation or other proceeding, even if resolved in Syros' favor, could be substantial. Syros will need to increase its insurance coverage if and when Syros commercializes any product that receives marketing approval. In addition, insurance coverage is becoming increasingly expensive. If Syros is unable to obtain or maintain sufficient insurance coverage at an acceptable cost or to otherwise protect against potential product liability claims, it could prevent or inhibit the development and commercial production and sale of Syros' product candidates, which could harm its business, financial condition, results of operations and prospects.

If the FDA or comparable foreign regulatory authorities approve generic versions of any of Syros' products that receive marketing approval, or such authorities do not grant Syros' products appropriate periods of data exclusivity before approving generic versions of Syros' products, the sales of Syros' products could be adversely affected.

Once an NDA is approved, the product covered thereby becomes a "reference-listed drug" in the FDA's publication, "Approved Drug Products with Therapeutic Equivalence Evaluations," or the Orange Book. Manufacturers may seek approval of generic versions of reference-listed drugs through submission of abbreviated new drug applications, or ANDAs, in the United States. In support of an ANDA, a generic manufacturer need not conduct clinical trials. Rather, the applicant generally must show that their product has the same active ingredient(s), dosage form, strength, route of administration and conditions of use or labeling as the reference-listed drug and that the generic version is bioequivalent to the reference-listed drug, meaning it is absorbed in the body at the same rate and to the same extent. Generic products may be significantly less costly to bring to market than the reference-listed drug and companies that produce generic products are generally able to

offer them at lower prices. Thus, following the introduction of a generic drug, a significant percentage of the sales of any branded product or reference-listed drug may be typically lost to the generic product.

The FDA may not approve an ANDA for a generic product until any applicable period ofnon-patent exclusivity for the reference-listed drug has expired. The Federal Food, Drug, and Cosmetic Act, or FDCA, provides a period of five years of non-patent exclusivity for a new drug containing a new chemical entity, or NCE. Specifically, in cases where such exclusivity has been granted, an ANDA may not be filed with the FDA until the expiration of five years unless the submission is accompanied by a Paragraph IV certification that a patent covering the reference-listed drug is either invalid or will not be infringed by the generic product, in which case the applicant may submit its application four years following approval of the reference-listed drug. Because the composition of matter patent for tamibarotene has expired and Syros' license rights to tamibarotene from TMRC are limited to human cancer indications, it is possible that another applicant could obtain approval for a similar product from the FDA before Syros, in which case its NDA for tamibarotene would not be eligible for NCE exclusivity. See "*Risks Related to Syros' Intellectual Property—Syros does not have composition of matter patent protection with respect to tamibarotene or the active pharmaceutical ingredient of SY-2101*." If any product Syros develops does not receive five years of NCE exclusivity, the FDA may approve generic versions of such product three years after its date of approval, subject to the requirement that the ANDA applicant certifies to any patents listed for Syros' products in the Orange Book. Manufacturers may seek to launch these generic products following the expiration of the applicable marketing exclusivity period, even if Syros still has patent protection for Syros' product.

Competition that Syros' products may face from generic versions of its products could negatively impact its future revenue, profitability and cash flows and substantially limit its ability to obtain a return on Syros' investments in those product candidates.

Risks Related to Syros' Dependence on Third Parties

Syros expects to rely on third parties to conduct Syros' clinical trials and certain aspects of its research and preclinical testing, and those third parties may not perform satisfactorily, including by failing to meet deadlines for the completion of such trials, research or testing.

Syros currently relies and expects to continue to rely on third parties to conduct certain aspects of Syros' research and preclinical testing. Any third parties on which Syros currently relies or may in the future rely may terminate their engagements with Syros at any time. If Syros needs to enter into alternative arrangements, it could delay its product development activities.

Syros additionally expects to rely on other third parties to store and distribute drug supplies for Syros' clinical trials. Any performance failure on the part of Syros' distributors could delay clinical development or marketing approval of its product candidates or commercialization of Syros' medicines, producing additional losses and depriving Syros of potential product revenue. Syros further expects to rely on third parties, such as CROS, clinical data management organizations, medical institutions and clinical investigators, to conduct Syros' clinical trials. Syros' reliance on these third parties for research and development activities will reduce Syros' control over these activities, but will not relieve Syros of its responsibilities. For example, Syros will remain responsible for ensuring that each of its clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA requires Syros to comply with standards, commonly referred to as good clinical practices, for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. Syros also is required to register ongoing clinical trials and post the results of completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within certain timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

Furthermore, these third parties may also have relationships with other entities, some of which may be Syros' competitors. If these third parties do not successfully carry out their contractual duties, meet expected deadlines

or conduct Syros' clinical trials in accordance with regulatory requirements or Syros' stated protocols, Syros will not be able to obtain, or may be delayed in obtaining, marketing approvals for Syros' product candidates and will not be able to, or may be delayed in its efforts to, successfully commercialize its medicines.

Syros currently depends on third-party manufacturers to produce its preclinical and clinical drug supplies and Syros intends to rely upon third-party manufacturers to produce commercial supplies of any approved product candidates.

Syros does not have any manufacturing facilities. Syros currently relies, and expect to continue to rely, on third-party manufacturers for the manufacture of Syros' product candidates for preclinical and clinical testing and for commercial supply of any of these product candidates for which Syros or its collaborators obtain marketing approval. Syros has engaged, and expects to continue engaging, third-party suppliers and manufacturers in China and India. Natural disasters such as earthquakes, tsunamis, power shortages or outages, floods or monsoons, public health crises such as the COVID-19 pandemic or other pandemics or epidemics, political crises such as terrorism, war, political insecurity or other conflict, or other events outside of Syros' control could adversely affect the ability of these third parties to perform their obligations as expected.

Syros also does not currently have a long-term supply agreement with any third-party manufacturers. Syros may be unable to establish any agreements with third-party manufacturers or to do so on acceptable terms. Even if Syros is able to establish agreements with third-party manufacturers, Syros faces risks such as the possible breach of the agreement by the third party or termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient to Syros. Syros also faces risks associated with reliance on third parties for regulatory compliance, quality assurance, and safety and pharmacovigilance reporting.

Third-party manufacturers may not be able to comply with current good manufacturing practices, or cGMP, regulations or similar regulatory requirements outside the United States. Syros' failure, or the failure of its third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on Syros, including fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or medicines, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of Syros medicines and harm its business and results of operations.

Any performance failure on the part of Syros' existing or future manufacturers could delay clinical development or marketing approval. Syros does not currently have arrangements in place for redundant supply of bulk drug substance or drug product. If any one of Syros' current contract manufacturers cannot perform as agreed, Syros may be required to replace that manufacturer. Although Syros believes that there are several potential alternative manufacturers who could manufacture its product candidates, Syros may incur added costs and delays in identifying and qualifying any such replacement.

Syros currently depends on a third-party manufacturer to develop and validate the clinical trial assay being used to select patients with its proprietary RARA biomarker, and if this assay does not perform as designed, Syros' clinical trials of tamibarotene may be adversely affected.

Syros is currently conducting SELECT-MDS-1, a Phase 3 clinical trial evaluating tamibarotene in combination with azacitidine inHR-MDS, patients who have been prospectively selected using Syros' proprietary RARA biomarker, and SELECT-AML-1, a randomized Phase 2 clinical trial evaluating tamibarotene in combination with venetoclax and azacitidine in RARA-positive newly diagnosed patients with AML who are not suitable candidates for standard intensive chemotherapy. Syros collaborates with a third party with respect to the clinical trial assay being used to select patients with the RARA biomarker for inclusion in these trials. The FDA has approved an investigational device exemption for the assay being used to select patients with the RARA biomarker, and Syros used this assay in its earlier Phase 2 trial evaluating the safety and efficacy of tamibarotene in certain AML and MDS patient populations. Based on data from patients screened in its clinical trials, Syros

believes approximately 50% of MDS patients and approximately 30% of AML patients are positive for the RARA biomarker. Syros' ability to continue to prospectively select RARA-positive patients for SELECT-MDS-1 and SELECT-AML-1 depends on the ability of this clinical trial assay to identify suitable patients for these clinical trials. If this assay does not perform as designed, it could adversely affect Syros' estimated timelines to enroll patients, or adversely impact the results of these trials, which could significantly harm its business and commercial prospects.

To the extent that Syros enters into collaborations with third parties for the development and commercialization of any product candidates, Syros' prospects with respect to those product candidates will depend in significant part on the success of those collaborations.

Syros expects to enter into collaborations for the development and commercialization of one or more product candidates Syros may develop, or to use its gene control platform to identify and validate disease targets, as Syros has with GBT to develop novel therapies for sickle cell disease and beta thalassemia and with Incyte to identify new drug targets in the field of myeloproliferative neoplasms. To the extent Syros enters into such collaborations, Syros will have limited control over the amount and timing of resources that its collaborators will dedicate to the development or commercialization of its product candidates. Syros' ability to generate revenues from these arrangements will depend on any collaborators' abilities to successfully perform the functions assigned to them in these arrangements. In addition, collaborators may have the right to abandon research or development projects and terminate applicable agreements, including funding obligations, prior to or upon the expiration of the agreed upon terms.

Collaborations involving Syros' product candidates pose a number of risks, including the following:

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborators may not perform their obligations as expected;
- collaborators may not pursue development and commercialization of Syros' product candidates or may elect not to continue or renew development or commercialization programs, based on clinical trial results, changes in the collaborators' strategic focus or available funding or external factors, such as an acquisition, that divert resources or create competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with Syros' product candidates;
- a collaborator with marketing and distribution rights to one or more products may not commit sufficient resources to the marketing and distribution of such product or products;
- disagreements with collaborators, including disagreements over proprietary rights, contract interpretation or the preferred course of development, might cause delays or termination of the research, development or commercialization of product candidates, might lead to additional responsibilities for Syros with respect to product candidates, or might result in litigation or arbitration, any of which would be time consuming and expensive;
- collaborators may not properly maintain or defend Syros' IP rights or may use Syros' proprietary information in such a way as to invite litigation that could jeopardize or invalidate Syros' IP or proprietary information or expose Syros to potential litigation;
- collaborators may infringe the IP rights of third parties, which may expose Syros to litigation and potential liability;

- Syros' collaboration agreements with GBT and Incyte contain, and any collaboration agreement that Syros enters into in the future may contain, restrictions on Syros' ability to enter into potential collaborations, to conduct research or development in certain fields, or to otherwise develop specified product candidates;
- there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential collaborators; and
- collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates.

Collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all. If any collaborator of Syros' is involved in a business combination, it could decide to delay, diminish or terminate the development or commercialization of any product candidate licensed to it by Syros.

Syros expects to seek to establish additional collaborations and, if Syros is not able to establish them on commercially reasonable terms, Syros may have to alter its development and commercialization plans.

Syros expects to seek one or more additional collaborators for the development and commercialization of one or more of its product candidates or to validate targets. Likely collaborators may include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies. In addition, if Syros is able to obtain marketing approval for product candidates from foreign regulatory authorities, Syros intends to enter into strategic relationships with international biotechnology or pharmaceutical companies for the commercialization of such product candidates outside of the United States.

Syros faces significant competition in seeking appropriate collaborators. Whether Syros reaches a definitive agreement for a collaboration will depend, among other things, upon its assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration, and the proposed collaborator's evaluation of a number of factors. Those factors may include the potential differentiation of Syros' product candidates from competing product candidates, design or results of clinical trials, the likelihood of approval by the FDA or comparable foreign regulatory authorities and the regulatory pathway for any such approval, the potential market for the product candidate, the costs and complexities of manufacturing and delivering the product to patients and the potential of competing products. The collaborator may also consider alternative product candidates or technologies for similar indications that may be available for collaboration and whether such a collaboration could be more attractive than the one with Syros for its product candidate.

Syros may not be able to negotiate new collaborations on a timely basis, on acceptable terms, or at all. If Syros is unable to do so, it may have to curtail the development of the product candidate for which Syros is seeking to collaborate, reduce or delay its development program or one or more of its other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase its expenditures and undertake development or commercialization activities at its own expense.

Risks Related to Syros' Intellectual Property

If Syros fails to comply with its obligations under its existing and any future intellectual property licenses with third parties, Syros could lose license rights that are important to its business.

Syros is party to several license agreements under which Syros licenses patent rights and other intellectual property, or IP, related to its business, including the TMRC license agreement, pursuant to which Syros was granted a license under specified patent rights, data, regulatory filings and other IP primarily for the North American and European development and commercialization of tamibarotene for the treatment of human cancer indications. Syros may enter into additional license agreements in the future. Syros' license agreements impose,

and Syros expects that future license agreements will impose, various diligence, milestone payment, royalty, insurance and other obligations on it. If Syros fails to comply with its obligations under these licenses, its licensors may have the right to terminate these license agreements, in which event Syros might not be able to market any product that is covered by these agreements, or its licensors may convert the license to a non-exclusive license, which could adversely affect the value of the product candidate being developed under the license agreement. Termination of these license agreements or reduction or elimination of Syros' licensed rights may also result in Syros having to negotiate new or reinstated licenses with less favorable terms.

Syros does not have composition of matter patent protection with respect to tamibarotene or the active pharmaceutical ingredient of SY-2101.

Syros owns certain patents and patent applications with claims directed to specific methods of using tamibarotene and Syros expects to have marketing exclusivity from the FDA and EMA for a period of no less than five and ten years, respectively, because tamibarotene has not been approved in these markets. Composition of matter patent protection in the United States and elsewhere covering tamibarotene has expired, however. In addition, Syros does not have composition of matter patent protection for ATO, the active pharmaceutical ingredient of SY-2101. Syros may be limited in its ability to list its method patents in the Orange Book if the use of Syros' products, consistent with its FDA-approved label, would not fall within the scope of Syros' patent claims. Also, Syros' competitors may be able to offer and sell products so long as these competitors do not infringe any other patents that Syros (or third parties) holds, including patents with claims directed to the manufacture of tamibarotene and/or method of use patents, or to the formulation of SY-2101 drug product and/or methods of manufacture of SY-2101. In general, method of use patents are more difficult to enforce than composition of matter patents because, for example, of the risks that the FDA may approve alternative uses of the subject compounds not covered by the method of use, formulation or manufacturing method patents, and others may engage in off-label sale or use of the subject compounds. Physicians are permitted to prescribe an approved product for uses that are not described in the product's labeling. Although off-label prescriptions may infringe Syros' method of use patents, the practice is common across medical specialties and such infringement is difficult to prevent or prosecute. FDA approval of uses of a generic version of tamibarotene or SY-2101 that are not covered by Syros' patents would limit its ability to generate revenue from the sale of such product candidates, if approved for commercial sale. In addition, any off-label use of a generic version of tamibarotene would limit Syros' ability to generate revenue from the sale of tamibarotene, if approved for commercial sale.

Syros' IP licenses with third parties may be subject to disagreements over contract interpretations, which could narrow the scope of Syros' rights to the relevant IP or technology or increase its financial or other obligations to its licensors.

The agreements under which Syros currently licenses IP or technology from third parties are complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what Syros believes to be the scope of its rights to the relevant IP or technology, or increase what Syros believes to be its financial or other obligations under the relevant agreement, either of which could harm its business, financial condition, results of operations and prospects.

Syros may not be successful in obtaining or maintaining necessary rights to current or future product candidates through acquisitions and in-licenses.

Syros currently has rights to certain IP, through ownership or licenses from third parties, to develop and commercialize tamibarotene for human cancers in North and South America and Europe, Israel, Russia and Australia, and for SY-2101 and SY-5609 for all potential uses in North America and major markets in Europe and elsewhere. Because Syros' programs may require the use of proprietary rights by third parties, the growth of its business likely will depend, in part, on Syros' ability to acquire, in-license or use these proprietary rights. Syros may be unable to acquire or in-license from third parties any IP rights directed to compositions, methods of

use, or processes that Syros identifies as necessary for any product candidates. The licensing or acquisition of third-party IP rights is a competitive area, and several more established companies may pursue strategies to license or acquire third-party IP rights that Syros may consider attractive. These established companies may have a competitive advantage over Syros due to their size, capital resources and greater clinical development and commercialization capabilities. In addition, companies that perceive Syros to be a competitor may be unwilling to assign or license rights to Syros. Syros also may be unable to license or acquire third-party IP rights on terms that would allow it to make an appropriate return on its investment.

Syros sometimes collaborates with non-profit and academic institutions to accelerate Syros' preclinical research or development under written agreements with these institutions. Typically, these institutions provide Syros with an option to negotiate a license to any of the institution's rights in technology resulting from the collaboration. Regardless of such option, Syros may be unable to negotiate a license within the specified timeframe or under terms that are acceptable to it, or Syros may decide not to execute such option if Syros believe such license is not necessary to pursue its program. If Syros is unable or opts not to do so, the institution may offer the IP rights to other parties, potentially blocking Syros' ability to pursue its program.

If Syros is unable to successfully obtain rights to required third-party IP rights or maintain the existing IP rights Syros has, Syros may be required to expend significant time and resources to redesign its product candidates or the methods for manufacturing them or to develop or license replacement technology, all of which may not be feasible on a technical or commercial basis. If Syros is unable to do so, it may be unable to develop or commercialize the affected product candidate, which could harm its business significantly.

Syros depends upon its license with TMRC, and Syros may not be able to maintain that license.

Syros has entered into a standby license with TMRC and Toko, providing that if at any time the license agreement between Toko and TMRC relating to the tamibarotene rights that TMRC has licensed to Syros terminates or otherwise ceases to be in effect for any reason, Toko will grant directly to Syros such rights and licenses with respect to tamibarotene as are necessary for Syros to continue to develop tamibarotene. If the TMRC license agreement terminates and this standby license terminates, then Syros may lose rights to tamibarotene that may be necessary to the development and commercialization of tamibarotene, which could have a material adverse impact on Syros' business.

If Syros is unable to obtain and maintain sufficient patent protection for any product candidates, or if the scope of the patent protection is not sufficiently broad, Syros' competitors could develop and commercialize products similar or identical to Syros', and Syros' ability to successfully commercialize its product candidates may be adversely affected.

Syros' success depends in large part on its ability to obtain and maintain patent protection in the United States and other countries with respect to its proprietary product candidates. If Syros does not adequately protect its IP, its competitors may be able to erode or negate any competitive advantage Syros may have, which could harm its business and ability to achieve profitability. To protect Syros' proprietary position, Syros files patent applications in the United States and abroad related to its novel product candidates that are important to its business. Syros also licenses or purchase patent applications filed by others. The patent application and approval processes are expensive and time consuming. Syros may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner.

Agreements through which Syros licenses patent rights may not give Syros control over patent prosecution or maintenance, so that Syros may not be able to control which claims or arguments are presented and may not be able to secure, maintain, or successfully enforce necessary or desirable patent protection from those patent rights. Syros has not had and does not have primary control over patent prosecution and maintenance for certain of the patents and patent applications Syros licenses, and therefore cannot guarantee that these patents and applications will be prosecuted in a manner consistent with the best interests of its business. Syros cannot be certain that

patent prosecution and maintenance activities by its licensors have been or will be conducted in compliance with applicable laws and regulations or will result in valid and enforceable patents.

Syros, or any partners, collaborators or licensees, may fail to identify patentable aspects of inventions made in the course of development and commercialization activities before it is too late to obtain patent protection for them. Therefore, Syros may miss potential opportunities to strengthen its patent position.

It is possible that defects of form in the preparation or filing of Syros' patents or patent applications may exist, or may arise in the future, for example with respect to proper priority claims, inventorship, claim scope or patent term adjustments. If Syros or its partners, collaborators, licensees, or licensors, whether current or future, fail to establish, maintain or protect such patents and other IP rights, such rights may be reduced or eliminated. If Syros' partners, collaborators, licensees or licensors, are not fully cooperative or disagree with Syros as to the prosecution, maintenance or enforcement of any patent rights, such patent rights could be compromised. If there are material defects in the form, preparation, prosecution, or enforcement of Syros' patents or patent applications, such patents may be invalid and/or unenforceable, and such applications may never result in valid, enforceable patents. Any of these outcomes could impair Syros' ability to prevent competition from third parties, which may have an adverse impact on Syros' business.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain. No consistent policy regarding the breadth of claims allowed in biotechnology and pharmaceutical patents has emerged to date in the United States or in many foreign jurisdictions. In addition, the determination of patent rights with respect to pharmaceutical compounds commonly involves complex legal and factual questions, which has in recent years been the subject of much litigation. As a result, the issuance, scope, validity, enforceability and commercial value of Syros' patent rights are highly uncertain.

Pending patent applications cannot be enforced against third parties practicing the technology claimed in such applications unless and until a patent issues from such applications. Assuming the other requirements for patentability are met, currently, the first to file a patent application is generally entitled to the patent except that, prior to March 16, 2013 in the United States, the first to invent was entitled to the patent. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases, not at all. Therefore, Syros cannot be certain that it was the first to make the inventions claimed in its patents or pending patent applications, or that Syros was the first to file for patent protection of such inventions. Similarly, Syros cannot be certain that parties from whom Syros does or may license or purchase patent rights were the first to make relevant claimed inventions, or were the first to file for patent protection for them. If third parties have filed patent applications on inventions claimed in Syros' patents or applications on or before March 15, 2013, an interference proceeding in the United States can be initiated by such third parties to determine who was the first to invent any of the subject matter covered by the patent claims of Syros' applications. If third parties have filed such applications after March 15, 2013, a derivation proceeding in the United States can be initiated by such third parties to determine whether Syros' invention was derived from theirs.

Moreover, because the issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, Syros' patents or pending patent applications may be challenged in the courts or patent offices in the United States and abroad. There is no assurance that all of the potentially relevant prior art relating to Syros' patents and patent applications has been found. If such prior art exists, it may be used to invalidate a patent, or may prevent a patent from issuing from a pending patent application. For example, such patent filings may be subject to a third-party pre-issuance submission of prior art to the U.S. Patent and Trademark Office, or USPTO, or to other patent offices around the world. Alternately or additionally, Syros may become involved in post-grant review procedures, oppositions, derivations, proceedings, reexaminations, *inter partes* review or interference proceedings, in the United States or elsewhere, challenging patents or patent applications in which Syros has rights, including patents on which Syros relies to protect its business. An adverse determination in any such challenges may result in loss of exclusivity or in patent claims being narrowed, invalidated or held

unenforceable, in whole or in part, which could limit Syros' ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of Syros' technology and products. In addition, given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized.

Pending and future patent applications may not result in patents being issued which protect Syros' business, in whole or in part, or which effectively prevent others from commercializing competitive products. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of Syros' patents or narrow the scope of its patent protection. In addition, the laws of foreign countries may not protect Syros' rights to the same extent or in the same manner as the laws of the United States.

Issued patents that Syros has or may obtain or license may not provide Syros with any meaningful protection, prevent competitors from competing with Syros or otherwise provide it with any competitive advantage. Syros' competitors may be able to circumvent Syros' patents by developing similar or alternative technologies or products in a non-infringing manner. Syros' competitors may also seek approval to market their own products similar to or otherwise competitive with Syros' products. Alternatively, Syros' competitors may seek to market generic versions of any approved products by submitting ANDAs to the FDA in which they claim that patents owned or licensed by Syros are invalid, unenforceable or not infringed. In these circumstances, Syros may need to defend or assert its patents, or both, including by filing lawsuits alleging patent infringement. In any of these types of proceedings, a court or other agency with jurisdiction may find Syros' patents invalid or unenforceable, or that Syros' competitors are competing in a non-infringing manner. Thus, even if Syros has valid and enforceable patents, these patents still may not provide protection against competing products or processes sufficient to achieve its business objectives.

Pursuant to the terms of some of Syros' license agreements with third parties, some of its third-party licensors have the right, but not the obligation, in certain circumstances to control enforcement of Syros' licensed patents or defense of any claims asserting the invalidity of these patents. Even if Syros is permitted to pursue such enforcement or defense, Syros will require the cooperation of its licensors, and cannot guarantee that Syros would receive it and on what terms. Syros cannot be certain that its licensors will allocate sufficient resources or prioritize their or Syros' enforcement of such patents or defense of such claims to protect its interests in the licensed patents. If Syros cannot obtain patent protection, or enforce existing or future patents against third parties, its competitive position and its financial condition could suffer.

If Syros is unable to protect the confidentiality of its trade secrets, the value of its technology could be materially adversely affected and its business would be harmed.

In addition to the protection afforded by patents, Syros may also rely on trade secret protection for certain aspects of its technology platform, including certain aspects of its gene control platform. Syros seeks to protect these trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as its employees, consultants, independent contractors, advisors, contract manufacturers, suppliers and other third parties. Syros also enters into confidentiality and invention or patent assignment agreements with employees and certain consultants. Any party with whom Syros has executed such an agreement may breach that agreement and disclose Syros' proprietary information, including any information Syros holds in confidence or as a trade secret, and Syros may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated confidential information or a trade secret is difficult, expensive and time consuming, and the outcome is unpredictable. Additionally, if the steps taken to maintain Syros' trade secrets are deemed inadequate, Syros may have insufficient recourse against third parties for misappropriating the trade secret. Further, if any of Syros' confidential information or trade secrets were to be lawfully obtained or independently developed by a competitor, Syros would have no right to prevent such third party, or those to whom they communicate such technology or information, from using that technology or information to compete with Syros. If any of Syros' trade secrets were to be disclosed to or independently developed by a competitor, Syros' business and competitive position could be harmed.

Syros may become involved in lawsuits to protect or enforce its patents or other IP, which could be expensive, time consuming and unsuccessful.

Competitors may infringe Syros' patents, trademarks, copyrights or other IP. To counter infringement or unauthorized use, Syros may be required to file infringement claims, which can be expensive and time consuming and divert the time and attention of its management and scientific personnel. Any claims Syros asserts against perceived infringers could provoke these parties to assert counterclaims against Syros alleging that Syros infringes their patents, in addition to counterclaims asserting that Syros' patents are invalid or unenforceable, or both. In any patent infringement proceeding, there is a risk that a court will decide that a patent of Syros' is invalid or unenforceable, in whole or in part, and that Syros does not have the right to stop the other party from using the invention at issue. There is also a risk that, even if the validity of such patents is upheld, the court will construe the patent's claims narrowly or decide that Syros does not have the right to stop the other party from using the invention at issue on the grounds that Syros' patent claims do not cover the invention. An adverse outcome in a litigation or proceeding involving one or more of Syros' patents could limit its ability to assert those patents against those parties or other competitors and may curtail or preclude Syros' ability to exclude third parties from making and selling similar or competitive products. Similarly, if Syros asserts trademark infringement claims, a court may determine that the marks Syros has asserted are invalid or unenforceable, or that the party against whom Syros has asserted trademark infringement has superior rights to the marks in question. In this case, Syros could ultimately be forced to cease use of such trademarks.

Even if Syros establishes infringement, the court may decide not to grant an injunction against further infringing activity and instead award only monetary damages, which may or may not be an adequate remedy. Furthermore, because of the substantial amount of discovery required in connection with IP litigation, there is a risk that some of Syros' confidential information could be compromised by disclosure during litigation. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could adversely affect the price of shares of Syros common stock. Moreover, there can be no assurance that Syros will have sufficient financial or other resources to file and pursue such infringement claims, which typically last for years before they are concluded. Even if Syros ultimately prevails in such claims, the monetary cost of such litigation and the diversion of the attention of Syros' management and scientific personnel could outweigh any benefit Syros receives as a result of the proceedings.

If Syros is sued for infringing IP rights of third parties, such litigation could be costly and time consuming and could prevent or delay Syros from developing or commercializing its product candidates.

Syros' commercial success depends, in part, on its ability to develop, manufacture, market and sell its product candidates and use its gene control technology without infringing the IP and other proprietary rights of third parties. Third parties may have U.S. and non-U.S. issued patents and pending patent applications relating to compounds and methods of use for the treatment of the disease indications for which Syros is developing its product candidates. If any third-party patents or patent applications are found to cover Syros' product candidates or their methods of use, Syros may not be free to manufacture or market its product candidates as planned without obtaining a license, which may not be available on commercially reasonable terms, or at all.

There is a substantial amount of IP litigation in the biotechnology and pharmaceutical industries, and Syros may become party to, or threatened with, litigation or other adversarial proceedings regarding IP rights with respect to its product candidates, including interference proceedings before the USPTO. There may be third-party patents or patent applications with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of Syros' product candidates. Because patent applications can take many years to issue, there may be currently pending patent applications which may later result in issued patents that Syros' product candidates may be accused of infringing. In addition, third parties may obtain patents in the future and claim that use of Syros' technologies infringes upon these patents. Accordingly, third parties may assert infringement claims against Syros based on existing or future IP rights. The outcome of IP litigation is subject to

uncertainties that cannot be adequately quantified in advance. The pharmaceutical and biotechnology industries have produced a significant number of patents, and it may not always be clear to industry participants, including Syros, which patents cover various types of products or methods of use. The coverage of patents is subject to interpretation by the courts, and the interpretation is not always uniform. If Syros was sued for patent infringement, Syros would need to demonstrate that its product candidates, products or methods either do not infringe the patent claims of the relevant patent or that the patent claims are invalid or unenforceable, and Syros may not be able to do this. Proving invalidity is difficult. For example, in the United States, proving invalidity requires a showing of clear and convincing evidence to overcome the presumption of validity enjoyed by issued patents. Even if Syros is successful in these proceedings, Syros may incur substantial costs and the time and attention of its management and scientific personnel could be diverted in pursuing these proceedings, which could significantly harm its business and operating results. In addition, Syros may not have sufficient resources to bring these actions to a successful conclusion.

If Syros is found to infringe a third party's IP rights, Syros could be forced, including by court order, to cease developing, manufacturing or commercializing the infringing product candidate or product. Alternatively, Syros may be required to obtain a license from such third party in order to use the infringing technology and continue developing, manufacturing or marketing the infringing product candidate or product. It is possible, however, that Syros would be unable to obtain any required license on commercially reasonable terms or at all. Even if Syros was able to obtain a license, it could be non-exclusive, thereby giving Syros' competitors access to the same technologies licensed to Syros. Alternatively, or additionally, it could include terms that impede or destroy Syros' ability to compete successfully in the commercial marketplace. In addition, Syros could be found liable for monetary damages, including treble damages and attorneys' fees if Syros is found to have willfully infringed a patent. A finding of infringement could prevent Syros from commercializing its product candidates or force Syros to cease some of its business operations, which could harm its business. Claims that Syros has misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on Syros' business.

Changes to the patent law in the United States and other jurisdictions could diminish the value of patents in general, thereby impairing Syros' ability to protect its products.

As is the case with other biopharmaceutical companies, Syros' success is heavily dependent on IP, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involves both technological and legal complexity and is therefore costly, time consuming and inherently uncertain. Patent reform legislation in the United States, including the Leahy-Smith America Invents Act, or the America Invents Act, could increase those uncertainties and costs.

The America Invents Act was signed into law on September 16, 2011, and many of the substantive changes became effective on March 16, 2013. The America Invents Act reforms U.S. patent law in part by changing the U.S. patent system from a "first to invent" system to a "first inventor to file" system, expanding the definition of prior art, and developing a post-grant review system. This legislation changes U.S. patent law in a way that may weaken Syros' ability to obtain patent protection in the United States for those applications filed after March 16, 2013.

Further, the America Invents Act created new procedures to challenge the validity of issued patents in the United States, including post-grant review and *inter partes* review proceedings, which some third parties have been using to cause the cancellation of selected or all claims of issued patents of competitors. For a patent with an effective filing date of March 16, 2013 or later, a petition for post-grant review can be filed by a third party in a nine-month window from issuance of the patent. A petition for *inter partes* review can be filed immediately following the issuance of a patent if the patent has an effective filing date prior to March 16, 2013. A petition for *inter partes* review can be filed after the nine-month period for filing a post-grant review petition has expired for a patent with an effective filing date of March 16, 2013 or later. Post-grant review proceedings can be brought on any ground of invalidity, whereas *inter partes* review proceedings can only raise an invalidity challenge based on

published prior art and patents. These adversarial actions at the USPTO review patent claims without the presumption of validity afforded to U.S. patents in lawsuits in U.S. federal courts and use a lower burden of proof than used in litigation in U.S. federal courts. Therefore, it is generally considered easier for a competitor or third party to have a U.S. patent invalidated in a USPTO post-grant review or *inter partes* review proceeding than invalidated in a litigation in a U.S. federal court. If any of Syros' patents are challenged by a third party in such a USPTO proceeding, there is no guarantee that Syros or its licensors or collaborators will be successful in defending the patent, which would result in a loss of the challenged patent right to Syros.

In addition, the USPTO continues to modify its guidelines regarding subject matter eligibility, a process that began with decisions rendered in *Association for Molecular Pathology v. Myriad Genetics, Inc.*; *BRCA1- & BRCA2-Based Hereditary Cancer Test Patent Litigation*; and *Promega Corp. v. Life Technologies Corp.* Those court decisions have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to Syros' ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents once obtained. Depending on future actions by the U.S. Congress, the U.S. courts, the USPTO and the relevant law-making bodies in other countries, the laws and regulations governing patents could change in unpredictable ways that would weaken Syros' ability to obtain new patents or to enforce its existing patents and patents that Syros might obtain in the future.

Syros may not be able to enforce its IP rights throughout the world.

Filing, prosecuting and defending patents on Syros' product candidates in all countries throughout the world would be prohibitively expensive, and Syros' IP rights in some countries outside the United States can be less extensive than those in the United States. The requirements for patentability may differ in certain countries, particularly in developing countries; thus, even in countries where Syros does pursue patent protection, there can be no assurance that any patents will issue with claims that cover its products.

Moreover, Syros' ability to protect and enforce its IP rights may be adversely affected by unforeseen changes in foreign IP laws. Additionally, laws of some countries outside of the United States and Europe do not afford IP protection to the same extent as the laws of the United States and Europe. Many companies have encountered significant problems in protecting and defending IP rights in certain foreign jurisdictions. The legal systems of some countries, including India, China and other countries, do not favor the enforcement of patents and other IP rights. This could make it difficult for Syros to stop the infringement of its patents or the misappropriation of its other IP rights. For example, many foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties. Consequently, Syros may not be able to prevent third parties from practicing its inventions in certain countries outside the United States and Europe. Competitors may use Syros' technologies in jurisdictions where Syros has not obtained patent protection to develop and market their own products and, further, may export otherwise infringing products to territories where Syros has patent protection, if Syros' ability to enforce its patents to stop infringing activities is inadequate. These products may compete with Syros' products, and Syros' patents or other IP rights may not be effective or sufficient to prevent them from competing.

Further, a decree was adopted by the Russian government in March 2022 allowing Russian companies and individuals to exploit inventions owned by patent holders from the United States without consent or compensation. Consequently, Syros would not be able to prevent third parties from practicing its inventions in Russia or from selling or importing products made using its inventions in and into Russia.

Agreements through which Syros licenses patent rights may not give Syros sufficient rights to permit it to pursue enforcement of its licensed patents or defense of any claims asserting the invalidity of these patents (or control of enforcement or defense) of such patent rights in all relevant jurisdictions as requirements may vary.

Proceedings to enforce Syros' patent rights in foreign jurisdictions, whether or not successful, could result in substantial costs and divert Syros' efforts and resources from other aspects of its business. Moreover, such

proceedings could put Syros' patents at risk of being invalidated or interpreted narrowly and its patent applications at risk of not issuing and could provoke third parties to assert claims against it. Syros may not prevail in any lawsuits that it initiates, and the damages or other remedies awarded, if any, may not be commercially meaningful. Furthermore, while Syros intends to protect its IP rights in major markets for its products, Syros cannot ensure that it will be able to initiate or maintain similar efforts in all jurisdictions in which Syros may wish to market its products. Accordingly, Syros' efforts to protect its IP rights in such countries may be inadequate.

Patent terms may be inadequate to protect Syros' competitive position on its products for an adequate amount of time.

Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. Syros expects to seek extensions of patent terms in the United States and, if available, in other countries where Syros is prosecuting patents. In the United States, the Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Amendments, permits a patent term extension of up to five years beyond the normal expiration of the patent, which is limited to the approved indication (or any additional indications approved during the period of extension). The applicable authorities, including the FDA and the USPTO in the United States, and any equivalent regulatory authority in other countries, may not agree, however, with Syros' assessment of whether such extensions are available, and may refuse to grant extensions to Syros' patents, or may grant more limited extensions than Syros requests. If this occurs, Syros' competitors may be able to take advantage of its investment in development and clinical trials by referencing its clinical and preclinical data and launch their product earlier than might otherwise be the case.

Syros may be subject to claims by third parties asserting that Syros' employees or Syros has misappropriated their IP or claiming ownership of what Syros regards as its own IP.

Many of Syros' employees and its licensors' employees, including its senior management, were previously employed at universities or at other biotechnology or pharmaceutical companies, some of which may be competitors or potential competitors. Some of these employees, including each member of Syros' senior management, executed proprietary rights, non-disclosure and non-competition agreements, or similar agreements, in connection with such previous employment. Although Syros tries to ensure that its employees do not use the proprietary information or know-how of others in their work for it, Syros may be subject to claims that it or these employees have used or disclosed IP, including trade secrets or other proprietary information, of any such third party. Litigation may be necessary to defend against such claims. If Syros fails in defending any such claims, in addition to paying monetary damages, Syros may lose valuable IP rights or personnel or sustain damages. Such IP rights could be awarded to a third party, and Syros could be required to obtain a license from such third party to commercialize Syros' technology or products. Such a license may not be available on commercially reasonable terms or at all. Even if Syros is successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.

In addition, while Syros typically requires its employees, consultants, contractors and vendors who may be involved in the development of IP to execute agreements assigning such IP to it, Syros may be unsuccessful in executing such an agreement with each party who in fact develops IP that Syros regards as its own, which may result in claims by or against Syros related to the ownership of such IP. If Syros fails in prosecuting or defending any such claims, in addition to paying monetary damages, Syros may lose valuable IP rights. Even if Syros is successful in prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to its senior management and scientific personnel.

Obtaining and maintaining patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and Syros' patent protection could be reduced or eliminated for non-compliance with these requirements.

Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and applications are required to be paid to the USPTO and various governmental patent agencies outside of the United States in several stages over the lifetime of the patents and applications. The USPTO and various non-U.S. governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process and after a patent has issued. There are situations in which non-compliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction.

Risks Related to Regulatory Approval and Marketing of Syros' Product Candidates and Other Legal Compliance Matters

Even if Syros completes the necessary preclinical studies and clinical trials, the regulatory approval process is expensive, time consuming and uncertain and may prevent Syros or any collaborators from obtaining approvals for the commercialization of some or all of Syros' product candidates. As a result, Syros cannot predict when or if, and in which territories, Syros, or any collaborators, will obtain marketing approval to commercialize a product candidate.

The research, testing, manufacturing, labeling, approval, selling, marketing, promotion and distribution of products are subject to extensive regulation by the FDA and comparable foreign regulatory authorities. Syros, and any collaborators, are not permitted to market Syros' product candidates in the United States or in other countries until Syros, or they, receive approval of an NDA from the FDA or marketing approval from applicable regulatory authorities outside the United States. Syros' product candidates are in various stages of development and are subject to the risks of failure inherent in drug development. Syros has not submitted an application for or received marketing approval for any of Syros' product candidates in the United States or in any other jurisdiction. Syros has limited experience in conducting and managing the clinical trials necessary to obtain marketing approvals, including FDA approval of an NDA.

The process of obtaining marketing approvals, both in the United States and abroad, is lengthy, expensive and uncertain. It may take many years, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. Securing marketing approval requires the submission of extensive preclinical and clinical data and supporting information, including manufacturing information, to regulatory authorities for each therapeutic indication to establish the product candidate's safety and efficacy. The FDA or other regulatory authorities may determine that Syros' product candidates are not safe and effective, only moderately effective or have undesirable or unintended side effects, toxicities or other characteristics that preclude Syros' obtaining marketing approval or prevent or limit commercial use. Moreover, the FDA or other regulatory authorities may fail to approve the companion diagnostics Syros contemplates developing with partners. Any marketing approval Syros ultimately obtains may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable.

In addition, changes in marketing approval policies during the development period, changes in or the enactment or promulgation of additional statutes, regulations or guidance or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application. Regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that Syros' data are insufficient for approval and require additional preclinical, clinical or other studies. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent marketing approval of a product candidate. Any marketing approval Syros, or any collaborators, ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable.

Any delay in obtaining or failure to obtain required approvals could negatively affect Syros' ability or that of any collaborators to generate revenue from the particular product candidate, which likely would result in significant harm to its financial position and adversely impact Syros' stock price.

If Syros is required by the FDA to obtain clearance or approval of a companion diagnostic in connection with approval of a candidate therapeutic product, and Syros does not obtain or there are delays in obtaining FDA clearance or approval of a diagnostic device, Syros will not be able to commercialize the product candidate and its ability to generate revenue will be materially impaired.

In August 2014, the FDA issued final guidance clarifying the requirements that will apply to approval of therapeutic products and *in vitro* companion diagnostics. According to the guidance, if the FDA determines that a companion diagnostic device is essential to the safe and effective use of a novel therapeutic product or indication, the FDA generally will not approve the therapeutic product or new therapeutic product indication if the companion diagnostic is not also approved or cleared for that indication. Under the FDCA, companion diagnostics are regulated as medical devices and the FDA has generally required companion diagnostics intended to select the patients who will respond to cancer treatment to obtain premarket approval, or a PMA. Consequently, Syros anticipates that certain of its companion diagnostics may require Syros or its collaborators to obtain a PMA.

The PMA process, including the gathering of clinical and preclinical data and the submission to and review by the FDA, involves a rigorous premarket review during which the sponsor must prepare and provide the FDA with reasonable assurance of the device's safety and effectiveness and information about the device and its components regarding, among other things, device design, manufacturing and labeling. PMA approval is not guaranteed and may take considerable time, and the FDA may ultimately respond to a PMA submission with a not approvable determination based on deficiencies in the application and require additional clinical trial or other data that may be expensive and time-consuming to generate and that can substantially delay approval. As a result, if Syros or its collaborators are required by the FDA to obtain approval of a companion diagnostic for a candidate therapeutic product, and Syros or its collaborators do not obtain or there are delays in obtaining FDA approval of a diagnostic device, Syros will not be able to commercialize the product candidate and its ability to generate revenue will be materially impaired.

In its August 2014 guidance, the FDA also indicated that companion diagnostics used to make treatment decisions in clinical trials of a therapeutic product generally will be considered investigational devices. When a companion diagnostic is used to make critical treatment decisions, such as patient selection, the FDA stated that the diagnostic will be considered a significant risk device requiring an investigational device exemption. The FDA may find that a companion diagnostic that Syros, alone or with a third party such as Qiagen, plan to develop does not comply with those requirements and, if this were to occur, Syros would not be able to proceed with its planned trial of the applicable product candidate in these patient populations.

Syros believes that adoption of screening and treatment into clinical practice guidelines is important for payer access, reimbursement, utilization in medical practice and commercial success, but both its collaborators and Syros may have difficulty gaining acceptance of the companion diagnostic into clinical practice guidelines. If such companion diagnostics fail to gain market acceptance, it would have an adverse effect on Syros' ability to derive revenues from sales, if any, of any of Syros' product candidates that are approved for commercial sale. In addition, any companion diagnostic collaborator or third party with whom Syros contracts may decide not to commercialize or to discontinue selling or manufacturing the companion diagnostic that Syros anticipates using in connection with development and commercialization of its product candidates, or Syros' relationship with such collaborator or third party may otherwise terminate. Syros may not be able to enter into arrangements with another provider to obtain supplies of an alternative diagnostic test for use in connection with the development and commercialization of its product candidates or do so on commercially reasonable terms, which could adversely affect and/or delay the development or commercialization of its product candidates.

Failure to obtain marketing approval in foreign jurisdictions would prevent Syros' product candidates from being marketed abroad. Any approval Syros is granted for its product candidates in the United States would not assure approval of its product candidates in foreign jurisdictions.

In order to market and sell Syros' products in the European Union and other foreign jurisdictions, Syros, and any collaborators, must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The marketing approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the United States, a product must be approved for reimbursement before the product can be approved for sale in that country. Syros, and any collaborators, may not obtain approvals from regulatory authorities outside the United States on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. Syros may file for marketing approvals but not receive necessary approvals to commercialize its products in any market.

In many countries outside the United States, a product candidate must also be approved for reimbursement before it can be sold in that country. In some cases, the price that Syros intends to charge for its products, if approved, is also subject to approval. Obtaining non-U.S. regulatory approvals and compliance with non-U.S. regulatory requirements could result in significant delays, difficulties and costs for Syros and any collaborators and could delay or prevent the introduction of Syros' product candidates in certain countries. In addition, if Syros or any collaborators fail to obtain the non-U.S. approvals required to market Syros' product candidates outside the United States or if Syros or any collaborators fail to comply with applicable non-U.S. regulatory requirements, Syros' target market will be reduced and its ability to realize the full market potential of its product candidates will be harmed and its business, financial condition, results of operations and prospects may be adversely affected.

Additionally, Syros could face heightened risks with respect to seeking marketing approval in the United Kingdom as a result of the recent withdrawal of the United Kingdom from the European Union, commonly referred to as Brexit. Effective January 1, 2021, the United Kingdom is no longer part of the European Single Market and European Union Customs Union. Since the regulatory framework for pharmaceutical products in the United Kingdom covering the quality, safety, and efficacy of pharmaceutical products, clinical trials, marketing authorization, commercial sales, and distribution of pharmaceutical products is derived from European Union directives and regulations, the consequences of Brexit and the impact the future regulatory regime that applies to products and the approval of product candidates in the United Kingdom remains unclear. As of January 1, 2021, the Medicines and Healthcare products Regulatory Agency, or the MHRA, became responsible for supervising medicines and medical devices in Great Britain, comprising England, Scotland and Wales under domestic law, whereas Northern Ireland will continue to be subject to European Union rules under the Northern Ireland Protocol. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, may force Syros to restrict or delay efforts to seek regulatory approval in the United Kingdom for its product candidates, which could significantly and materially harm its business.

Syros, or any collaborators, may not be able to obtain orphan drug designation or orphan drug exclusivity for Syros' product candidates and, even if Syros does, that exclusivity may not prevent the FDA or the EMA from approving competing products.

Regulatory authorities in some jurisdictions, including the United States and Europe, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is a drug intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals annually in the United States. Generally, a product with orphan drug designation only becomes entitled to orphan drug exclusivity if it receives the first marketing

approval for the indication for which it has such designation, in which case the FDA or the EMA will be precluded from approving another marketing application for the same product for that indication for the applicable exclusivity period. The applicable exclusivity period is seven years in the United States and ten years in Europe. The European exclusivity period can be reduced to six years if a product no longer meets the criteria for orphan drug designation or if the product is sufficiently profitable so that market exclusivity is no longer justified.

Syros has obtained orphan drug designation for tamibarotene for the treatment of MDS in the United States, and for the treatment of AML in the United States and in Europe. In addition, the EMA has issued a positive opinion on our application for orphan drug designation for tamibarotene for the treatment of MDS in Europe. SY-2101 has also received orphan drug designation for the treatment of APL in the United States, and for the treatment of AML in Europe. In the future, Syros or any collaborators may seek orphan drug designations for tamibarotene or SY-2101 in other indications or territories or for other product candidates and may be unable to obtain such designations. Even if Syros does secure such designations and orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different products can be approved for the same condition. Further, the FDA can subsequently approve the same drug for the same condition if the FDA concludes that the later product is clinically superior in that it is shown to be safer, to be more effective or to make a major contribution to patient care. Finally, orphan drug exclusivity may be lost if the FDA or the EMA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the product to meet the needs of patients with the rare disease or condition.

The FDA may further reevaluate the Orphan Drug Act and its regulations and policies. This may be particularly true in light of a decision from the Court of Appeals for the 11th Circuit in September 2021 finding that, for the purpose of determining the scope of exclusivity, the term “same disease or condition” means the designated “rare disease or condition” and could not be interpreted by the Agency to mean the “indication or use.” Syros does not know if, when, or how the FDA may change the orphan drug regulations and policies in the future, and it is uncertain how any changes might affect Syros’ business. Depending on what changes the FDA may make to its orphan drug regulations and policies, Syros’ business could be adversely impacted.

Any product candidate for which Syros or its collaborators obtain marketing approval is subject to ongoing regulation and could be subject to restrictions or withdrawal from the market, and Syros may be subject to substantial penalties if it fails to comply with regulatory requirements, when and if any of its product candidates are approved.

Any product candidate for which Syros or its collaborators obtain marketing approval will be subject to continual requirements of and review by the FDA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, cGMP requirements relating to quality control and manufacturing, quality assurance and corresponding maintenance of records and documents, and requirements regarding the distribution of samples to physicians and recordkeeping. In addition, the approval may be subject to limitations on the indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the medicine, including the requirement to implement a risk evaluation and mitigation strategy, or REMS. Accordingly, if Syros receives marketing approval for one or more of its product candidates, Syros would continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production, product surveillance and quality control. If Syros fails to comply with these requirements, Syros could have the marketing approvals for its products withdrawn by regulatory authorities and Syros’ ability to market any products could be limited, which could adversely affect its ability to achieve or sustain profitability.

Syros and its collaborators must also comply with requirements concerning advertising and promotion for any of Syros’ product candidates for which it obtains marketing approval. Promotional communications with respect to prescription products are subject to a variety of legal and regulatory restrictions and must be consistent with the

information in the product's approved labeling. Thus, Syros will not be able to promote any products it develops for indications or uses for which they are not approved.

The FDA and other agencies, including the U.S. Department of Justice, or the DOJ, closely regulate and monitor the post-approval marketing and promotion of products to ensure that they are marketed and distributed only for the approved indications and in accordance with the provisions of the approved labeling. Violations of the FDCA and other statutes, including the False Claims Act, relating to the promotion and advertising of prescription products may lead to investigations and enforcement actions alleging violations of federal and state health care fraud and abuse laws, as well as state consumer protection laws.

Failure to comply with regulatory requirements, may yield various results, including:

- restrictions on such products, manufacturers or manufacturing processes;
- restrictions on the labeling or marketing of a product;
- restrictions on distribution or use of a product;
- requirements to conduct post-marketing studies or clinical trials;
- warning letters or untitled letters;
- withdrawal of the products from the market;
- refusal to approve pending applications or supplements to approved applications that Syros submits;
- recall of products;
- damage to relationships with collaborators;
- unfavorable press coverage and damage to Syros' reputation;
- fines, restitution or disgorgement of profits or revenues;
- suspension or withdrawal of marketing approvals;
- refusal to permit the import or export of Syros' products;
- product seizure;
- injunctions or the imposition of civil or criminal penalties; and
- litigation involving patients using Syros' products.

Non-compliance with EU requirements regarding safety monitoring or pharmacovigilance, and with requirements related to the development of products for the pediatric population, can also result in significant financial penalties. Similarly, failure to comply with the EU's requirements regarding the protection of personal information can also lead to significant penalties and sanctions.

Syros may seek certain designations for its product candidates, including Breakthrough Therapy and Fast Track designations, but it might not receive such designations, and even if it does, such designations may not lead to a faster development or regulatory review or approval process.

Syros may seek certain designations for one or more of its product candidates that could expedite review and approval by the FDA. A Breakthrough Therapy product is defined as a product that is intended, alone or in combination with one or more other products, to treat a serious condition, and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For products that have been designated as Breakthrough Therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens. Products designated as Breakthrough Therapies by

the FDA may also be eligible for priority review if supported by clinical data at the time the NDA is submitted to the FDA.

The FDA may also designate a product for Fast Track review if it is intended, whether alone or in combination with one or more other products, for the treatment of a serious or life-threatening disease or condition, and it demonstrates the potential to address unmet medical needs for such a disease or condition. For Fast Track products, sponsors may have greater interactions with the FDA and the FDA may initiate review of sections of a Fast Track product's application before the application is complete. This rolling review may be available if the FDA determines, after preliminary evaluation of clinical data submitted by the sponsor, that a Fast Track product may be effective. The sponsor must also provide, and the FDA must approve, a schedule for the submission of the remaining information and the sponsor must pay applicable user fees.

Designation as a Breakthrough Therapy or Fast Track is within the discretion of the FDA. Accordingly, even if Syros believes that one of its product candidates meets the criteria for these designations, the FDA may disagree and instead determine not to make such designation. Further, even if Syros receives Breakthrough Therapy or Fast Track designation, the receipt of such designation for a product candidate may not result in a faster development or regulatory review or approval process compared to products considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of Syros' product candidates qualifies for these designations, the FDA may later decide that the product candidates no longer meet the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

Inadequate funding for the FDA, the SEC and other government agencies, including from government shut downs, or other disruptions to these agencies' operations, could hinder their ability to hire and retain key leadership and other personnel, prevent new products and services from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal business functions on which the operation of Syros' business may rely, which could negatively impact Syros' business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory and policy changes. Average review times at the agency have fluctuated in recent years as a result. Disruptions at the FDA and other agencies may also slow the time necessary for new product candidates to be reviewed and/or approved by necessary government agencies, which would adversely affect Syros' business. In addition, government funding of the SEC and other government agencies on which Syros' operations may rely, including those that fund research and development activities, is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA and other agencies may also slow the time necessary for new product candidates to be reviewed and/or approved by necessary government agencies, which would adversely affect Syros' business. For example, over the last several years the U.S. government has shut down several times and certain regulatory agencies, such as the FDA and the SEC, have had to furlough critical FDA, SEC and other government employees and stop critical activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process Syros' regulatory submissions, which could have a material adverse effect on Syros' business. Further, future government shutdowns could impact Syros' ability to access the public markets and obtain necessary capital in order to properly capitalize and continue its operations.

Separately, in response to the COVID-19 pandemic, a number of companies announced receipt of complete response letters due to the FDA's inability to complete required inspections for their applications. As of May 26, 2021, the FDA noted it was continuing to ensure timely reviews of applications for medical products during the ongoing COVID-19 pandemic in line with its user fee performance goals and conducting mission critical domestic and foreign inspections to ensure compliance of manufacturing facilities with FDA quality standards. However, the FDA may not be able to continue its current pace and review timelines could be extended,

including where a pre-approval inspection or an inspection of clinical sites is required and due to the ongoingCOVID-19 pandemic and travel restrictions, the FDA is unable to complete such required inspections during the review period. Regulatory authorities outside the U.S. may adopt similar restrictions or other policy measures in response to the COVID-19 pandemic and may experience delays in their regulatory activities. If a prolonged government shutdown or other disruption occurs, it could significantly impact the ability of the FDA to timely review and process Syros' regulatory submissions, which could have a material adverse effect on Syros' business. Future shutdowns or other disruptions could also affect other government agencies such as the SEC, which may also impact Syros' business by delaying review of Syros' public filings, to the extent such review is necessary, and its ability to access the public markets.

Current and future legislation may result in more rigorous coverage and reimbursement criteria for product candidates, which could increase the difficulty and cost for Syros and any collaborators to obtain marketing approval of Syros' product candidates.

In the United States and foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of Syros' product candidates, restrict or regulate post-approval activities and affect its ability to profitably sell any product candidates for which Syros obtains marketing approval.

In March 2010, President Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively the ACA.

In addition, other legislative changes have been proposed and adopted since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. These changes included aggregate reductions to Medicare payments to providers of up to 2% per fiscal year which went into effect in April 2013 and will remain in effect through 2031 under the Coronavirus Aid, Relief, and Economic Security Act, or the CARES Act. The American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices Syros may obtain for any of its product candidates for which Syros may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used.

Since enactment of the ACA, there have been and continue to be, numerous legal challenges and Congressional actions to repeal and replace provisions of the law. For example, with enactment of the Tax Cuts and Jobs Act, or the Tax Act, Congress repealed the "individual mandate." The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, became effective in 2019. Further, on December 14, 2018, a U.S. District Court judge in the Northern District of Texas ruled that the individual mandate portion of the ACA is an essential and inseverable feature of the ACA and therefore because the mandate was repealed as part of the Tax Act, the remaining provisions of the ACA are invalid as well. The U.S. Supreme Court heard this case on November 10, 2020 and on June 17, 2021, dismissed this action after finding that the plaintiffs do not have standing to challenge the constitutionality of the ACA. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

The Trump administration also took executive actions to undermine or delay implementation of the ACA, including directing federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. On January 28, 2021, however, President Biden issued a new Executive Order which directs federal agencies to reconsider rules and other policies that limit Americans' access to health

care, and consider actions that will protect and strengthen that access. Under this Executive Order, federal agencies are directed to re-examine: policies that undermine protections for people with pre-existing conditions, including complications related to COVID-19; demonstrations and waivers under Medicaid and the ACA that may reduce coverage or undermine the programs, including work requirements; policies that undermine the Health Insurance Marketplace or other markets for health insurance; policies that make it more difficult to enroll in Medicaid and the ACA; and policies that reduce affordability of coverage or financial assistance, including for dependents.

The Tax Act, as amended by the CARES Act, additionally contains changes in tax law that could adversely affect Syros' business or financial condition. The Tax Act contains significant changes to corporate taxation, including a reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, the limitation of the tax deduction for net interest expense to 30% of adjusted taxable income (except for certain small businesses), the limitation of the deduction for net operating losses to 80% of current year taxable income and elimination of net operating loss carrybacks, in each case, for losses arising in taxable years beginning after December 31, 2017 (though any such net operating losses may be carried forward indefinitely and such net operating losses arising in taxable years beginning before January 1, 2021 are generally eligible to be carried back up to five years), one-time taxation of offshore earnings at reduced rates regardless of whether they are repatriated, the elimination of U.S. tax on foreign earnings (subject to certain important exceptions), the allowance of immediate deductions for certain new investments instead of deductions for depreciation expense over time, and the modification or repeal of many business deductions and credits. In addition to the CARES Act, as part of Congress' response to the COVID-19 pandemic, economic relief legislation has been enacted in 2020 and 2021 containing tax provisions. Regulatory guidance under the Tax Act and such additional legislation is and continues to be forthcoming, and such guidance could ultimately increase or lessen the impact of these laws on Syros' business and financial condition. Also, as a result of the changes in the U.S. presidential administration and control of the U.S. Senate, additional tax legislation may be enacted; any such additional legislation could have an impact on Syros.

Current laws, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that Syros, or any collaborators, may receive for any approved products. If reimbursement of Syros' products is unavailable or limited in scope or amount, its business could be materially harmed.

Current and future legislation designed to reduce prescription drug costs may affect the prices Syros and any collaborators may obtain for Syros' product candidates.

The prices of prescription pharmaceuticals have also been the subject of considerable discussion in the United States. There have been several recent U.S. congressional inquiries, as well as proposed and enacted state and federal legislation designed to, among other things, bring more transparency to pharmaceutical pricing, review the relationship between pricing and manufacturer patient programs, and reduce the costs of pharmaceuticals under Medicare and Medicaid. In 2020, President Trump issued several executive orders intended to lower the costs of prescription products and certain provisions in these orders have been incorporated into regulations. These regulations include an interim final rule implementing a most favored nation model for prices that would tie Medicare Part B payments for certain physician-administered pharmaceuticals to the lowest price paid in other economically advanced countries, effective January 1, 2021. That rule, however, has been subject to a nationwide preliminary injunction and, on December 29, 2021, the Centers for Medicare & Medicaid Services, or CMS, issued a final rule to rescind it. With issuance of this rule, CMS stated that it will explore all options to incorporate value into payments for Medicare Part B pharmaceuticals and improve beneficiaries' access to evidence-based care.

In addition, in October 2020, U.S. Department of Health and Human Services, or HHS, and the FDA published a final rule allowing states and other entities to develop a Section 804 Importation Program, or SIP, to import certain prescription drugs from Canada into the United States. The final rule is currently the subject of ongoing

litigation, but at least six states (Vermont, Colorado, Florida, Maine, New Mexico, and New Hampshire) have passed laws allowing for the importation of drugs from Canada with the intent of developing SIPs for review and approval by the FDA. Further, on November 20, 2020, HHS finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The implementation of the rule has been delayed by the Biden administration from January 1, 2022 to January 1, 2023 in response to ongoing litigation. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a new safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers, the implementation of which have also been delayed by the Biden administration until January 1, 2023.

At the state level, legislatures are increasingly passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional health care authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other health care programs. These measures could reduce the ultimate demand for Syros' products, once approved, or put pressure on its product pricing. Syros expects that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for Syros' product candidates or additional pricing pressures.

Finally, outside the United States, in some nations, including those of the European Union, the pricing of prescription pharmaceuticals is subject to governmental control and access. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, Syros, or its collaborators may be required to conduct a clinical trial that compares the cost-effectiveness of Syros' product to other available therapies. If reimbursement of Syros' products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, its business could be materially harmed.

Syros may be subject to certain healthcare laws and regulations, which could expose it to criminal sanctions, civil penalties, contractual damages, reputational harm, fines, disgorgement, exclusion from participation in government healthcare programs, curtailment or restricting of its operations, and diminished profits and future earnings.

Healthcare providers, third-party payors and others will play a primary role in the recommendation and prescription of any products for which Syros obtains marketing approval. Syros' future arrangements with healthcare providers and third-party payors will expose it to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which Syros markets, sells and distributes any products for which it obtains marketing approval. Potentially applicable U.S. federal and state healthcare laws and regulations include the following:

Anti-Kickback Statute. The federal Anti-Kickback Statute prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under federal healthcare programs such as Medicare and Medicaid;

False Claims Laws. The federal false claims laws, including the civil False Claims Act, impose criminal and civil penalties, including those from civil whistleblower or *qui tam* actions against individuals or entities for knowingly presenting, or causing to be presented to the federal government, claims for payment that are false or

fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government;

HIPAA. The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for executing or attempting to execute a scheme to defraud any healthcare benefit program;

HIPAA and HITECH. HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or the HITECH Act, also imposes obligations on certain types of individuals and entities, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information. While these provisions likely will not apply to Syros directly, they will apply to many of Syros' partners and other entities assisting with its clinical trials and future activities, and therefore may impact its relationships with these entities and related costs;

False Statements Statute. The federal false statements statute prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services;

Transparency Requirements. The federal Physician Payments Sunshine Act requires certain manufacturers of drugs, devices, biologics, and medical supplies for which payment is available under Medicare, Medicaid, or the Children's Health Insurance Program, with specific exceptions, to report annually to HHS information related to payments and other transfers of value, including ownership and investment interests, to physicians and other healthcare providers; and

Analogous State and Foreign Laws. Analogous state laws and regulations, such as state anti-kickback and false claims laws, and transparency laws, may apply to sales or marketing arrangements, and claims involving healthcare items or services reimbursed by non-governmental third party payors, including private insurers, and some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, in addition to requiring drug manufacturers to report information related to payments to physicians and other healthcare providers or marketing expenditures. Many state laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts. Foreign laws also govern the privacy and security of health information in many circumstances.

Efforts to ensure that Syros' business arrangements with third parties, and its business generally, will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that Syros' business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If Syros' operations are found to be in violation of any of these laws or any other governmental regulations that may apply to it, Syros may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, exclusion of products from government funded healthcare programs, such as Medicare and Medicaid, disgorgement, contractual damages, and reputational harm, any of which could substantially disrupt Syros' operations. If any of the physicians or other providers or entities with whom Syros expects to do business is found not to be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

Compliance with global privacy and data security requirements could result in additional costs and liabilities to Syros or inhibit its ability to collect and process data globally, and the failure to comply with such requirements could subject Syros to significant fines and penalties, which may have a material adverse effect on its business, financial condition or results of operations.

The regulatory framework for the collection, use, safeguarding, sharing, transfer and other processing of information worldwide is rapidly evolving and is likely to remain uncertain for the foreseeable future. Globally,

virtually every jurisdiction in which Syros operates has established its own data security and privacy frameworks with which Syros must comply.

For example, the collection, use, disclosure, transfer, or other processing of personal data regarding individuals in the European Union, including personal health data, is subject to EU General Data Protection Regulation, or the GDPR, which applies to all member states of the European Economic Area, or EEA. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data. The GDPR imposes significant obligations on Syros with respect to clinical trials conducted in the EEA. In addition, the GDPR also imposes strict rules on the transfer of personal data to countries outside the European Union, including the United States and, as a result, increases the scrutiny that clinical trial sites located in the EEA should apply to transfers of personal data from such sites to countries that are considered to lack an adequate level of data protection, such as the United States. The scope of contractual and data security protections required for these transfers is undergoing ongoing evolution, and likely will increase Syros' costs of contracting with service providers and partners as well as Syros' own data security requirements. The GDPR also permits data protection authorities to require destruction of improperly gathered or used personal information and/or impose substantial fines for violations of GDPR, and it also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies and obtain compensation for damages resulting from violations of GDPR. In addition, the GDPR provides that EU member states may make their own further laws and regulations limiting the processing of personal data, including genetic, biometric or health data. As with other issues related to Brexit, there are open questions about how personal data will be protected in the United Kingdom and whether personal information can transfer from the European Union to the United Kingdom. Following the withdrawal of the United Kingdom from the European Union, the U.K. Data Protection Act 2018 applies to the processing of personal data that takes place in the United Kingdom and includes parallel obligations to those set forth by GDPR. While the Data Protection Act of 2018 in the United Kingdom that "implements" and complements the GDPR has achieved Royal Assent on May 23, 2018 and is now effective in the United Kingdom, it is still unclear whether transfer of data from the EEA to the United Kingdom will remain lawful under the GDPR. The United Kingdom government has already determined that it considers all European Union and EEA member states to be adequate for the purposes of data protection, ensuring that data flows from the United Kingdom to the European Union/EEA remain unaffected. In addition, a recent decision from the European Commission appears to deem the United Kingdom as being "essentially adequate" for purposes of data transfer from the European Union to the United Kingdom, although this decision may be re-evaluated in the future.

Beyond the GDPR, there are privacy and data security laws in a growing number of countries around the world. While many loosely follow the GDPR as a model, other laws contain different or conflicting provisions. These laws will impact Syros' ability to conduct its business activities, including both its clinical trials and any eventual sale and distribution of commercial products.

Given the breadth and depth of changes in data protection obligations, complying with the GDPR's requirements is rigorous and time intensive and requires significant resources and a review of Syros' technologies, systems and practices, as well as those of any third-party collaborators, service providers, contractors or consultants that process or transfer personal data collected in the European Union. The GDPR and other changes in laws or regulations associated with the enhanced protection of certain types of sensitive data, such as healthcare data or other personal information from Syros' clinical trials, could require Syros to change its business practices and put in place additional compliance mechanisms, may interrupt or delay Syros' development, regulatory and commercialization activities and increase Syros' cost of doing business, and could lead to government enforcement actions, private litigation and significant fines and penalties against it and could have a material adverse effect on its business, financial condition or results of operations. Similarly, failure to comply with international, federal and state laws regarding privacy and security of personal information could expose Syros to fines and penalties under such laws. Even if Syros is not determined to have violated these laws, government investigations into these issues typically require the expenditure of significant resources and generate negative publicity, which could harm its reputation and its business.

Similar privacy and data security requirements are either in place or underway in the United States. There are a broad variety of data protection laws that are applicable to Syros' activities now or that will be in the future, and a wide range of enforcement agencies at both the state and federal levels that can review companies for privacy and data security concerns based on general consumer protection laws. The Federal Trade Commission and state Attorneys General all are aggressive in reviewing privacy and data security protections for consumers. New laws also are being considered at both the state and federal levels. For example, the California Consumer Privacy Act, or the CCPA, which went into effect on January 1, 2020, is creating similar risks and obligations as those created by GDPR, though the CCPA does exempt certain information collected as part of a clinical trial subject to the Federal Policy for the Protection of Human Subjects (the Common Rule). The CCPA already has been revised through the California Privacy Rights Act, or the CPRA, which will significantly expand the CCPA to incorporate additional provisions including requiring that the use, retention and sharing of personal information of California residents be reasonably necessary and proportionate to the purposes of collection or processing, granting additional protections for sensitive personal information, and requiring greater disclosures related to notice to residents regarding retention of information. Virginia and Colorado also have already passed similar laws. Many other states are considering similar legislation. A broad range of legislative measures also have been introduced at the federal level. Accordingly, failure to comply with current and any future federal and state laws regarding privacy and security of personal information could expose Syros to fines and penalties. Syros also faces a threat of consumer class actions related to these laws and the overall protection of personal data. Even if Syros is not determined to have violated these laws, government investigations into these issues typically require the expenditure of significant resources and generate negative publicity, which could harm Syros' reputation and its business. Moreover, these laws create substantial complications for any business, particularly for one that deals with health information, and these laws likely will increase Syros' operating costs and the costs needed for both compliance and negotiation of agreements with service providers, customers and others.

In addition to the foregoing, any breach of privacy laws or data security laws, particularly one resulting in a significant security incident or breach involving the misappropriation, loss or other unauthorized use or disclosure of sensitive or confidential patient or consumer information, could have a material adverse effect on Syros' business, reputation and financial condition. As a data controller, Syros will be accountable for any third-party service providers it engages to process personal data on Syros' behalf, including its CROs. There is no assurance that privacy and security-related safeguards Syros implements will protect it from all risks associated with the third-party processing, storage and transmission of such information. In certain situations, both in the United States and in other countries, Syros also may be obligated as a result of a security breach to notify individuals and/or government entities about these breaches.

Syros is subject to U.S. and foreign anti-corruption and anti-money laundering laws with respect to its operations and non-compliance with such laws can subject it to criminal and/or civil liability and harm its business.

Syros is subject to the U.S. Foreign Corrupt Practices Act of 1977, as amended, or the FCPA, the U.S. domestic bribery statute contained in 18 U.S.C. § 201, the U.S. Travel Act, the USA PATRIOT Act, and possibly other state and national anti-bribery and anti-money laundering laws in countries in which Syros conducts activities. Anti-corruption laws are interpreted broadly and prohibit companies and their employees, agents, third-party intermediaries, joint venture partners and collaborators from authorizing, promising, offering, or providing, directly or indirectly, improper payments or benefits to recipients in the public or private sector. Syros may have direct or indirect interactions with officials and employees of government agencies or government-affiliated hospitals, universities, and other organizations. In addition, Syros may engage third party intermediaries to promote its clinical research activities abroad and/or to obtain necessary permits, licenses, and other regulatory approvals. Syros can be held liable for the corrupt or other illegal activities of these third-party intermediaries, its employees, representatives, contractors, partners, and agents, even if Syros does not explicitly authorize or have actual knowledge of such activities.

Syros has adopted a Code of Business Conduct and Ethics that mandates compliance with the FCPA and other anti-corruption laws applicable to its business throughout the world. Syros cannot assure you, however, that its

employees and third-party intermediaries will comply with this code or such anti-corruption laws. Noncompliance with anti-corruption and anti-money laundering laws could subject Syros to whistleblower complaints, investigations, sanctions, settlements, prosecution, other enforcement actions, disgorgement of profits, significant fines, damages, other civil and criminal penalties or injunctions, suspension and/or debarment from contracting with certain persons, the loss of export privileges, reputational harm, adverse media coverage, and other collateral consequences. If any subpoenas, investigations, or other enforcement actions are launched, or governmental or other sanctions are imposed, or if Syros does not prevail in any possible civil or criminal litigation, its business, results of operations and financial condition could be materially harmed. In addition, responding to any action will likely result in a materially significant diversion of management's attention and resources and significant defense and compliance costs and other professional fees. In certain cases, enforcement authorities may even cause Syros to appoint an independent compliance monitor which can result in added costs and administrative burdens.

Syros is subject to governmental export and import controls that could impair its ability to compete in international markets due to licensing requirements and subject Syros to liability if it is not in compliance with applicable laws.

Syros' products and solutions are subject to export control and import laws and regulations, including the U.S. Export Administration Regulations, U.S. Customs regulations, and various economic and trade sanctions regulations administered by the U.S. Treasury Department's Office of Foreign Assets Controls. Exports of Syros' products and solutions outside of the United States must be made in compliance with these laws and regulations. If Syros fails to comply with these laws and regulations, Syros and certain of its employees could be subject to substantial civil or criminal penalties, including the possible loss of export or import privileges; fines, which may be imposed on Syros and responsible employees or managers; and, in extreme cases, the incarceration of responsible employees or managers.

In addition, changes in Syros' products or solutions or changes in applicable export or import laws and regulations may create delays in the introduction, provision, or sale of its products and solutions in international markets, prevent customers from using its products and solutions or, in some cases, prevent the export or import of its products and solutions to certain countries, governments or persons altogether. Any limitation on Syros' ability to export, provide, or sell its products and solutions could adversely affect its business, financial condition and results of operations.

If Syros fails to comply with environmental, health and safety laws and regulations, Syros could become subject to fines or penalties or incur costs that could harm its business.

Syros is subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. From time to time and in the future, Syros' operations may involve the use of hazardous and flammable materials, including chemicals and biological materials, and may also produce hazardous waste products. Even if Syros contracts with third parties for the disposal of these materials and waste products, it cannot completely eliminate the risk of contamination or injury resulting from these materials. In the event of contamination or injury resulting from the use or disposal of Syros' hazardous materials, it could be held liable for any resulting damages, and any liability could exceed its resources. Syros also could incur significant costs associated with civil or criminal fines and penalties for failure to comply with such laws and regulations.

Syros maintains workers' compensation insurance to cover it for costs and expenses it may incur due to injuries to its employees resulting from the use of hazardous materials, but this insurance may not provide adequate coverage against potential liabilities. Syros does not, however, maintain insurance for environmental liability or toxic tort claims that may be asserted against it.

In addition, Syros may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. Current or future environmental laws and regulations may impair Syros' research,

development or production efforts. In addition, failure to comply with these laws and regulations may result in substantial fines, penalties or other sanctions.

Unfavorable global economic conditions could adversely affect Syros' business, financial condition or results of operations.

Syros' results of operations could be adversely affected by general conditions in the global economy and in the global financial markets. The most recent global financial crisis caused extreme volatility and disruptions in the capital and credit markets, and it is unclear what impact the decision by the United Kingdom to leave the European Union will have on the global economy. A severe or prolonged economic downturn, such as the most recent global financial crisis, could result in a variety of risks to Syros' business, including weakened demand for its product candidates and its ability to raise additional capital when needed on acceptable terms, if at all. A weak or declining economy could strain Syros' suppliers, possibly resulting in supply disruption, or cause delays in payments for Syros' services by third-party payors or Syros' collaborators. Any of the foregoing could harm Syros' business and it cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact its business.

Syros' internal computer systems, or those of any collaborators or contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of Syros' product development programs.

Despite the implementation of security measures and certain data recovery measures, Syros' internal computer systems and those of its current and any future collaborators and other contractors or consultants are vulnerable to damage from cyber-attacks, computer viruses, unauthorized access, sabotage, natural disasters, terrorism, war and telecommunication and electrical failures. Syros has experienced, and may experience in the future, security breaches of its information technology systems. Any system failure, accident or security breach that causes interruptions in Syros' operations, for it or those third parties with which Syros contracts, could result in a material disruption of Syros' product development programs and its business operations, whether due to a loss of Syros' trade secrets or other proprietary information or other similar disruptions, in addition to possibly requiring substantial expenditures of resources to remedy. For example, the loss of clinical trial data from an ongoing, completed or future clinical trial could result in delays in Syros' regulatory approval efforts and significantly increase Syros' costs to recover or reproduce the data. To the extent that any disruption or security breach results in a loss of, or damage to, Syros' data or applications, or inappropriate disclosure of confidential or proprietary information, Syros may incur liabilities, its competitive position could be harmed and the further development and commercialization of its product candidates may be delayed. In addition, Syros may not have adequate insurance coverage to provide compensation for any losses associated with such events.

Syros could be subject to risks caused by misappropriation, misuse, leakage, falsification or intentional or accidental release or loss of information maintained in the information systems and networks of its company, including personal information of its employees. In addition, outside parties have attempted, and may in the future attempt, to penetrate Syros' systems or those of its vendors or fraudulently induce its employees or employees of its vendors to disclose sensitive information to gain access to Syros' data. Like other companies, Syros may experience threats to its data and systems, including malicious codes and viruses, and other cyber-attacks. The number and complexity of these threats continue to increase over time. If a material breach of Syros' security or that of its vendors occurs, the market perception of the effectiveness of Syros' security measures could be harmed, Syros could lose business and its reputation and credibility could be damaged. Syros could be required to expend significant amounts of money and other resources to repair or replace information systems or networks. Although Syros develops and maintains systems and controls designed to prevent these events from occurring, and Syros has a process to identify and mitigate threats, the development and maintenance of these systems, controls and processes is costly and requires ongoing monitoring and updating as technologies change and efforts to overcome security measures become more sophisticated. Moreover, despite Syros' efforts, the possibility of these events occurring cannot be eliminated entirely.

Syros' employees may engage in misconduct or other improper activities, includingnon-compliance with regulatory standards and requirements, which could cause significant liability for Syros and harm its reputation.

Syros is exposed to the risk of employee fraud or other misconduct, including intentional failures to comply with FDA regulations or similar regulations of comparable foreign regulatory authorities, provide accurate information to the FDA or comparable foreign regulatory authorities, comply with manufacturing standards Syros has established, comply with federal and state healthcare fraud and abuse laws and regulations and similar laws and regulations established and enforced by comparable foreign regulatory authorities, report financial information or data accurately or disclose unauthorized activities to Syros. Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to Syros' reputation. It is not always possible to identify and deter employee misconduct, and the precautions Syros takes to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting Syros from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws, standards or regulations. If any such actions are instituted against Syros, and it is not successful in defending itself or asserting its rights, those actions could have a significant impact on its business and results of operations, including the imposition of significant fines or other sanctions.

Risks Related to Syros' Business Operations, Employee Matters and Managing Growth

Syros' future success depends on its ability to attract and retain key management and scientists, development, medical and commercial staff, consultants and advisors.

Syros' ability to compete in the biotechnology and pharmaceuticals industries depends upon its ability to attract and retain highly qualified managerial, scientific and medical personnel. Syros is highly dependent on the pharmaceutical research and development and business development expertise of Nancy Simonian, M.D., its president and chief executive officer; Conley Chee, its chief commercial officer; Jason Haas, its chief financial officer; Eric R. Olson, Ph.D., its chief scientific officer; David A. Roth, M.D., its chief medical officer; and Kristin Stephens, its chief development officer. Each member of Syros' management team is employed "at will," meaning any of them may terminate his or her employment with Syros at any time with or without notice and for any reason or no reason. Syros also relies on consultants and advisors, including scientific and clinical advisors, to assist Syros in formulating its research and development and commercialization strategy.

Syros' industry has experienced a high rate of turnover of management, scientific, clinical, medical and commercial personnel in recent years. If Syros loses one or more of its executive officers or other key employees, its ability to implement its business strategy successfully could be seriously harmed. Replacing executive officers or other key employees may be difficult and may take an extended period of time because of the limited number of individuals in Syros' industry with the breadth of skills and experience required to develop, gain marketing approval of and commercialize products successfully. Syros faces intense competition for qualified individuals from numerous pharmaceutical and biotechnology companies, universities, governmental entities and other research institutions, many of which have substantially greater resources with which to attract and reward qualified individuals than Syros does. In addition, due to the risks associated with developing a new class of medicine, Syros may face additional challenges in attracting and retaining employees. If Syros is unable to continue to attract and retain highly qualified personnel, its ability to develop and commercialize its product candidates will be limited.

Syros expects to expand its organization, and as a result, Syros may encounter difficulties in managing its growth, which could disrupt its operations.

Syros expects to experience significant growth in the number of its employees and the scope of its operations, particularly in the areas of clinical development, drug manufacturing, regulatory affairs and sales, marketing and distribution. To manage these growth activities, Syros must continue to implement and improve its managerial,

operational and financial systems, expand its facilities and continue to recruit and train additional qualified personnel. Syros' management may need to devote a significant amount of its attention to managing these growth activities. Due to Syros' limited financial resources and the limited experience of its management team in managing a company with such anticipated growth, Syros may not be able to effectively manage the expansion or relocation of its operations, retain key employees, or identify, recruit and train additional qualified personnel. Syros' inability to manage the expansion or relocation of its operations effectively may result in weaknesses in its infrastructure, give rise to operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees. Syros' expected growth could also require significant capital expenditures and may divert financial resources from other projects, such as the development of additional product candidates. If Syros is unable to effectively manage its expected growth, its expenses may increase more than expected, its ability to generate revenues could be reduced and Syros may not be able to implement its business strategy, including the successful commercialization of its product candidates.

Syros may engage in acquisitions that could disrupt its business, cause dilution to its stockholders or reduce its financial resources.

In the future, Syros may enter into transactions to acquire other businesses, products or technologies. Because Syros has not made any acquisitions to date, its ability to do so successfully is unproven. If Syros does identify suitable candidates, it may not be able to make such acquisitions on favorable terms, or at all. Any acquisitions Syros makes may not strengthen its competitive position, and these transactions may be viewed negatively by customers or investors. Syros may decide to incur debt in connection with an acquisition or issue Syros common stock or other equity securities to the stockholders of the acquired company, which would reduce the percentage ownership of Syros' existing stockholders. Syros could incur losses resulting from undiscovered liabilities of the acquired business that are not covered by the indemnification Syros may obtain from the seller. In addition, Syros may not be able to successfully integrate the acquired personnel, technologies and operations into its existing business in an effective, timely and non-disruptive manner. Acquisitions may also divert management attention from day-to-day responsibilities, increase Syros' expenses and reduce its cash available for operations and other uses. Syros cannot predict the number, timing or size of future acquisitions or the effect that any such transactions might have on its operating results.

Syros' operations or those of the third parties upon whom Syros depends might be affected by the occurrence of a catastrophic event, such as a terrorist attack, war or other armed conflict, geopolitical tensions or trade wars, pandemic or natural disaster.

Syros depends on its employees, consultants, CROs, as well as regulatory agencies and other parties, for the continued operation of its business. Despite any precautions that Syros or any third parties on whom Syros depends take for catastrophic events, including terrorist attacks, wars or other armed conflicts, geopolitical tensions or trade wars, pandemics or natural disasters, these events could result in significant disruptions to Syros' research and development, manufacturing, preclinical studies, clinical trials, and, ultimately, if approved, the commercialization of its products. Long-term disruptions in the infrastructure caused by these types of events, such as natural disasters, which are increasing in frequency due to the impacts of climate change, the outbreak of wars or other armed conflicts, the escalation of hostilities, geopolitical tensions or trade wars, acts of terrorism or "acts of God," particularly involving geographies in which Syros or third parties on whom Syros depends have offices, manufacturing or clinical trial sites, could adversely affect Syros' businesses. Syros cannot be certain what the overall impact of such events will be on its business or on the business of any third parties on whom Syros depends. Although Syros carries business interruption insurance policies and typically have provisions in its contracts that protect it in certain events, Syros' coverage might not include or be adequate to compensate it for all losses that may occur. Any catastrophic event affecting Syros, its CROs, regulatory agencies or other parties with which Syros is engaged could have a material adverse effect on its operations and financial performance.

Risks Related to Tyme

Risks Related to the Proposed Merger

The announcement and pendency of the merger may result in disruptions to Tyme's business.

The Merger Agreement generally requires Tyme to operate its business in the ordinary course pending completion of the merger and restricts it from taking certain specified actions until the merger is completed or the Merger Agreement is terminated. These restrictions may affect Tyme's ability to execute its business strategies and attain product development and other goals and may impact its financial condition, results of operations and cash flows. Further, in connection with the merger, Tyme's current and prospective employees may experience uncertainty about their future roles with Tyme following the consummation of the merger, which may materially adversely affect its ability to attract, motivate and retain key personnel. Additionally, the pursuit of the merger may place a significant burden on Tyme management and internal resources, and will divert management's time and attention from its day-to-day operations and the execution of its other strategic initiatives. This could adversely affect Tyme's financial results. In addition, Tyme has incurred and will continue to incur other significant costs, expenses and fees for professional services and other transaction costs in connection with the merger, and many of these fees and costs are payable regardless of whether or not the merger is consummated. Any of the foregoing could adversely affect Tyme's business, its financial condition, and its results of operations.

Risks Related to Owning Tyme Stock

Each of Tyme's co-founders holds a substantial ownership interest in Tyme, which gives them the ability to influence certain decision making and Mr. Hoffman has certain rights to Tyme's IP that may allow them to use Tyme's IP in ways that could be inconsistent with Tyme's use.

Steve Hoffman, Tyme's former Chief Science Officer and current director, owned approximately 11.6% of Tyme's outstanding common stock as of June 30, 2022. Additionally, Michael Demurjian, Tyme's former Chief Operating Officer, also owned approximately 13.4% of Tyme's outstanding common stock as of June 30, 2022. As such, Mr. Hoffman and Mr. Demurjian will each be positioned to exercise significant influence over Tyme's affairs, including, but not limited to, electing members of Tyme's Board and exercising influence and voting rights in connection with structural defenses and anti-takeover measures, and fundamental corporate transactions, and they may seek action that may not reflect the best interests of all of the Tyme stockholders.

Tyme entered into voting agreements with Messrs. Hoffman and Demurjian on March 24, 2022 and April 18, 2022 respectively. Mr. Hoffman agreed to vote all shares of Tyme common stock beneficially owned by him in accordance with the Tyme board's recommendation with respect to any matter presented to the stockholders for a period of one year and Mr. Demurjian agreed to do so for a period of two years from the date of the agreement.

Additionally, Tyme has granted Mr. Hoffman perpetual, exclusive non-royalty bearing license rights with respect to certain patents and patent applications that Tyme uses for SM-88 in all fields other than in connection with the treatment of cancer. Further, in his employment agreement, Mr. Hoffman agreed that all IP he had developed during his employment with Tyme that related to Tyme's or any of its affiliates' businesses, research and development or existing products (or products under development) or services is the property of Tyme, but only with respect to the treatment of cancer in humans and certain other indications. Likewise, Mr. Demurjian agreed that all IP he had developed during his employment with Tyme is the property of Tyme, but only with respect to the treatment of cancer in humans.

The license to Mr. Hoffman may limit Tyme's ability to profit from alternative uses of SM-88, were such uses to be discovered. Further, the use of the patents or patent applications that are used for SM-88 or that otherwise overlap with Tyme's IP could be associated with a negative event outside of the control of Tyme and outside the treatment of cancer in humans, which, in either case, may have an adverse effect on Tyme's business.

Tyme's share price is likely to be volatile due to factors beyond Tyme's control and may drop below prices paid by investors; investors could lose all of their investment in Tyme.

All readers of this joint proxy statement/prospectus should consider an investment in Tyme's common stock as speculative, involving a high degree of risk, and invest in Tyme's common stock only if the purchaser can withstand a significant loss and wide fluctuations in the market value of an investment. Potential investors should be aware that the value of an investment in Tyme's may go down as well as up. In addition, there can be no certainty that the market value of an investment in Tyme's will fully reflect its underlying value.

Investors may be unable to sell their shares of Tyme's common stock at or above the price they paid for their shares due to fluctuations in the market price of Tyme's common stock arising from factors affecting Tyme's drug discovery and development objectives as well as changes in Tyme's operating performance or prospects. In addition, the stock market is subject to significant volatility, particularly with respect to pharmaceutical, biotechnology and other life sciences company stocks. The volatility of pharmaceutical, biotechnology and other life sciences company stocks often does not relate to the operating performance of the companies represented by the stock. Some of the factors that may cause the market price of Tyme's common stock to fluctuate include, but are not limited to:

- results and timing of Tyme's clinical trials and clinical trials of Tyme's competitors' products;
- the failure or discontinuation of clinical trials in which Tyme's product candidates are being studied or of any of Tyme's development programs;
- limitations on the availability of acceptable-quality clinical supplies or issues in manufacturing Tyme's drug candidates, the methoxsalen, phenytoin, and sirolimus, or MPS, components or any future drugs Tyme may develop and receive governmental approval to market;
- regulatory developments or enforcement in the United States andnon-U.S. countries with respect to Tyme's or Tyme's competitors' products;
- failure to achieve pricing and reimbursement levels expected by Tyme or the market;
- competition from existing products or new products that may emerge;
- developments or disputes concerning patents or other proprietary rights;
- introduction of technological innovations or new commercial products by Tyme or Tyme's competitors;
- announcements by Tyme, Tyme's collaborators or Tyme's competitors of significant acquisitions, strategic partnerships, joint ventures, collaborations, capital commitments or strategic reviews;
- changes in estimates or recommendations by securities analysts, to the extent any cover Tyme's common stock;
- fluctuations in the valuation of companies perceived by investors to be comparable to us;
- public concern over Tyme's drug candidates or any future drugs Tyme may develop and receive governmental approval to market;
- litigation or the threat of litigation;
- future issuances and sales of Tyme's common stock;
- share price and volume fluctuations attributable to inconsistent trading volume levels of Tyme's shares;
- additions or departures of key personnel;
- changes in the structure of healthcare payment systems in the United States or overseas;
- the failure of Tyme's drug candidates, if approved, or any other approved drug product Tyme may develop, to achieve commercial success;

- economic and other external factors or disasters, military conflicts or widespread health or other crises;
- period-to-period fluctuations in Tyme's financial condition and results of operations, including the timing of receipt of any milestone or other payments under commercialization or licensing agreements, if any;
- general market conditions and market conditions for biopharmaceutical stocks; and
- overall fluctuations in U.S. equity markets.

Due to these risks and the other risks described in this joint proxy statement/prospectus, investors could lose their entire investment in Tyme.

Tyme's common stock has historically been characterized by low and/or erratic trading volume, and the intraday per share price of Tyme's common stock has fluctuated from $0.28 to $2.02 between April 1, 2021 and March 31, 2022, the date of Tyme's last completed fiscal year.

As of July 31, 2017, Tyme's common stock became quoted on The Nasdaq Capital Market under the symbol "TYME." Historically, the public market for Tyme's common stock has been characterized by low and/or erratic trading volume, often resulting in price volatility. For the fiscal year ended March 31, 2022, the average daily trading volume for Tyme's common stock was approximately 2,883,757 shares. In addition, the price of Tyme's common stock has been volatile. Tyme's common stock had a closing price of $1.87 on April 1, 2021, and ended fiscal year 2022 at a closing price of $0.35. During the fiscal year 2022, Tyme's common stock had a low closing price of $0.2850, which occurred on March 15, 2022, and had a high closing price of $1.87, which occurred on April 1, 2021.

The market price of Tyme's common stock is subject to wide fluctuations due to a number of factors, including the results of preclinical and clinical testing of Tyme's products under development, Tyme's strategic plans regarding product development, decisions by collaborators regarding product development, regulatory developments, market conditions in the pharmaceutical and biotechnology industries, announcements concerning Tyme's competitors, adverse developments concerning proprietary rights, public concern as to the safety or commercial value of any products, impacts of public health crises, including the ongoing COVID-19 pandemic, and general economic conditions, many of which Tyme cannot control.

Furthermore, the stock market has experienced significant price and volume fluctuation unrelated to the operating performance of particular companies. These market fluctuations can adversely affect the market price and volatility of Tyme's common stock.

Tyme may be unable to regain and maintain compliance with The Nasdaq Capital Market continued listing requirements, which could cause Tyme's common stock to be delisted from The Nasdaq Capital Market. This could result in the lack of a market for Tyme's common stock, cause a decrease in the value of an investment in Tyme, and adversely affect Tyme's business, financial condition, and results of operations.

Tyme's common stock is currently listed on The Nasdaq Capital Market. To maintain the listing of Tyme's common stock on The Nasdaq Capital Market, Tyme is required to meet certain listing requirements, including, among others, a minimum closing bid price of $1.00 per share.

On December 22, 2021, Tyme received notice from The Nasdaq Capital Market that the closing bid price for Tyme's common stock had been below $1.00 per share for the previous 30 consecutive business days, and that Tyme is therefore not in compliance with the minimum bid price requirement for continued inclusion on The Nasdaq Capital Market under Nasdaq Listing Rule 5550(a)(2), or Rule 5550(a)(2). The Nasdaq Capital Market's notice has no immediate effect on the listing or trading of Tyme's common stock on The Nasdaq Capital Market.

The notice indicates that Tyme will have 180 calendar days, until June 20, 2022, to regain compliance with this requirement. Tyme can regain compliance with the $1.00 minimum bid listing requirement if the closing bid price of Tyme's common stock is at least $1.00 per share for a minimum of ten (10) consecutive business days during the 180-day compliance period. Tyme requested and was granted an additional180-day compliance period and now has until December 19, 2022 to regain compliance.

A delisting of Tyme's common stock could negatively impact Tyme by, among other things, reducing the liquidity and market price of Tyme's common stock and reducing the number of investors willing to hold or acquire shares, which would further restrict Tyme's ability to obtain equity financing. A suspension or delisting could also adversely affect Tyme's reputation, Tyme's relationships with Tyme's business partners and suppliers, which would have a material, adverse impact on Tyme's business, operating results and financial condition. In addition, a suspension or delisting would impair Tyme's ability to raise additional capital through equity or debt financing as well as Tyme's ability to attract and retain employees by means of equity compensation.

As of the date hereof, Tyme had not regained compliance with Rule 5550(a)(2). Tyme has asked its stockholders to approve an amendment to Tyme's Certificate of Incorporation to implement a reverse stock split in an effort to regain compliance with the $1.00 minimum bid listing requirement and avoid delisting.

Raising additional capital may cause dilution to Tyme's stockholders, restrict Tyme's operations or require Tyme to relinquish substantial rights.

Until such time, if ever, as Tyme can generate substantial revenue, Tyme expects to finance its cash needs through a combination of equity offerings, debt financings, grants and licensing and development agreements in connection with any collaborations. Tyme does not have any committed external source of funds and no revenue source. To the extent that Tyme raises additional capital through the sale of equity, equity-linked securities or convertible debt securities, as Tyme expects it will, then outstanding stockholders' ownership interests in Tyme will be diluted and the terms of these new securities may include liquidation or other preferences that adversely affect rights of holders of Tyme's common stock. For example, as further described in "*Tyme Business-Collaboration with Eagle Pharmaceuticals*" in this joint proxy statement/prospectus, in January 2020, Tyme entered into a securities purchase agreement with Eagle Pharmaceuticals, Inc., or Eagle, pursuant to which Eagle would be required, upon Tyme's achievement of certain milestone events, to purchase Series A Preferred Stock of Tyme that is convertible into common stock, which, upon conversion, if any, would result in additional dilution. Debt financing, if available at all, may involve agreements that include covenants limiting or restricting Tyme's ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. Tyme cannot give any assurance that it will be able to obtain additional funding if and when necessary or on satisfactory terms. If Tyme is unable to obtain adequate financing on a timely basis, it could be required to delay, scale back or eliminate one or more of its development programs or grant rights to develop and market product candidates that Tyme would otherwise prefer to develop and market on its own.

Future issuances of Tyme's common stock or rights to purchase Tyme's common stock pursuant to Tyme's equity incentive plan or outstanding options and warrants could result in additional dilution of the percentage ownership of Tyme's stockholders and could cause Tyme's share price to fall.

Tyme is authorized to grant equity awards, including stock grants and stock options, to Tyme's employees, directors and consultants, covering up to 12.5% of Tyme's shares of common stock outstanding from time to time pursuant to Tyme's 2015 Equity Incentive Plan, as amended, or the 2015 Plan, and up to 5,750,000 shares of Tyme's common stock, pursuant to Tyme's amended and restated 2016 Director Plan, or the 2016 Director Plan. Future issuances, as well as the possibility of future issuances, under Tyme's 2015 Plan or 2016 Director Plan or other equity incentive plans could cause the market price of Tyme's common stock to decrease.

Investors may experience dilution of their ownership interests because of the future issuance of additional shares of Tyme's common or preferred stock or other securities that are convertible into or exercisable for Tyme's common or preferred stock.

In the future, to raise needed financing, Tyme is likely to issue its authorized but previously unissued equity securities, resulting in the dilution of the ownership interests of Tyme's stockholders at the time of such issuances. Tyme is authorized to issue an aggregate of 300,000,000 shares of common stock and 10,000,000 shares of "blank check" preferred stock. Tyme also has an effective "shelf" registration statement on Form S-3 that allows Tyme to issue securities in registered offerings as well as an available at-the-market, or ATM, financing facility that allows Tyme to sell shares of Tyme's common stock through a placement agent at market prices. Tyme may issue additional shares of Tyme's common stock or other securities that are convertible into or exercisable for Tyme's common stock in connection with hiring or retaining employees, future acquisitions, future sales of Tyme's securities for capital raising purposes or for other business purposes. The future issuance of any such additional shares of Tyme's common stock may create downward pressure on the trading price of Tyme's common stock. Tyme will need to raise additional capital in the near future to meet Tyme's working capital needs, and Tyme regularly evaluates its capital needs and available sources of financing. There can be no assurance that Tyme will not be required to issue additional shares, warrants or other convertible securities in the future in conjunction with these capital raising efforts, including at a price (or exercise prices) below the price a stockholder at the time of such securities issuance paid for such stockholder's stock.

The ability of Tyme's board of directors to issue additional stock may prevent or make more difficult certain transactions, including a sale or merger of Tyme. Tyme's board of directors is authorized to issue up to 10,000,000 shares of preferred stock with powers, rights and preferences designated by it. On January 7, 2020, the Tyme board of directors designated and reserved 10,000 shares as Series A Preferred in connection with the Eagle SPA (as further described in "*Tyme's Business—Collaboration with Eagle Pharmaceuticals*" in this joint proxy statement/prospectus). Shares of Series A Preferred or other voting or convertible preferred stock could be issued or rights to purchase such shares could be issued, to create voting impediments or to frustrate persons seeking to affect a takeover or otherwise gain control of Tyme. The ability of Tyme's board of directors to issue such additional shares of preferred stock, with rights and preferences it deems advisable, could discourage an attempt by a party to acquire control of Tyme by tender offer or other means. Such issuances could therefore deprive stockholders of benefits that could result from such an attempt, such as the realization of a premium over the market price for their shares in a tender offer or the temporary increase in market price that such an attempt could cause. Moreover, the issuance of such additional shares of preferred stock to persons friendly to Tyme's board of directors could make it more difficult to remove incumbent managers and directors from office even if such change were to be favorable to stockholders generally.

If securities or industry analysts do not publish research or publish inaccurate or unfavorable research about Tyme's business, its stock price and trading volume could decline.

The trading market for Tyme's common stock will depend, in part, on the research and reports that securities or industry analysts publish about Tyme and its business. Securities and industry analysts may choose not to publish research on Tyme. If an insufficient number of securities or industry analysts provide coverage of Tyme, the trading price for Tyme's common stock would likely be negatively impacted. If one or more of the analysts who cover Tyme downgrade Tyme's stock or publish inaccurate or unfavorable research about Tyme's business, Tyme's stock price would likely decline. In addition, if Tyme's operating results fail to meet the forecast of analysts, its stock price would likely decline. Further, if one or more of these analysts cease coverage of Tyme or fail to publish reports on Tyme regularly, demand for Tyme's stock could decrease, which might cause its stock price and trading volume to decline.

Provisions in Tyme's corporate charter documents and under Delaware law could make an acquisition of Tyme more difficult and may prevent attempts by Tyme's stockholders to replace or remove Tyme's current management.

Provisions in Tyme's Certificate of Incorporation and its By-laws may discourage, delay or prevent a merger, acquisition or other change in control of Tyme that stockholders may consider favorable, including transactions in which stockholders might otherwise receive a premium for their shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of Tyme's common stock, thereby depressing the market price of Tyme's common stock. In addition, these provisions may frustrate or prevent any attempts by Tyme's stockholders to replace or remove Tyme's current management by making it more difficult for stockholders to replace members of Tyme's board of directors. Because Tyme's board of directors is responsible for appointing the members of Tyme's management team, these provisions could, in turn, affect any attempt by Tyme's stockholders to replace current members of Tyme's management team. Among others, these provisions:

- establish a board of directors having three classes of directors with a three-year term of office that expires as to one class each year, commonly referred to as a "staggered board";
- limit the manner in which stockholders can remove directors from Tyme's board of directors;
- exclusively empower the board to fill any and all vacancies on the board;
- authorize the board of directors to exclusively have the power to change and set the size of the board of directors;
- limit who may call stockholder meetings;
- include advance notice requirements for stockholder proposals that can be acted on at stockholder meetings and for nominations to Tyme's board of directors, which include, among other things, requirements for proposing stockholders to disclose information about derivative or short positions; and
- authorize Tyme's board of directors to issue, without stockholder approval, shares of preferred stock; such ability to issue previously undesignated preferred stock makes it possible for Tyme's board of directors to establish a "poison pill" and issue preferred stock with voting or other rights or preferences that could impede the success of any attempt to acquire Tyme.

Moreover, because Tyme is incorporated in Delaware, it is governed by the provisions of Section 203 of the DGCL, which prohibits a person who owns in excess of 15% of Tyme's outstanding voting stock from merging or combining with Tyme for a period of three years after the date of the transaction in which the person acquired in excess of 15% of Tyme's outstanding voting stock, unless the merger or combination is approved in a prescribed manner. However, in connection with entering into a securities purchase agreement between Tyme and Eagle in January 2020, the Tyme board of directors agreed to waive the provisions of Section 203 to the extent it is or could become applicable to Eagle.

Additionally, Tyme's by-laws provide that the Court of Chancery of the State of Delaware (or, if the Court of Chancery does not have jurisdiction, the federal district court for the District of Delaware) will be the exclusive forum for actions or proceedings for: (i) any derivative action or proceeding brought on Tyme's behalf; (ii) any action asserting a breach of fiduciary duty owed to Tyme or its stockholders; (iii) any action asserting a claim against Tyme arising under the DGCL, Tyme's Certificate of Incorporation, or Tyme's by-laws; or (iv) any action asserting a claim against Tyme that is governed by the internal affairs doctrine. Tyme's by-laws further provide that the federal district courts of the United States of America will be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act.

Tyme does not anticipate paying dividends on Tyme's common stock.

Cash dividends have never been declared or paid on Tyme's common stock and Tyme does not anticipate such a declaration or payment for the foreseeable future. Tyme expects to use future earnings, if any, to fund business

growth. Therefore, Tyme's stockholders will likely not receive any funds absent a sale of their shares of Tyme's common stock. If Tyme does not pay dividends, Tyme's common stock may be less valuable because a return on an investment in shares of Tyme's common stock will only occur if Tyme's stock price appreciates. Tyme cannot assure stockholders of a positive return on their investment when they sell their shares, nor can Tyme assure that stockholders will not lose the entire amount of their investment.

Risks Related to Tyme's Business and the Development, Regulatory Approval, and Commercialization of Tyme's Product Candidates.

The novel coronavirus (COVID-19) and its impact on business and economic conditions could adversely affect Tyme's business, results of operations and financial condition, and the extent and duration of those effects will be uncertain.

Tyme continues to monitor the effect of the novel strain of coronavirus, COVID-19, which has spread worldwide and has caused significant disruptions due to the pandemic and efforts to mitigate it. Tyme may continue to experience disruptions because of the COVID-19 pandemic that could impact Tyme's business. These disruptions may be made more likely to occur or may be exacerbated the longer the crisis continues.

In particular, Tyme's clinical trials will likely continue to be affected by the pandemic. Site initiation, participant recruitment and enrollment, participant dosing, distribution of clinical trial materials, study monitoring, data analysis, dissemination of product information and regulatory review have been disrupted and may be paused or delayed due to changes in hospital or university policies, federal, state or local regulations, prioritization of hospital resources toward pandemic efforts, or other reasons related to the pandemic.

Although many pandemic-related restrictions have been loosened, COVID-19 continues to evolve and counter measures have also changed and been re-imposed from time to time. Should this continue or should government countermeasures become more restrictive, Tyme's business operations, results of operations and financial condition may further be affected as follows:

- The continuation of the coronavirus pandemic may adversely impact Tyme's operations and risk a delay, default and/or nonperformance under existing agreements, which may increase Tyme's costs. These cost increases may not be fully recoverable or adequately covered by insurance.
- Tyme's supply chain may be disrupted, limiting Tyme's ability to manufacture Tyme's product candidates for Tyme's clinical trials and research and development operations, if Tyme's third party suppliers are adversely impacted.
- Tyme's business may experience a material economic effect due to the additional work and resource demands for Tyme's employees and vendors.
- Tyme's ability to file on a routine and timely basis Tyme's periodic reports or other filings under federal securities or other laws and regulations may be adversely impacted.
- Tyme's business may experience a material economic effect. Tyme's ability to access capital either at all or on favorable terms may be reduced. In addition, a recession, depression or other sustained adverse market event resulting from the spread of the coronavirus could materially and adversely affect Tyme's business and the value of Tyme's common stock.

The ultimate impact of the current pandemic, or any other health epidemic, is highly uncertain and subject to change. The extent to which the coronavirus further impacts Tyme's business and operating results will depend on future developments that are highly uncertain and cannot be accurately predicted. Tyme does not yet know the full extent of potential delays or impacts on Tyme's business, Tyme's clinical trials, Tyme's research programs, healthcare systems or the global economy as a whole. Management will continue to monitor the situation closely and implement business continuity and emergency response plans as needed.

Tyme's proprietary lead drug product, SM-88, is in clinical development in two principal areas. Tyme is currently participating in the advancement of clinical trials for breast cancer and sarcoma. Tyme is considering additional clinical trials in other solid tumors and/or hematologic malignancies. Clinical drug development is expensive, time-consuming and uncertain, and Tyme may ultimately not be able to obtain regulatory approval for the commercialization of its lead candidate.

The risk of failure for drugs in clinical development is high and it is impossible to predict whether Tyme's lead drug candidate for the treatment of cancer, SM-88, will prove safe and effective for use in humans or if it will receive regulatory approval. The research, testing, manufacturing, labeling, approval, selling, marketing and distribution of drug products are subject to extensive regulation by the FDA, the EMA, national competent authorities in Europe and other non-U.S. regulatory authorities, which establish regulations that differ from country to country. Tyme is not permitted to market SM-88 and any other drug product it may develop in the United States or in other countries until Tyme receives approval of an NDA from the FDA or marketing approval from applicable regulatory authorities outside the United States. Since SM-88 is in clinical development, it is subject to the risk of failure inherent in the drug development process. Tyme has limited experience in conducting and managing the clinical trials necessary to obtain regulatory approvals, including approval by the FDA or EMA. Obtaining approval of an NDA or a marketing authorization application, or an MAA, can be a lengthy, expensive and uncertain process, and Tyme may experience delays as an impact of COVID-19. In addition, failure to comply with the FDA, EMA and/or other non-U.S. regulatory requirements prior to or following regulatory approval, could subject Tyme to administrative or judicially imposed sanctions, which include, but are not limited to:

- restrictions on Tyme's ability to conduct clinical trials, including issuing full or partial clinical holds or other regulatory objections to ongoing or planned trials;
- recalls;
- restrictions on the use of drugs, manufacturers or Tyme's planned manufacturing process;
- warning letters;
- clinical investigator disqualification;
- civil and criminal penalties;
- injunctions;
- suspension or withdrawal of regulatory approvals;
- drug seizures, detentions or import/export bans or restrictions;
- voluntary or mandatory drug recalls and publicity requirements;
- total or partial suspension of drug manufacturing;
- imposition of restrictions on operations, including costly new manufacturing requirements; and
- refusal to approve pending NDAs or supplements to approved NDAs in the United States and refusal to grant marketing approvals in other jurisdictions, such as a MAA in the European Union.

The FDA, the EMA and other non-U.S. regulatory authorities also have substantial discretion in the drug approval process. Generally, the number of nonclinical and clinical trials that will be required for regulatory approval varies depending on the drug candidate, the disease or condition that the drug candidate is designed to address and the regulations applicable to any particular drug candidate. Regulatory agencies can delay, limit or deny approval of a drug for many reasons, which include, but are not limited to:

- the drug candidate may be deemed unsafe or ineffective;
- future results may not continue to confirm any or all of the positive results from earlier nonclinical or clinical trials;

- failure to select optimal drug doses and suitable trial endpoints;
- populations studied did not reflect populations likely to use the drug;
- mortality rates in clinical trials for drug candidates such as SM-88 are shown to be numerically higher, given the fact that subjects are being treated for late stage cancers than participants in other clinical trial programs;
- regulatory agencies may not find the data from nonclinical and clinical trials sufficient or well-controlled;
- regulatory agencies might not approve or might require changes to manufacturing processes or facilities; and
- regulatory agencies may change their approval policies or adopt new regulations.

Any delay in obtaining or failure to obtain, required approvals could materially adversely affect Tyme's ability to generate revenue fromSM-88, which would likely result in significant harm to Tyme's financial position and adversely impact Tyme's share price. Furthermore, any regulatory approval to market SM-88 may be subject to limitations on the indications for use for which Tyme may market the drug or to restrictions or post-approval commitments that render SM-88 not commercially viable. These limitations may limit the size of the market forSM-88 and any other drug product Tyme may develop.

Tyme has limited experience with completing large-scale or pivotal Phase II or III clinical trials, obtaining FDA approvals or commercializing pharmaceutical products, which may make it difficult to evaluate the prospects for Tyme's future viability or could result in delays or the failure to obtain required regulatory approval of Tyme's products.

Although some members of Tyme's management team have experience in creating, seeking approval and marketing various products, Tyme's operations to date have been limited to financing and staffing Tyme, developing Tyme's technology platform, SM-88, TYME-19 and Tyme's other drug candidates, conducting Tyme's small-scale completed Phase I or Phase II clinical trials for Tyme's drug candidates, and initiating or partnering to initiate pivotal trials for SM-88. Tyme has initiated Tyme's commercialization strategy and marketing plan. Accordingly, as a company, Tyme has not had experience completing a large-scale or pivotal clinical trial (whether Phase II, III, or otherwise), obtaining marketing approval, manufacturing product on a commercial scale or conducting sales and marketing activities. If a product candidate is approved, Tyme will need to transition from a company with a research and development focus to a company capable of supporting successful commercial activities. Tyme may not be successful in any step in such a transition. Consequently, predictions about Tyme's future success or viability may not be as accurate as they could be if Tyme had a history of successfully developing and commercializing pharmaceutical products.

Moreover, this lack of experience could result in delays in obtaining necessary regulatory approvals, both in conducting clinical trials and final marketing approvals; additional costs; and the possibility that approvals will not be obtained due to the failure to comply with the regulatory approval process. Such delays, costs and/or failure would likely adversely affect Tyme's business, financial condition and results of operations and could possibly cause Tyme to cease Tyme's operations in their entirety.

If Tyme is unable to identify, recruit and retain enough qualified patients for its clinical trials, it could delay or prevent development of Tyme's drug candidates and adversely affect Tyme's future business prospects.

The timing and length of Tyme's clinical trials depends in part on the speed at which Tyme can identify and recruit patients to participate in clinical trials of Tyme's product candidates. SM-88 is currently being studied in two investigator-initiated clinical trials, including the Phase II OASIS trial forSM-88 in patients with metastatic HR+/HER2- breast cancer, for which patient enrollment commenced in 2021. Difficulties with enrollment or

finding eligible patients and retaining them may cause delays in current and future clinical trials. If patients are unwilling or unable to participate or remain in Tyme's clinical trials due to any negative publicity in the industry, interest in trials for other third-party product candidates, or for other reasons, including fears or restrictions related to the COVID-19 pandemic, Tyme's clinical trials could be delayed or terminated.

Tyme or its clinical trial sites may not be able to identify, recruit, enroll and retain enough patients, or those with the required or desired characteristics in a clinical trial, to complete Tyme's clinical trials in a timely manner. Patient enrollment is affected by factors including the design of clinical trial protocols, size of patient populations, eligibility criteria, proximity and availability of clinical trial sites, perceived risks and benefits of the product candidate under study, and other factors. If Tyme has difficulty enrolling and retaining enough patients to conduct Tyme's clinical trials as planned, Tyme may need to delay, limit or terminate ongoing or planned clinical trials, any of which could have an adverse effect on Tyme's business. For example, due in part to COVID-19, Tyme experienced slower-than-expected enrollment in its TYME-88-Panc trial, which Tyme has since discontinued.

If clinical trials for Tyme's drug candidates are prolonged, delayed or stopped, Tyme may be unable to obtain regulatory approval and commercialize its drug candidates on a timely basis, which would require Tyme to incur additional costs and delay revenue.

All Tyme's current drug candidates are in clinical development. Tyme conducted several Phase I and Phase II trials for SM-88. Tyme is collaborating with Georgetown University to support a Phase II trial, OASIS, to study effects of SM-88 in breast cancer. SM-88 is also being studied in an open label Phase II investigator-sponsored trial, HoPES, to study SM-88 therapy in sarcoma. The successful completion of these and future trials will be subject to numerous factors that can cause interruptions or delays, many of which may be beyond Tyme's control. For example, Tyme also partnered with Pancreatic Cancer Action Network, or PanCAN to study SM-88 in an adaptive randomized Phase II/III trial with registration intent known as Precision Promise. In January 2022, Tyme announced the discontinuation of the Precision Promise trial upon learning that the trial sponsor had discontinued the SM-88 arm due to futility. Should Tyme experience any interruption, delay, or discontinuation of its current trials, Tyme's plans and expected future revenue could be adversely affected and could result in Tyme's inability to continue its operations.

Many factors could substantially delay or prevent the timely completion of Tyme's planned clinical trials, which include, but are not limited to the following:

- slower than expected rate of subject recruitment and enrollment;
- slower than projected IRB or independent ethics committee, or IEC, review and approval;
- the data monitoring committee, or DMC, or DSMB for a clinical trial requires the clinical trial be delayed or stopped or requests major or minor modifications to the clinical trial;
- failure of subjects to complete their full participation in clinical trial or return for post-treatment follow-up, which Tyme has experienced in the TYME-88-Panc trial;
- unforeseen safety issues, including severe or unexpected drug-related adverse effects, or AEs, experienced by subjects, including the possibility of death;
- lack of drug candidate efficacy during the clinical trials;
- poor trial design for one or more of Tyme's clinical trials;
- withdrawal of participation by a principal investigator in one or more of Tyme's clinical trials;
- withdrawal of participation by one of Tyme's CROs;
- inability or unwillingness of subjects or clinical investigators to comply with clinical trial procedures;
- resolution of data discrepancies;

- inadequate CRO management and/or monitoring in one or more of Tyme's clinical trials;
- the need to repeat, reconstruct or terminate a clinical trial due to inconclusive or negative results or unforeseen complications in testing; and
- a request by the FDA to suspend or terminate Tyme's current drug development programs.

Changes in regulatory requirements and guidance may also occur and Tyme may need to significantly amend ongoing clinical trial protocols or revise planned prospective clinical trial protocols to reflect such changes mandated by regulatory authorities. Amendments may require Tyme to renegotiate terms with CROs or clinical trial sites or to resubmit clinical trial protocols and other documents to IRBs or IECs for re-review, which may impact the costs, timing or successful completion of a clinical trial. Tyme's clinical trials may be suspended or terminated at any time by the FDA, the EMA, other regulatory authorities or the IRB/IEC overseeing the clinical trial, due to a number of factors, which include, but are not limited to:

- failure to conduct the clinical trial in accordance with regulatory requirements or compliance with the clinical protocol;
- unforeseen safety issues or any determination that a clinical trial presents unacceptable health risks to subjects;
- lack of adequate funding to continue the clinical trial due to higher or additional unforeseen costs or other business decisions; and
- upon a breach or pursuant to the terms of any agreement with or for any other reason by, current or future collaborators that have responsibility for the clinical development of SM-88.

Any failure or significant delay in clinical and regulatory development plans for current or future drug candidates would likely adversely affect Tyme's ability to obtain regulatory approval for the drug and would diminish Tyme's ability to generate revenue.

The results of previous studies may not be predictive of future results, Tyme's progress in future trials for one drug candidate may not be indicative of progress in trials for other drug candidates and the results of Tyme's current and planned clinical trials may not satisfy the requirements of the FDA, the EMA or other non-U.S. regulatory authorities.

Tyme currently has no products approved for sale and Tyme cannot guarantee that Tyme will ever have marketable products. Before obtaining marketing approval from regulatory authorities any sale of SM-88, Tyme must conduct extensive clinical trials to demonstrate the safety and efficacy of Tyme's drug candidates in humans. Clinical testing is expensive, difficult to design and implement, can take many years to complete and has a risk of uncertainty as to its outcome.

Clinical failure can occur at any stage of clinical development and the outcome of early clinical trials may not be predictive of the success of later clinical trials. Additionally, interim results of a clinical trial do not necessarily predict final trial results. In addition, nonclinical and clinical data are often susceptible to varying interpretations and analyses. In this regard, many companies that have believed their drug performed satisfactorily in clinical trials have nonetheless failed to obtain marketing approval of their products from regulatory organizations. Furthermore, changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations or changes in regulatory review for each submitted product application may cause delays in the approval or rejection of an application.

Drug candidates that have shown promising results in early clinical trials (such as Tyme's first-in-human, or FIH, study) and compassionate use programs (such as Tyme's Compassionate Use Patients) may still suffer significant setbacks in subsequent clinical trials. For example, despite promising results in prior trials in pancreatic cancer, the Phase II/III trial with registrational intent, Precision Promise, was discontinued due to futility in January

2022. Many companies in the pharmaceutical industry, including those with greater resources and experience than Tyme, as well as those that have conducted large-scale clinical trials under an IND (in contrast to Tyme's limited number of FIH study patients and Compassionate Use Patients, all of whom were treated outside of an IND approved clinical trial) have suffered significant setbacks in advanced clinical trials, even after obtaining promising results in earlier clinical trials. In light of these factors, and the fact that Tyme's dosage and method of delivery from Tyme's FIH study and Compassionate Use Patients differ from Tyme's current clinical trials, and may differ from future clinical trials, no assurance can be given that Tyme's ongoing or future clinical trials may produce results similar to Tyme's FIH study or those experienced by Compassionate Use Patients.

Tyme may, from time to time, publish interim or preliminary data from its clinical trials. Adverse changes from the published data from Tyme's FIH study, Compassionate Use Patients, and interim data to the final data obtained from Tyme's future clinical trials could harm Tyme's business prospects. In the 30 patients who received SM-88 in Tyme's FIH study, treatment-related AEs were reported in all participating patients, of which hyperpigmentation was the only consistent, lasting AE. The most common treatment-related AEs were hyperpigmentation (100%), mild transient fatigue (57%), and mild transient pain (13%). Many of these patients who were treated with SM-88 were late-stage cancer patients with one or more previous treatments or existing medical conditions, which can cause AEs unrelated to SM-88. Patients may also report additional AEs that have not yet been previously experienced or otherwise predicted. Patients who will be administered SM-88 in Tyme's clinical trials are, or may be, seriously ill and as more patient data becomes available, there is a risk that future clinical outcomes may materially differ from interim or preliminary data, FIH study data or Compassionate Use Patient data. Any negative material changes could have an adverse effect on Tyme's business and product development efforts.

Clinical trials may also produce negative or inconclusive results and Tyme may decide to, or regulators may require Tyme to, conduct additional clinical or nonclinical testing. Tyme will be required to demonstrate with substantial evidence through well-controlled clinical trials that any of Tyme's drug candidates are safe and effective for use in diverse populations before Tyme can seek regulatory approvals for its commercial sale.

In addition, the design of a clinical trial can determine whether its results will support approval of a drug. Flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced. Tyme may be unable to design and execute a clinical trial to support regulatory approval in general, or in an efficient manner given Tyme's limited resources.

In some instances, there may be significant variability in safety and/or efficacy results between different trials of the same drug due to numerous factors, including amendment to trial protocols, variability in size and type of the patient populations, adherence to the dosing regimen and other trial procedures and the rate of dropout among clinical trial subjects. Tyme does not know whether any of the clinical trials in Tyme's current development plans will demonstrate consistent or adequate efficacy and safety to obtain regulatory approval to market Tyme's drug candidates, and Tyme may need to further refine or redesign Tyme's combination drug candidate formula or modify production methodology based on such clinical trials, each of which could result in delays in the regulatory approval process.

There is always the possibility that none of Tyme's drug candidates gain regulatory approval if they do not achieve their primary endpoints in its clinical trials, and other factors, such as product safety or nonclinical registration requirements, may prevent such drug candidates from gaining regulatory approval even if it achieves its primary endpoints. The FDA, the EMA or other global regulatory authorities may disagree with Tyme's trial design and/or Tyme's interpretation of data from nonclinical and clinical trials. In addition, any of these regulatory authorities may change requirements for the approval of a drug even after reviewing and providing comments or advice on a protocol for a clinical trial. In addition, any of these regulatory authorities may also approve a drug for fewer or more limited indications than requested or may grant approval that is contingent on the performance of costly post-marketing clinical trials. Further, the FDA, the EMA or other non-U.S. regulatory authorities may not accept the proposed labeling or labeling claims that Tyme believes would be necessary or desirable for the successful commercialization of Tyme's drug candidates.

Preclinical development programs and preclinical mechanism research activities are uncertain. Tyme's preclinical programs and activities may experience delays or may never advance to clinical trials, which would adversely affect Tyme's ability to obtain regulatory approvals or commercialize these programs on a timely basis or at all.

Tyme is conducting a range of preclinical experiments with external CROs and academic partners to more fully understand and illustrate the mechanism of action of SM-88 in oncology and have recently expanded Tyme's activity in this area through a biomarker initiative. However, it is unknown if the impact of SM-88 on processes studied in cultured cells or animal models would be replicated in humans or provide a clinical benefit. The FDA is interested in understanding the general biologic properties of SM-88, and there is a risk that the results produced by Tyme's planned preclinical activities might not satisfy their requirements to support a regulatory approval. Therefore, additional activity may be required to address the FDA's questions, or Tyme might not be able to effectively address these questions.

In addition to SM-88, Tyme has researched other drug platforms, such as TYME-18 and TYME-19. Before Tyme can commence human clinical trials for a product candidate, Tyme must complete extensive preclinical testing. Preclinical development is highly speculative and carries a high risk of failure. Preclinical studies and early-stage clinical trials are primarily designed to test safety, to study pharmacokinetics and pharmacodynamics, to understand the side effects of product candidates at various doses and schedules, and may not advance to later-stage clinical trials. Furthermore, the results of preclinical studies and early-stage clinical trials may not be predictive of the future results of later-stage, large scale efficacy clinical trials.

Tyme may not be successful in its efforts to use and expand its technology platform to build a pipeline of product candidates.

A key element of Tyme's business strategy has been to further develop and expand Tyme's technology platform in order to build a steady pipeline that could be successful in the treatment of a variety of cancers, as well as other diseases. However, Tyme may not be able to develop and obtain approval to market its drugs if regulators do not conclude that they are safe and effective. Furthermore, the potential product candidates that Tyme discovers may not be suitable for further clinical development, whether due to the potential that they produce harmful AEs or possess other characteristics that indicate that they are unlikely to receive marketing approval and/or market acceptance. In addition, unexpected technical issues involving such product candidates could be encountered that could cause the products to be prohibitively expensive to manufacture and market. If Tyme does not continue the steady development and commercialization of products utilizing Tyme's technology platform, Tyme will face difficulty in achieving increased revenues in future periods, which could result in significant harm to its financial position and adversely affect Tyme's share price.

The FDA and other regulatory authorities have not approved products that utilize this technology platform.

In the future, Tyme plans to develop additional product candidates based on its technology platform. This platform incorporates novel technologies and methods and actions. Since regulators have not yet approved such a platform, the approval of the product candidates in Tyme's pipeline is less certain than approval of drugs that do not employ such novel technologies or methods of action. Tyme intends to work closely with the FDA, the EMA and other non-U.S. regulatory authorities to perform the requisite scientific analyses and evaluation of Tyme's methods to obtain regulatory approval for these future product candidates. It is possible that the validation process may take time and significant expenditures of resources, require independent third-party analyses or not be accepted by the FDA, the EMA and other non-U.S. regulatory authorities. Delays or failure to obtain regulatory approval of any of Tyme's future product candidates could adversely affect Tyme's business prospects and the value of Tyme's common stock.

Even if Tyme obtains marketing approval for one or more of Tyme's drug candidates in a major pharmaceutical market such as the United States or Europe, Tyme may never obtain approval or commercialize in other major markets, which would limit Tyme's ability to realize the drug's full market potential.

In order to market any products in a country or territory, Tyme must establish and comply with numerous and varying regulatory requirements of such countries or territories regarding safety and efficacy. Clinical trials conducted in one country may not be acceptable for review by regulatory authorities in other countries and regulatory approval in one country does not mean that regulatory approval will be obtained in any other country. Approval procedures differ among countries and can involve additional testing and validation as well as varying administrative review periods. Seeking regulatory approvals in multiple countries could result in significant delays, difficulties and costs and may require additional nonclinical or clinical trials, which would be costly and time-consuming or even delay or prevent the introduction of Tyme's drug candidates in those countries. In addition, Tyme's failure to obtain regulatory approval in one country may delay or have negative effects on the process for regulatory approval in other countries. Tyme does not have any drug candidates approved for sale in any jurisdiction, including international markets and Tyme therefore does not have experience in obtaining regulatory approval. If Tyme fails to comply with regulatory requirements in international markets or to obtain and maintain required approvals, Tyme's target market will be reduced and its ability to create stockholder value from its drug candidates will be harmed.

In the United States, Tyme may seek fast track or breakthrough designation forSM-88 or other drug candidates. There is no assurance that the FDA will grant either designation and even if it does, such designation may not actually lead to a faster development process, regulatory review or ultimate approval compared to conventional FDA procedure. Any achievement of fast track or breakthrough designation for SM-88 would not increase the likelihood that Tyme's drug candidates will receive marketing approval in the United States.

The FDA has broad discretion whether or not to grant fast track or breakthrough designation, which are further discussed in the sections titled "*Tyme Business—Fast Track Program*" and "*—Breakthrough Therapy Approvals*" of this joint proxy statement/prospectus. Accordingly, even if Tyme believes SM-88 or any other drug candidate meets the criteria for fast track or breakthrough designation, the FDA may disagree and instead determine not to make such designation. In any event, the receipt of fast track or breakthrough designation for a drug candidate may not result in a faster development process, review or approval compared to drug candidates considered for approval under conventional FDA procedures and, in any event, does not assure ultimate approval by the FDA. The FDA may even withdraw fast track designation if it believes that the designation is no longer supported by data from Tyme's clinical development program. Further, in connection with fast track designation, Tyme may be required to provide government regulators with additional manufacturing and production information, some of which Tyme may not be able to provide in a timely manner or to the extent required by such regulators, in particular because Tyme is using contract manufacturers.

Although Tyme has obtained orphan drug designation from the FDA for SM-88 as a potential treatment for patients with pancreatic cancer, Tyme may be unable to obtain orphan drug designation for any other drug candidate Tyme may develop. If Tyme's competitors instead can obtain orphan drug exclusivity for their products in the same indications of any other drug candidate Tyme may develop, Tyme may be at a competitive disadvantage and may not be able to have Tyme's products approved by the applicable regulatory authority for a significant period of time, if at all. In addition, Tyme may not be able to fully benefit from the associated marketing exclusivity of SM-88's orphan drug designation or for any other drug Tyme develops that is granted that designation.

As further described under the caption "*Tyme Business—Orphan Drug Designation*" in this joint proxy statement/prospectus, regulatory authorities in some jurisdictions, including the United States and Europe, may designate drugs for relatively small patient populations as orphan drugs. In July 2020, Tyme received from the FDA orphan drug designation for SM-88 as a potential treatment for patients with pancreatic cancer, however,

Tyme does not currently have any active clinical trials in pancreatic cancer. Nonetheless, SM-88, or any other drug candidate Tyme may develop that receives orphan drug designation, may not have market exclusivity in particular markets. There is no assurance Tyme will be able to receive orphan drug designation for any other drug candidate Tyme is developing or may develop. Associated marketing exclusivity for SM-88 or another drug candidate for which Tyme may receive orphan drug designation may not effectively protect it from competition because that exclusivity can be suspended under certain circumstances. Further, the granting of a request for orphan drug designation does not alter the standard regulatory requirements and process for obtaining marketing approval.

SM-88, TYME-18, TYME-19 or any other drug product Tyme may develop may have serious adverse, undesirable or unacceptable side effects, which may delay or prevent marketing approval. If such side effects are identified during the development of a product candidate Tyme may develop or following such candidate's approval, if any, Tyme may need to abandon its development of such product candidate, the commercial profile of any approved label may be limited and/or Tyme may be subject to other significant negative consequences following marketing approval, if any.

Although Tyme's drug candidates will undergo safety testing to the extent possible and agreed to with regulatory authorities, not all AEs of drugs can be predicted or anticipated. SM-88, Tyme's proprietary drug product, is based on a mechanism designed to utilize oxidative stress, among other techniques, to selectively kill cancer cells, yet is powerful and could lead to serious side effects that Tyme can only discover in clinical trials. Unforeseen side effects from SM-88 or Tyme's other drug candidates could arise either during clinical development or, if such side effects are sporadic, after it has been approved by regulatory authorities and the approved drug has been marketed, resulting in the exposure of additional patients. While Tyme's trials to date for SM-88 have generally demonstrated a favorable safety profile, the results from future trials of SM-88 may not confirm these results. Any new therapy to kill cancer tumors is risky and may have unintended consequences. Tyme has not fully demonstrated that SM-88 or its other drug candidates is safe in humans and Tyme may not be able to do so.

Furthermore, Tyme is initially developing SM-88 for patients with cancer for whom no other therapies have succeeded and survival times are frequently short. Therefore, Tyme expects that certain subjects may die during the clinical trials and it may be difficult to ascertain whether such deaths are attributable to the underlying disease, complications from the disease, SM-88 or a combination of such factors.

The results of future clinical trials may show that one of Tyme's drug candidates causes undesirable or unacceptable side effects, which could interrupt, delay or halt Tyme's clinical trials and result in delay of or failure to obtain, marketing approval from the FDA, the European Commission and other non-U.S. regulatory authorities or result in marketing approval from the FDA, the European Commission and othernon-U.S. regulatory authorities with restrictive label warnings or potential drug liability claims.

If SM-88 or Tyme's other product candidates receive marketing approval and it is later identified as undesirable or has unacceptable side effects, Tyme is at risk for the following actions:

- regulatory authorities may require Tyme to take such drug product off the market;
- regulatory authorities may require the addition of labeling statements, specific warnings, a contraindication or field alerts to physicians and pharmacies;
- regulatory authorities may require post-market clinical trials to assess possible serious risks associated with such drug product, which will require Tyme to provide the FDA or other regulatory authorities with additional data;
- Tyme may be required to change the way such drug product is administered, conduct additional clinical trials or change the labeling of the drug;
- Tyme may be subject to limitations on how it may promote such drug product;

- sales of such drug product may never gain traction or could decrease significantly;
- Tyme may be subject to litigation or drug liability claims; and
- Tyme's reputation may suffer.

Any of these events could prevent Tyme from achieving or maintaining market acceptance ofSM-88 or other drug candidates or could substantially increase commercialization costs and expenses, which in turn could delay or prevent Tyme from generating significant revenue from the sale of such drug product.

Enacted and future legislation may increase the difficulty and cost for Tyme to obtain marketing approval and commercialization of Tyme's product candidates and may affect the prices Tyme obtains. Tyme's successful commercialization will depend in part on the extent to which governmental authorities and health insurers establish adequate coverage, reimbursement and pricing policies.

In the United States, the European Union, its member states and other foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes that affect the healthcare industry. These changes could prevent or delay marketing approval of Tyme's drug candidates, restrict or regulate post-approval activities and affect Tyme's ability to sell and recognize revenue. Among policy makers and payors in the United States and elsewhere, there is continued interest in promoting changes in the healthcare industry, with stated goals that include containing health care costs, improving quality and/or expanding access to health care.

In the United States, there have been a number of proposals for increased federal and state government regulation of, or involvement in, the pricing and/or purchasing of drugs. For example, the Prescription Drug Price Relief Act of 2021, introduced in the Senate in March 2021, would require the HHS Secretary to assure that Americans do not pay more for prescription drugs than the median price of five countries (Canada, United Kingdom, France, Germany and Japan). There have also been state legislative efforts to address drug costs, which generally have focused on increasing transparency about drug costs and limiting drug prices. Some such legislation has been subject to legal challenges.

In addition, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or the Medicare Modernization Act, established the Medicare Part D program and provided authority for limiting the number of drugs that will be covered in any therapeutic class thereunder. The Medicare Modernization Act, including its cost reduction initiatives, could limit the coverage and reimbursement rate that Tyme receives for any of its approved products. Private payors may follow Medicare coverage policies and payment limitations in setting their own reimbursement rates resulting in similar limits in payments from private payors.

Further, the ACA, is a far-reaching law intended to broaden access to health insurance, reduce or constrain the growth of health care spending, enhance remedies against fraud and abuse, add new transparency requirements for health care and health insurance industries, impose new taxes and fees on the health industry and impose additional health policy reforms. The law has continued the downward pressure on the pricing of medical items and services, especially under the Medicare program, and increased the industry's regulatory burdens and operating costs. Since its enactment, there have been executive, judicial and Congressional challenges to certain aspects of the ACA, which are further described in this section, and Tyme expects there will be additional challenges and amendments to the ACA in the future.

Other legislative changes have been proposed and adopted since the ACA was enacted. In August 2011, President Obama signed into law the Budget Control Act of 2011, which, among other things, created the Joint Select Committee on Deficit Reduction to recommend to Congress proposals in spending reductions. The Joint Select Committee on Deficit Reduction did not achieve a targeted deficit reduction, which triggered the legislation's automatic reduction to several government programs. This includes aggregate reductions to Medicare payments to providers of 2% per fiscal year through 2030 due to subsequent legislative amendments to the statute, with the exception of a temporary suspension from May 1, 2020 through March 31, 2021 due to the

COVID-19 pandemic, unless additional Congressional action is taken. In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, further reduced Medicare payments to several providers (including hospitals and cancer treatment centers), and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. Further, in response to the COVID-19 pandemic, the CARES Act was signed into law in March 2020. The CARES Act is aimed at providing emergency assistance and health care for individuals, families and businesses affected by the COVID-19 pandemic and generally supporting the U.S. economy. The effects of the COVID-19 pandemic may introduce temporary or permanent healthcare reform measures, which could have negative financial implications on Tyme's business.

There has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices. Specifically, there have been several recent U.S. Congressional inquiries and proposed federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. At the federal level, the Trump administration used several means to propose or implement drug pricing reform, including through federal budget proposals, executive orders and policy initiatives. For example, on July 24, 2020 and September 13, 2020, the Trump administration announced several executive orders related to prescription drug pricing that seek to implement several of the administration's proposals. As a result, the FDA released a final rule on September 24, 2020, effective November 30, 2020, providing guidance for states to build and submit importation plans for drugs from Canada. Further, on November 20, 2020, HHS finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Medicare Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The implementation of the rule has been delayed by the Biden administration from January 1, 2022 to January 1, 2023 in response to ongoing litigation. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a new safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers, the implementation of which have also been delayed pending review by the Biden administration. On November 20, 2020, the CMS issued an interim final rule implementing the Trump administration's Most Favored Nation executive order, which would tie Medicare Part B payments for certain physician-administered drugs to the lowest price paid in other economically advanced countries, effective January 1, 2021. On December 28, 2020, the U.S. District Court in Northern California issued a nationwide preliminary injunction against implementation of the interim final rule. It is unclear whether the Biden administration will work to reverse these measures or pursue similar policy initiatives. In addition, there have been and continue to be similar initiatives at the state level to reduce drug costs. Tyme cannot be sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of SM-88 or Tyme's other existing or future product candidates, if any, may be. In addition, increased scrutiny by the U.S. Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject Tyme to more stringent product labeling and post-marketing testing and other requirements.

The ACA and other healthcare reform measures adopted in the future may result in more rigorous coverage criteria new payment methodologies and additional downward pressure on the price that Tyme receives for any approved product. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent Tyme from being able to generate revenue, attain profitability, or commercialize Tyme's products.

Individual states in the United States have also become increasingly active in passing legislation and implementing regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products to purchase and which suppliers will be included in their

prescription drug and other healthcare programs. Furthermore, there has been increased interest by third party payors and governmental authorities in reference to pricing systems and publication of discounts and list prices. These reforms could also reduce the ultimate demand for Tyme's product candidates or put pressure on Tyme's product pricing.

In the European Union, similar political, economic and regulatory developments may affect Tyme's ability to profitably commercialize its product candidates, if approved. In addition to continuing pressure on prices and cost containment measures, legislative developments at the European Union or member state level may result in significant additional requirements or obstacles that may increase Tyme's operating costs. The delivery of healthcare in the European Union, including the establishment and operation of health services and the pricing and reimbursement of medicines, is almost exclusively a matter for national, rather than European Union, law and policy. National governments and health service providers have different priorities and approaches to the delivery of health care and the pricing and reimbursement of products in that context. In general, however, the healthcare budgetary constraints in most European Union member states have resulted in restrictions on the pricing and reimbursement of medicines by relevant health service providers. Coupled with ever-increasing European Union and national regulatory burdens on those wishing to develop and market products, this could prevent or delay marketing approval of Tyme's product candidates, restrict or regulate post-approval activities and affect Tyme's ability to commercialize its product candidates, if approved. In markets outside of the United States and European Union, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies.

There have been, and likely will continue to be, legislative and regulatory proposals at the foreign, federal and state levels directed at broadening the availability of healthcare and containing or lowering the cost of healthcare. The implementation of cost containment measures or other healthcare reforms may prevent Tyme from being able to generate revenue, attain profitability, or commercialize its product candidates. Such reforms could have an adverse effect on anticipated revenue from product candidates that Tyme may successfully develop and for which it may obtain regulatory approval and may affect Tyme's overall financial condition and ability to develop product candidates.

Tyme cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If Tyme is slow or unable to adapt to new requirements or policies, or if Tyme is not able to maintain regulatory compliance, its product candidates may lose any regulatory approval that may have been obtained and Tyme may not achieve or sustain profitability, which would adversely affect its business.

Tyme currently has very limited marketing, sales or distribution infrastructure. If Tyme is unable to develop full sales, marketing and distribution capabilities on its own or through collaborations or if Tyme fails to achieve adequate pricing and/or reimbursement, Tyme will not be successful in commercializing its candidates.

Tyme currently has very limited marketing, sales and distribution capabilities because Tyme's lead drug candidate,SM-88, is still in clinical development and initial trials and Tyme's other drug candidates are only in the initial stages of development. If any of Tyme's drug candidates is approved, Tyme intends either to have established a sales and marketing organization with technical expertise and supporting distribution capabilities to commercialize Tyme's drug or to have outsourced this function or portions, to one or more experienced third parties. Either of these options is expensive and time-consuming. Some of these costs may be incurred well in advance of any regulatory approvals for such drug candidate. In addition, Tyme may not be able to hire a sales force that is sufficient in size or has adequate expertise in the medical markets that Tyme intends to target. Any failure or delay in the development of Tyme's internal sales, marketing and distribution capabilities or to outsource these functions, in whole or part, would adversely affect the commercialization of Tyme's products.
To the extent that Tyme enters into collaborative agreements for marketing, sales and/or distribution, its revenue may be lower than if it directly marketed and sold an approved drug product. For example, as further discussed in

the "*Tyme's Business—Collaboration with Eagle Pharmaceuticals*" section in this joint proxy statement/prospectus, under the Co-Promote (as defined in the section therein), Eagle will receive 15% of the net sales of all SM-88 products in the United States during the term of the agreement. In addition, any revenue Tyme receives will depend in whole or in part upon the efforts and success of these third-party collaborators, which are likely not to be entirely within Tyme's control. If Tyme is unable to enter into these arrangements on acceptable terms or at all, it may not be able to successfully commercialize SM-88 or other drug candidates. If Tyme is not successful in commercializing its drug candidates, either on its own or through collaborations with one or more third parties, Tyme's future revenues will suffer, Tyme may incur significant and additional losses and it may be forced to curtail operations. These factors would have an adverse effect on Tyme's share price.

Even if SM-88 obtains regulatory approval, it will remain subject to ongoing regulatory requirements and oversight.

If marketing authorization is obtained for Tyme's lead drug candidate, SM-88, it will continue to be under review by regulatory authorities and be subject to regulatory requirements. As a result, authorization could be subsequently withdrawn or restricted at any time for many reasons, including safety issues. Tyme will be subject to ongoing obligations and oversight by regulatory authorities, including AE reporting requirements, marketing restrictions and, potentially, other post-marketing obligations, all of which may result in significant expense and limit Tyme's ability to successfully commercialize Tyme's drug product and generate revenue.

If there are changes in the application of legislation or regulatory policies or if problems are discovered with SM-88 or Tyme's manufacturer(s) or if Tyme or one of its distributors, licensees or co-marketers fails to comply with regulatory requirements, the regulators could take various actions. These include imposing fines on Tyme, imposing restrictions on the drug or its manufacture and requiring Tyme to recall or remove the drug from the market. The regulators could also suspend or withdraw Tyme's marketing authorizations, requiring Tyme to conduct additional clinical trials, change Tyme's drug labeling or submit additional applications for marketing authorization. If any of these events occurs, Tyme's ability to sell SM-88 may be impair and it may incur substantial additional expense to comply with regulatory requirements, which could adversely affect its business, financial condition and the results of operations and the value of its share price.

Even if approved, if SM-88 does not achieve broad market acceptance among physicians, patients, the medical community and third-party payors, Tyme's revenue generated from its sales will be limited.

The commercial success of Tyme's drug candidates will depend upon its acceptance among physicians, patients and the overall medical community. The degree of market acceptance of the drug candidates Tyme develops will depend on a number of factors, which include, but are not limited to:

- limitations or warnings contained in the approved labeling for such drug candidate;
- changes in the standard of care for the targeted therapy;
- limitations in the approved clinical indications for such drug candidate;
- demonstrated clinical safety and efficacy of such drug candidate compared to other drugs;
- lack of significant AEs;
- limitations on how Tyme promotes such drug candidate;
- sales, marketing and distribution support;
- availability and extent of reimbursement from managed care plans and other third-party payors;
- timing of market introduction and perceived effectiveness of competitive drugs;
- the degree of cost-effectiveness of such drug candidate;

- availability of alternative therapies, whether or not at a similar or lower cost, including generic andover-the-counter drugs;
- the extent to which such drug candidate is approved for inclusion on formularies of hospitals and managed care organizations;
- whether such drug candidate is designated under physician treatment guidelines as a first-line therapy or as a second- or third-line therapy;
- adverse publicity about such drug candidate or favorable publicity about competitive drugs;
- convenience and ease of administration; and
- potential drug liability claims.

If any of Tyme's drug candidates are approved but does not achieve an adequate level of acceptance by physicians, patients and the overall medical community, Tyme may not generate sufficient revenue to become profitable or to sustain operations. In addition, efforts to educate the medical community and third-party payors on the benefits of such drug candidate may require significant resources and may never be successful.

Tyme is subject to manufacturing risks that could substantially increase Tyme's costs and limit the supply of its current drug candidates and any other drug product it may develop.

As is likely to be common with any other product candidate Tyme may develop, the process of manufacturingSM-88, TYME-18 and TYME-19 is complex, highly regulated and subject to several risks, which include, but are not limited to the following risks:

- Tyme does not have experience in manufacturing Tyme's drug candidates in bulk quantity or at commercial scale. Tyme would expect to contract with external manufacturers to develop a larger scale process for manufacturing SM-88 in parallel with Tyme's involvement in any larger-scale trials of SM-88 should Tyme pursue participation in such trials. Tyme expects to do the same for its other current drug candidates. Tyme may not succeed in the scaling up of Tyme's process or it may need a larger manufacturing process for its drug candidates than what it has planned. Any changes to its manufacturing processes may result in the need to obtain additional regulatory approvals. Difficulties in achieving commercial-scale production or the need for additional regulatory approvals could delay the development and regulatory approval of Tyme's drug candidates and ultimately affect its success.
- The process of manufacturing drugs, such as SM-88, is extremely susceptible to loss due to contamination, equipment failure or improper installation or operation of equipment, vendor or operator error, inconsistency in yields, variability in drug characteristics and difficulties in scaling the production process. Even minor deviations from normal manufacturing processes could result in reduced production yields, drug defects and other supply disruptions. If microbial, viral or other contaminations are discovered in Tyme's drug candidates or in the manufacturing facilities in which any of Tyme's drug candidates is made, such manufacturing facilities may need to be closed for an extended time to investigate and remedy the contamination.
- A shortage of drug product and/or the agents used with Tyme's drug candidates.
- The manufacturing facilities in which Tyme's drug candidates are made could have delays in manufacturing due to delays created by other sponsor company drug manufacturing runs, which could affect Tyme's manufacturing runs.
- An unforeseen increase in ingredients procurement or other manufacturing costs.
- An unforeseen production shortage resulting from any events, including interruptions to business operations and supply chain disruption as a result of worldwide economic and political disruptions including the impacts of military conflict between Russia and Ukraine, and widespread health crises, such as the COVID-19 pandemic, affecting raw material and or intermediate supply or manufacturing capabilities abroad and domestically.

- The manufacturing facilities in which Tyme's drug candidates are made could be adversely affected by equipment failures, labor shortages, labor strikes, extreme weather events and other natural disasters, widespread disease and other public health crises, including COVID-19, power failures, lack of phone or internet services, riots, crime, act of foreign enemies, war, nationalization, government sanction, blockage, embargo, any extraordinary event or circumstance beyond control and numerous other factors.
- Tyme and its manufacturing partners must comply with applicable cGMP and local and state regulations and guidelines. Compliance with cGMP can be time consuming and expensive. Further, cGMP may not be flexible in situations where business pressures would normally call for immediate ingenuity. Tyme or its manufacturing partners may encounter difficulties in achieving quality controls and quality assurance and may experience shortages in qualified personnel. Tyme and its manufacturing partners will be subject to inspections by the FDA and comparable agencies in other jurisdictions to confirm compliance with applicable regulatory requirements. Any failure to follow cGMPs or other regulatory requirements or delay, interruption or other issues that arise in the manufacture, fill-finish, packaging or storage of Tyme's drug candidates that result from a failure at the facilities or the facilities or operations of third parties to comply with regulatory requirements or pass any regulatory authority inspection could significantly impair Tyme's ability to develop and commercialize its drug candidates. This could lead to significant delays in the availability of Tyme's drug candidates for clinical trials or the termination or clinical hold on a trial or the delay or prevention of a filing or approval of marketing applications for Tyme's drug candidates. Significant noncompliance could also result in the imposition of sanctions, including fines, injunctions, civil penalties, failure of regulatory authorities to grant marketing approvals for Tyme's drug candidates, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of products, operating restrictions and criminal prosecutions, any of which could damage Tyme's reputation. If Tyme and/or its manufacturing partners are not able to maintain regulatory compliance, Tyme may not be permitted to market its drug candidates and/or may be subject to drug recalls, seizures, injunctions or criminal prosecution.
- Any adverse developments affecting manufacturing operations for Tyme's drug candidates, if approved for marketing by the FDA, may result in shipment delays, inventory shortages, lot inspection failures, drug withdrawals or recalls or other interruptions in the supply of Tyme's drug candidates. Tyme may also have to take inventory write-offs and incur other charges and expenses for products that fail to meet regulator-approved manufacturing specifications, undertake costly remediation efforts or seek more costly manufacturing alternatives.
- Drug products that have been produced and stored for later use may degrade, become contaminated or suffer other quality defects, which could cause the affected products to no longer be suitable for its intended use in clinical trials or other development activities. If the defective drug cannot be replaced in a timely fashion, Tyme may incur significant delays in Tyme's development programs that could adversely affect the value of Tyme's drug candidates.
- As further described under the caption "*Tyme's Business—Manufacturing*"in this joint proxy statement/prospectus, SM-88 drug substance is being manufactured by a FDA registered and inspected third party and to date that manufacturer is Tyme's sole supplier of this drug substance. Tyme believes that replacement for this supplier, in the event it becomes necessary, is not impossible, but would cause Tyme to lose time that could otherwise be devoted to development. Currently, Tyme does not have an arrangement in place for a secondary supplier for this drug substance.
- Third parties may hold IP rights that impact, restrict or inhibit manufacturing or sale of a commercial version of any of Tyme's drug candidates.

The drug candidates that Tyme may develop will face significant competition and, if competitors develop and market products that are more effective, safer or less expensive than Tyme's drug, Tyme's commercial opportunity will be negatively impacted.

The anti-cancer and antiviral treatment industries are highly competitive and subject to rapid and significant technological changes. Tyme has been developing SM-88 to compete with other drugs that currently exist or are being developed. Drugs Tyme may develop in the future are also likely to face competition from other drugs, some of which Tyme may not be currently aware of. In marketing Tyme's products, Tyme will have domestic and international competitors, including major multinational pharmaceutical companies, established biotechnology companies, specialty pharmaceutical companies, universities and other research institutions. Many of Tyme's competitors have significantly greater financial, manufacturing, marketing, drug development, technical and human resources than Tyme does. Large pharmaceutical companies, in particular, have extensive experience in clinical testing, obtaining regulatory approvals, patient recruitment and manufacturing pharmaceutical products. These companies also have significantly greater research and marketing capabilities than Tyme does and may also have products that have been approved or are in more advanced stages of development or collaborative arrangements in Tyme's target markets with leading companies and research institutions. Established pharmaceutical companies also may invest heavily to accelerate discovery and development of novel compounds or to in-license novel compounds that could make Tyme's drug candidates and any other drug product Tyme may develop obsolete. Some or all of these factors may contribute to Tyme's competitors succeeding in obtaining patent protection and/or marketing approval or developing and commercializing products in Tyme's field before it does.

There are a large number of companies working to develop and/or market various types of anti-cancer treatments. These treatments consist both of small molecule drugs, as well as biological drugs that work by using next-generation technology platforms to address specific cancer targets. These treatments are often combined with one another in an attempt to maximize a response rate. In addition, several companies are developing drugs that work by targeting additional specificities using a single recombinant molecule.

Tyme's commercial opportunity could be reduced or eliminated if Tyme's competitors develop and commercialize products that are safer, more effective, have fewer or less severe effects, are more convenient or are less expensive than Tyme's drug candidates. Tyme's competitors also may obtain FDA, EU or other non-U.S. regulatory approval for their products more rapidly than Tyme may, which could result in Tyme's competitors establishing a strong market position before Tyme is able to enter the market. If third parties obtain regulatory approval for their products before Tyme does, such products may change the treatment landscape for Tyme's product candidates and affect Tyme's ability to successfully launch and commercialize any products for which Tyme receives regulatory approval. Even if Tyme's drug candidates achieve marketing approval, they may be priced at a significant premium over competitive products, if any have been approved by then, resulting in Tyme's product's reduced competitiveness. In addition, the costs and restrictions effected by the ACA may impact Tyme's competitiveness or availability opportunity.

Further, Tyme's future ability to compete may be affected in many cases by insurers or other third-party payors seeking to encourage the use of generic or biosimilar products if and when they become available.

Smaller and other early-stage companies also may prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with Tyme in recruiting and retaining qualified scientific and management personnel, recruiting clinical trial sites and recruiting subjects for clinical trials, as well as in acquiring technologies complementary to or necessary for, Tyme's drug candidates. In addition, the biopharmaceutical industry is characterized by rapid technological changes. If Tyme fails to stay at the forefront of technological change, it may be unable to compete effectively. Technological advances or products developed by Tyme's competitors may render Tyme's technologies or product candidates obsolete, less competitive or not economical.

In addition, generic therapies, as further discussed under the caption "*Tyme's Business—Competition*" n this joint proxy statement/prospectus, are typically sold at lower prices than branded therapies and are generally preferred by hospital formularies and managed care providers of health services. Tyme anticipates that, if approved, Tyme's product candidates will face increasing competition in the form of generic versions of branded products of competitors, including those that have lost or will lose their patent exclusivity. In the future, Tyme may face additional competition from a generic form of Tyme's own candidates when the patents covering them begin to expire, or earlier if the patents are successfully challenged. If Tyme is unable to demonstrate to physicians and payers that the key differentiating features of its product candidates translate to overall clinical benefit or lower cost of care, it may not be able to compete with generic alternatives.

If any drug liability lawsuits are successfully brought against Tyme or any of its collaborators, Tyme may incur substantial liabilities and may be required to limit commercialization of Tyme's drug candidates and any other drug product Tyme may develop.

Tyme faces an inherent risk of drug liability lawsuits related to the testing ofSM-88, TYME-18, TYME-19 and any other product candidate Tyme may develop that is intended to treat seriously ill patients and that is approved by regulatory authorities and introduced commercially. Drug liability claims may be brought against Tyme or its collaborators, if any, by subjects enrolled in Tyme's clinical trials, patients, health care providers or others using, administering or selling drug products. If Tyme cannot successfully defend itself against any such claims, Tyme may incur substantial liabilities. Regardless of their merit or eventual outcome, liability claims may result in, but are not limited to:

- decreased demand for Tyme's drug candidates or any other product candidate Tyme may develop;
- injury to Tyme's reputation;
- withdrawal of subjects in Tyme's clinical trials;
- withdrawal of clinical trial sites or entire trial programs;
- increased regulatory scrutiny;
- significant litigation costs;
- substantial monetary awards to or costly settlements with patients or other claimants;
- drug recalls or a change in the indications for which they may be used;
- loss of revenue;
- diversion of management and scientific resources from Tyme's business operations; and
- the inability to commercialize SM-88 or such other drug product.

Adverse results, side effects of injuries may happen and may lead to product liability claims. Liability claims could divert management's attention from Tyme's core business, be expensive to defend, result in sizable damage awards against Tyme that may not be covered by liability insurance, and could harm Tyme's reputation in the marketplace among physicians and patients. Any of these events could harm Tyme's business and results of operations and cause Tyme's stock price to decline.

If any of Tyme's drug candidates are approved for commercial sale, Tyme will be highly dependent upon consumer perception and the safety, effectiveness and quality of such drug candidate. Tyme could be adversely affected if it is subject to negative publicity or if such drug candidate proves to be or is asserted to be, harmful to patients. Because of Tyme's dependence upon consumer perceptions, any adverse publicity associated with illness or other AEs resulting from patients' use or misuse of Tyme's drug candidates could have a material adverse impact on its financial condition or results of operations. This would also be true with respect to any other drug product Tyme may develop, receive regulatory approval of and, thereafter, seek to market.

Tyme holds clinical trial insurance for its ongoing clinical trials. Tyme also intends to obtain drug liability insurance coverage at appropriate levels for Tyme's operations, which will vary as the level of Tyme's operations vary during its growth from a research and development, or R&D, company to a company manufacturing and/or marketing drugs to the public. Tyme's current and planned insurance coverage may not be adequate to cover all liabilities that Tyme may incur. Tyme also may need to increase its insurance coverage when Tyme begins the commercialization of SM-88, TYME-18 or TYME-19. Insurance coverage can be expensive for pharmaceutical products and candidates. As a result, Tyme may be unable to obtain or maintain sufficient liability insurance at a reasonable cost to protect Tyme against losses, which could have a material adverse effect on its business. A successful drug liability claim or series of claims brought against Tyme, particularly if judgments exceed any insurance coverage Tyme may have, could decrease Tyme's cash resources and adversely affect its business, financial condition and results of operations and could possibly cause Tyme to cease its operations in their entirety.

Risks Related to Tyme's Financial Condition and Need for Additional Capital

Tyme has incurred significant losses since inception and anticipates that it will continue to incur losses for the foreseeable future. Tyme has no products approved for commercial sale and to date Tyme has not generated any revenue or profit from drug sales. Tyme may never realize revenue or profitability.

Tyme is a clinical-stage pharmaceutical company with a limited operating history. Tyme has incurred significant losses since its inception. As of March 31, 2022, Tyme's accumulated deficit was $160,420,062. Tyme's losses have resulted principally from expenses incurred in the discovery and development of SM-88 and from general and administrative expenses incurred while building its business infrastructure. Tyme expects to continue to incur losses for the near future. Furthermore, if Tyme continues its research and development of and seeks regulatory approval for its drug candidates and any other product candidates it may develop, prepare for development or commercialize, it expects these losses to increase. Any such drug or product candidates may also require additional infrastructure and personnel to support further drug development and commercialization efforts. The net losses and negative cash flows from operations incurred to date, together with expected future losses, have had and likely will continue to have, an adverse effect on Tyme's stockholders' equity and working capital. The amount of future net losses will depend, in part, on the rate of future growth of Tyme's expenses and its ability to generate revenue.

To become and remain profitable, Tyme must succeed in the development and commercialization of drug products with significant market potential. This will require Tyme to be successful in a range of challenging activities for which Tyme is only in the preliminary stages, including, with respect to the near term, developing Tyme's drug candidates, obtaining regulatory approval and manufacturing, marketing and selling its drug candidates. Tyme may never succeed with these activities or generate revenue from drug sales that is significant enough to achieve profitability. Tyme's ability to generate future revenue from drug sales depends heavily on Tyme's success in many areas, which include, but are not limited to:

- completing research and clinical development of Tyme's drug candidates, including successful completion of required clinical trials;
- obtaining marketing approval for Tyme's drug candidates;
- developing a sustainable and scalable manufacturing process for Tyme's drug candidates and maintaining supply and manufacturing relationships with third parties that can conduct the process and provide adequate (in amount and quality) drugs to support clinical development and the market demand for Tyme's drug candidates, if approved;
- launching and commercializing Tyme's drug candidates, either directly or with a collaborator or distributor;
- establishing sales, marketing and distribution capabilities in the United States and in other markets, such as the European Union;

- obtaining market acceptance of Tyme's drug candidates as a viable treatment option;
- addressing any competing technological and market developments;
- identifying, assessing, acquiring and/or developing new product candidates;
- negotiating favorable terms in any collaboration, licensing or other arrangements into which Tyme may enter;
- maintaining, protecting and expanding Tyme's portfolio of IP rights, including patents, trade secrets andknow-how; and
- attracting, hiring and retaining qualified personnel.

These factors would likely be applicable to any other product candidate Tyme may develop. Even if a product candidate that Tyme develops is approved for commercial sale, Tyme anticipates incurring significant costs associated with commercialization. Because of the numerous risks and uncertainties with drug development, Tyme is unable to accurately predict the timing or amount of increased expenses and when or if Tyme will be able to achieve profitability. For example, Tyme's expenses could increase if the FDA or EMA require Tyme to conduct supplemental clinical trials not included in Tyme's current development plan or if there are any delays in completing Tyme's planned clinical trials or in the development of Tyme's drug candidates or any other drug product Tyme may pursue. Even if Tyme achieves profitability in the future, Tyme may not be able to sustain profitability in subsequent periods. Tyme's failure to realize revenue or become or remain profitable could depress Tyme's market value and could impair Tyme's ability to raise capital, expand its business, develop other product candidates or continue its operations. A decline in the value of Tyme's shares could also cause investors in Tyme's common stock (or other securities Tyme may issue in the future) to lose all or part of their investment.

To achieve on Tyme's long-term development objectives, Tyme will require substantial additional funding, which may require Tyme to agree to restrictions on its operations or may not be available to Tyme on acceptable terms or at all and, if not available, may require Tyme to delay, scale back or cease Tyme's drug development programs or operations.

In addition to SM-88, Tyme has been seeking to advance multiple product candidates through Tyme's research and clinical development process. The completion of the development, regulatory approval and the potential commercialization of Tyme's drug candidates will require substantial funds. Tyme's future financing requirements will depend on many factors, some of which are beyond Tyme's control, which include, but are not limited to:

- the number and characteristics of product candidates that Tyme pursues;
- the scope, progress, timing, cost and results of nonclinical and clinical development and research;
- the costs, timing and outcome of Tyme's seeking and obtaining FDA, EMA and other non-U.S. regulatory approvals;
- the costs associated with manufacturing SM-88, as well as other potential product candidates, and establishing sales, marketing and distribution capabilities, including in collaboration with others;
- Tyme's ability to maintain, expand and defend the scope of Tyme's IP portfolio, including the amount and timing of any payments Tyme may be required to make in connection with the licensing, filing, defense and enforcement of any patents or other IP rights;
- the extent to which Tyme acquires or in-licenses other products or technologies;
- Tyme's need and ability to increase its overall capacity and hire additional administrative, managerial, scientific, operational and medical personnel;
- the effect of competing products that may limit market penetration of Tyme's drug candidates;

- the amount and timing of revenues, if any, Tyme receives from commercial sales of Tyme's drug candidates for which Tyme receives marketing approval in the future, which is expected to be offset by revenues Tyme must share with collaborators;
- Tyme's need to implement additional internal systems and infrastructure, including financial and reporting systems; and
- the economic and other terms, timing of and ultimate success of any future collaboration, licensing or other arrangements, including the timing of achievement of milestones and receipt of any milestone or royalty payments under such agreements.

Until Tyme can generate sufficient drug and royalty revenue to finance Tyme's cash requirements, which Tyme may never achieve, Tyme expects to finance future cash needs through a combination of public or private equity offerings, debt financings, collaborations, strategic alliances, licensing arrangements, royalty agreements and other marketing and distribution arrangements. The demand for the equity and debt of biotechnology companies like Tyme is dependent upon many factors, including the general state of the financial markets. During times of extreme market volatility, capital may not be available on favorable terms, if at all. Any additional fundraising efforts may divert management's attention from day-to-day activities and financing may not be available to Tyme when Tyme needs it or financings may not be available on favorable terms. If Tyme raises additional capital through marketing and distribution arrangements or other collaborations, strategic alliances, royalty rights or licensing arrangements with third parties, Tyme may have to relinquish certain valuable rights to Tyme's product candidates, technologies, future revenue streams or research programs and/or grant licenses on terms that may not be favorable to Tyme. If Tyme raises additional capital through public or private equity offerings, as Tyme expects to do, the ownership interests of Tyme's then existing stockholders could be diluted and the terms of these securities may include liquidation or other preferences that adversely affect stockholders' rights.

While Tyme regularly considers options and opportunities to raise additional capital and obtain financing and will continue to seek capital through a number of means, there can be no assurance that additional financing will be available on acceptable terms, if at all, and Tyme's negotiating position in capital generating efforts may worsen as existing resources are used. Additionally, if Tyme raises additional capital through debt financing, Tyme may be subject to covenants limiting or restricting Tyme's ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. Any debt financing or additional equity that Tyme raises may contain terms, such as liquidation and other preferences, which are not favorable to Tyme or its stockholders. If Tyme raises additional funds through collaborations, strategic alliances or licensing arrangements with third parties, Tyme may have to relinquish valuable rights to its technologies, product candidates or future revenue streams or have to grant licenses on terms that are not favorable to Tyme. For example, as described in the "*Tyme's Business—Collaboration with Eagle Pharmaceuticals*" subsection in this joint proxy statement/prospectus, under the Co-Promote, Eagle will receive 15% of the net sales of all SM-88 products in the U.S. during the term of the agreement. See "*Tyme's Business—Collaboration with Eagle Pharmaceuticals*" in this joint proxy statement/prospectus for a further discussion of this collaboration with Eagle. In addition, general market conditions, as well as market conditions for companies in Tyme's financial and business position, as well as the ongoing issues arising from the COVID-19 pandemic, may make it difficult for Tyme to seek financing from the capital markets, and the terms of any financing may adversely affect the holdings or the rights of Tyme's stockholders. Should the financing Tyme requires to sustain Tyme's working capital needs be unavailable or prohibitively expensive when Tyme requires it, Tyme's business, operating results, financial condition and prospects could be materially and adversely affected, and Tyme may be unable to continue its operations.

Tyme may expend its limited resources to pursue approval of Tyme's drug candidates to treat certain indications that may not be the most profitable or do not have the greatest likelihood of success.

Because Tyme has limited financial and managerial resources, Tyme has been focused on Tyme's research programs on SM-88 for the treatment of specified cancer therapies and on the pre-clinical development of

TYME-19. Tyme is also engaged in a biomarker initiative in an effort to better inform Tyme's development activities and areas of focus. As a result of Tyme's limited returns, Tyme may forego or delay pursuit of opportunities with other product candidates or other indications that later prove to have greater commercial potential. Tyme's resource allocation decisions may cause Tyme to fail to capitalize on viable commercial products or profitable market opportunities. For example, in June 2021, Tyme announced the discontinuation of its TYME-88-Panc trial. Tyme's spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable products.

If Tyme does not accurately evaluate the commercial potential or target market forSM-88 or any other product candidate, Tyme may relinquish valuable rights through collaboration, licensing or other royalty arrangements in cases where it would have been advantageous for Tyme to retain sole development and commercialization rights.

If Tyme does not achieve its projected development goals in the periods Tyme announces and expects, the commercialization of its products may be delayed and, as a result, its stock price may decline.

Over the course of Tyme's development efforts, Tyme will estimate the successful completion of various scientific, clinical, regulatory and other drug development goals, which Tyme refers to as milestones. These milestones may include the commencement or completion of clinical trials and the submission of planned regulatory filings. Occasionally, Tyme may publicly announce the expected timing of some of these milestones. All of these projected milestone timelines will be based on a variety of assumptions. The actual timing of achieving these milestones can vary dramatically compared to Tyme's estimates, in some cases for reasons beyond Tyme's control. If Tyme does not meet these milestones as publicly announced, the commercialization of Tyme's products may be delayed and, as a result, its stock price may decline.

Risks Related to Tyme's Reliance on Third Parties

Tyme relies on third parties to conduct its clinical trials and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of these trials.

Tyme currently relies on, and will likely continue to rely on, third parties, such as CROs, clinical data management organizations, medical institutions and clinical investigators to study Tyme's product candidates in clinical trials. Tyme may independently conduct future clinical trials for any drug product Tyme may develop, including SM-88, but will continue to collaborate with such parties to study SM-88 in their clinical trials of SM-88 or other drug candidates. This strategy necessarily relies upon clinical data and other results obtained by third parties that may ultimately prove to be inaccurate or unreliable. For example, Tyme partnered with PanCAN to study SM-88 in its adaptive randomized Phase II/III trial with registration intent known as Precision Promise, but the trial sponsor terminated the SM-88 arm of the trial due to futility, as described below in the "*Tyme's Business—Discontinuing Programs*" section of this joint proxy statement/prospectus. Also, HoPES is a Phase II investigator-initiated trial evaluating SM-88 monotherapy in late-stage sarcomas, under the direction of principal investigator Dr. Sant Chawla and in collaboration with The Joseph Ahmed Foundation. Tyme is collaborating with Georgetown University to support a clinical trial evaluating SM-88 in breast cancer. Tyme's reliance on these third parties for clinical development activities reduces Tyme's control over these activities, relieves Tyme of certain rights Tyme otherwise would have and puts Tyme at risk for the acts or omissions of these third parties, but it does not relieve Tyme of its responsibilities. For example, the FDA requires Tyme to comply with standards, commonly referred to as good clinical practices, for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of subjects in clinical trials are protected even though Tyme is not in control of these processes. If the third-party data and results Tyme relies upon prove to be inaccurate, unreliable or not applicable to Tyme's product candidates or future product candidate, Tyme could make inaccurate assumptions and conclusions about Tyme's product candidates and its research and development efforts could be compromised. These third parties also may have relationships with other entities, some of which may be Tyme's competitors. If

these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct Tyme's clinical trials in accordance with regulatory requirements or Tyme's stated protocols, Tyme will not be able to obtain, or may be delayed in obtaining, regulatory approvals for its drug candidates and will not be able to, or may be delayed in Tyme's efforts to, successfully commercialize its drug candidates.

In addition, if any of Tyme's relationships with third-party CROs or site management organizations terminate, Tyme may not be able to enter into arrangements with alternative CROs or site management organizations or to do so on commercially reasonable terms. Switching or adding additional CROs or site management organizations involves additional cost and requires management time and focus. Further, there is a natural transition period when a new CRO or site management organization commences work. As a result, delays could occur, which could compromise Tyme's ability to meet its desired development timelines. Though Tyme carefully manages its relationships with its CROs or site management organizations, there can be no assurance that Tyme will not encounter similar challenges or delays in the future. Forces beyond Tyme's control, including the impacts of COVID-19, could disrupt the ability of Tyme's third-party CROs, site management organizations, clinical data management organizations, medical institutions and clinical investigators to conduct Tyme's preclinical studies and Tyme's clinical trials for its product candidates and for any future product candidate.

Tyme also will rely on other third parties to store and distribute supplies for its clinical trials. Any performance failure on the part of Tyme's existing or future distributors could delay clinical development or regulatory approval of SM-88, producing additional losses and depriving Tyme of potential revenue.

Tyme intends to rely on third-party contract manufacturing organizations to manufacture and supply Tyme's drug candidates for Tyme. If one of Tyme's suppliers or manufacturers fails to perform adequately or fulfill Tyme's needs, Tyme may be required to incur significant costs and devote significant efforts to find new suppliers or manufacturers. Tyme may also face delays in the development and commercialization of its drug candidates and any other drug product Tyme may develop.

Tyme currently has limited experience in and does not own facilities for, clinical-scale manufacturing ofSM-88, TYME-18 and TYME-19, and expects to rely upon third-party contract manufacturing organizations to manufacture and supply drugs for Tyme's clinical trials. However, Tyme may be unable to establish any agreements with third-party manufacturers or to do so on acceptable terms. Even if Tyme is able to establish agreements with third-party manufacturers, reliance on third-party manufacturers entails additional risks, including the possible breach of the manufacturing agreement by the third party or the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for Tyme. In addition, the manufacture of pharmaceutical products in compliance with the FDA's cGMP requires significant expertise and capital investment, including the development of advanced manufacturing techniques and process controls. Manufacturers of pharmaceutical products often encounter difficulties in production, including difficulties with production costs and yields, quality control, including drug stability, quality assurance testing, shortages of qualified personnel, as well as compliance with strictly enforced cGMP requirements and other federal and state regulatory requirements and foreign regulations. If Tyme's manufacturers were to encounter any of these difficulties or otherwise fail to comply with their obligations to Tyme or under applicable regulations, it would jeopardize Tyme's ability to supply investigational drug for its clinical trials. Any delay or interruption in the supply of clinical trial materials, including as a result of restrictions put in place because of the COVID-19 pandemic or other supply chain disruptions, could delay the completion of Tyme's clinical trials, increase the costs associated with maintaining Tyme's clinical development programs and, depending upon the period of delay, require Tyme to commence new trials at significant additional expense or terminate the ongoing trials.

All manufacturers used to formulate the components of Tyme's drug candidates must comply with cGMP requirements, which are enforced by the FDA through its facilities inspection program. These requirements include, among other things, quality control, quality assurance and the documentation and maintenance of records. Manufacturers of Tyme's product candidates may be unable to comply with cGMP requirements and/or with other FDA, state and foreign regulatory requirements. The FDA or similar foreign regulatory agencies may

also implement new standards at any time or change their interpretation and enforcement of existing standards for the manufacture, packaging or testing of drug products. Tyme has little control over its manufacturers' compliance with these regulations and standards and a failure to comply with these requirements may result in fines and civil penalties, suspension of production, suspension or delay in drug approval, drug seizure or recall or withdrawal of a drug approval. If the safety of any drug supplied is compromised due to a manufacturers' failure to adhere to applicable laws or for other reasons, Tyme may not be able to obtain regulatory approval for or successfully commercialize SM-88 and as a result, may be held liable for any injuries sustained. Any of these factors could cause a delay of clinical trial completion, regulatory submission, approval or commercialization of Tyme's drug candidates, increase Tyme's costs or impair its reputation.

Tyme currently relies on third party suppliers for its drug candidates, including for the components of MPS used withSM-88. Supplies are obtained through limited term supply agreements under individual purchase orders. At this time, no supply agreements in place exceed 18 months. Although Tyme believes alternative sources of supplies exist, the number of third-party suppliers with the necessary manufacturing and regulatory expertise and facilities is limited, could be more expensive and it could take a significant amount of time to source, any of which would adversely affect Tyme's business. New suppliers would be required to qualify under applicable regulatory requirements and would need to have sufficient rights under applicable IP laws to the method of manufacturing the drug candidate. Obtaining the necessary FDA approvals or other qualifications under applicable regulatory requirements and ensuring non-infringement of third-party IP rights could result in a significant interruption of supplies and could require the new manufacturer(s) to bear significant additional costs which may be passed on to Tyme.

Tyme's reliance on third parties may require Tyme to share its trade secrets, which increases the possibility that a competitor could discover them or that Tyme's trade secrets could be misappropriated or disclosed.

Because Tyme relies on third parties to assist in the research, development and manufacture ofSM-88, TYME-18 and TYME-19, and may do so with any other product candidate Tyme may develop, Tyme must, at times, share trade secrets with such third parties. Tyme will seek to protect its proprietary technology in part by initially entering into confidentiality agreements and, if applicable, material transfer agreements, consulting agreements or other similar agreements with Tyme's advisors, employees and third-party contractors prior to disclosing any proprietary information. These agreements typically limit the rights of third parties to use or disclose Tyme's confidential information, which include its trade secrets. Despite the contractual provisions employed when working with third parties, the need to share trade secrets and other confidential information increases the risk that such trade secrets could become known by Tyme's competitors, are inadvertently incorporated into the technology of others or are disclosed or used in violation of these agreements. Given that Tyme's proprietary position is based, in part, on its know-how and trade secrets, a competitor's independent discovery of Tyme's trade secrets or other unauthorized use or disclosure could impair Tyme's competitive position and could have a material adverse effect on Tyme's business.

In addition, these agreements would typically restrict the ability of Tyme's advisors, employees, third-party contractors and consultants to publish data that could potentially relate to Tyme's trade secrets, even though Tyme's agreements may contain certain limited publication rights. For example, any academic institution that Tyme may collaborate with in the future can be, based on customary practice, expected to be granted rights to publish data arising out of such collaboration, provided that Tyme is notified in advance and given the opportunity to delay publication for a limited time period in order for Tyme to secure patent protection of IP rights arising from the collaboration, in addition to the opportunity to remove confidential or trade secret information from any such publication. In the future, Tyme may also conduct joint research and develop programs that may require Tyme to share trade secrets under the terms of such research. Despite Tyme's efforts to protect its trade secrets, Tyme's competitors may discover its trade secrets, either through breach of Tyme's agreements with third parties, independent development, publication of information by any of Tyme's third-party collaborators or otherwise. A competitor's discovery of Tyme's trade secrets could impair Tyme's competitive position and could have an adverse impact on Tyme's business.

Tyme has entered into a co-promotion agreement and may enter into additional license or collaboration agreements with third parties with respect to SM-88 and any other product candidates Tyme may develop that may place the development or promotion of Tyme product candidates partially or entirely outside of Tyme's control, may require Tyme to relinquish important rights or may otherwise be on terms unfavorable to Tyme. If such collaborations are not successful, then Tyme's drug candidates may not reach their full market potential.

As described under the heading "*Tyme's Business—Collaboration with Eagle Pharmaceuticals*" in this joint proxy statement/prospectus, Tyme entered into a co-promotion agreement with Eagle, whereby Eagle agreed to provide sales representatives to cover 25% of Tyme's sales force requirements and will receive 15% of the net sales of all SM-88 products in the U.S. during the term of the agreement. Tyme remains responsible for the remaining promotional effort. The co-promotion of SM-88 in the United States will be supervised by a joint sales operations committee composed of representatives from Tyme and Eagle. Under the agreement, Tyme will remain responsible for clinical development and commercial strategy and for the costs of seeking regulatory approval, manufacturing and distribution of SM-88. Tyme has the ability to purchase back the Eagle 15% share of the net U.S. sales for $200 million.

The co-promotion agreement provides parameters and sales requirements, but certain specific requirements related to promotional activities and requirements will be defined in more detail and finalized as any product nears commercialization. If Tyme and Eagle disagree on these matters, it could lead to disputes or be disruptive to sales efforts. Additionally, Eagle may change its strategic focus or pursue alternative technologies or treatments in a manner that results in reduced or delayed revenue to Tyme. If Eagle fails to effectively promote and assist in the commercialization of Tyme's SM-88 products, Tyme's business, financial condition, results of operations and prospects could be harmed. In addition, any material alteration of the collaboration agreements, or dispute or litigation proceedings Tyme may have with Eagle in the future could delay development programs, distract management from other business activities and generate substantial expense.

Tyme may in the future enter into additional license or collaboration arrangements with other third parties with respect to Tyme's drug candidates that may place the development or promotion of Tyme's product candidates partially or entirely outside of Tyme's control, may require Tyme to relinquish important rights or may otherwise be on terms unfavorable to Tyme, and could be subject to similar types of risks as described above. In particular, Tyme could seek partners for activities related to its TYME-18 and TYME-19 product candidates. In addition, any collaborations are and will be subject to numerous risks, which may include, but are not limited to:

- collaborators may have significant discretion in determining the efforts and resources that they will apply to collaborations;
- collaborators may not perform their obligations as expected;
- collaborators may not pursue development and commercialization of Tyme's drug candidates or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in their strategic focus due to the acquisition of competitive products, availability of funding or other external factors, such as a business combination that diverts resources or creates competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical program, stop a clinical trial, abandon Tyme's drug candidates, repeat or conduct new clinical trials or require a new formulation of Tyme's drug candidates;
- collaborators may be more established companies with a competitive advantage due to their larger size and cash resources or greater clinical development and commercialization capabilities and, as a result, Tyme may not be able to obtain favorable terms for Tyme's arrangements;
- collaborators could independently develop or develop with third parties, products that compete directly or indirectly with Tyme's drug candidates;

- a collaborator with marketing, manufacturing and distribution rights to one or more products may not commit sufficient resources to or otherwise not perform satisfactorily in carrying out these activities;
- Tyme could grant exclusive rights to Tyme's collaborators that would prevent Tyme from collaborating with others;
- collaborators may not properly maintain or defend Tyme's IP rights or may use Tyme's IP or proprietary information in a way that gives rise to actual or threatened litigation that could jeopardize or invalidate Tyme's IP or proprietary information or expose Tyme to potential liability;
- collaborators may not aggressively or adequately pursue litigation against ANDA filers or may settle such litigation on unfavorable terms;
- collaborations may be terminated, sometimes at-will, without penalty;
- collaborators may own or co-own IP covering Tyme's products that results from Tyme's collaborating with them and, in such cases, Tyme would not have the exclusive right to commercialize such IP;
- a collaborator's sales and marketing activities or other operations may not be in compliance with applicable laws and could result in civil or criminal proceedings; and
- disputes may arise between Tyme and a collaborator that causes the delay or termination of the research, development or commercialization of Tyme's drug candidates or any other product candidate Tyme may develop or results in costly litigation or arbitration that diverts management attention and resources.

If Tyme's collaborations are not successful, or Tyme is unable to reach agreement with a collaboration partner or disputes arise under collaboration arrangements, Tyme's drug candidates may not reach their full market potential, and its business, financial condition, results of operations and prospects could be harmed.

Risks Related to the Operation of Tyme

Tyme's future operational success depends on its ability to retain its key executives and to attract, retain and motivate qualified personnel.

Tyme is highly dependent on its chief executive officer and other members of its executive and scientific teams. Tyme's executives may terminate their employment with Tyme at any time. The loss of any of their services could impede the achievement of Tyme's research, development and commercialization objectives. Tyme does not currently maintain "key person" insurance on any of its executives or employees. While Tyme may, in the future, seek to obtain key person insurance , it may not be able to obtain the insurance at favorable rates or at all. Any insurance proceeds Tyme may receive under such "key person" insurance may not adequately compensate Tyme for the loss of the insured's services.

Recruiting and retaining qualified scientific, clinical, administrative, operations, manufacturing and sales and marketing personnel will also be critical to Tyme's success. An overall tightening and increasingly competitive labor market has been observed in the U.S. employment market generally, especially in response to the COVID-19 pandemic. Specific to the biotechnology industry, there is significant demand and competition for the highly specialized talent that Tyme requires. Tyme may not be able to attract and retain these personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. In addition, Tyme relies on consultants and advisors, including scientific and clinical advisors, to assist Tyme in formulating its research and development, preparing filings and communicating with the FDA and other regulatory authorities, preparing for and the conducting of clinical trials and formulating commercialization strategies. Tyme's consultants and advisors may be employed or contracted by other businesses in addition to Tyme's and may have commitments with other entities that may limit their availability to Tyme.

Until March 21, 2022, Tyme's drug discovery process and development program had been led by Steve Hoffman, Tyme's former chief science offer and former chief executive officer. Mr. Hoffman continues to serve as a member of Tyme's board of directors. As chief science officer, he had been instrumental in providing scientific, technical and business expertise. Development of SM-88 will continue without Mr. Hoffman's direct contributions, but future development of SM-88 and all other drug products in Tyme's pipeline may be adversely affected without his continued active involvement.

Tyme is highly reliant on its executives, but certain of them, including Tyme's acting chief medical officer, Jan M Van Tornout, have other business interests to which they devote their attention. From time to time, these other interests may distract their attention from Tyme, generate reputational risk for Tyme or give rise to conflicts of interest that must be resolved through the exercise of sound judgment consistent with their fiduciary duties to Tyme. Tyme's ability to attract and retain investors, collaborators, and employees could be adversely affected by damage to Tyme's reputation resulting from various sources, such as Tyme's executives' other business interests, employee misconduct, litigation, or regulatory outcomes.

Business disruptions (domestic and/or international) could seriously harm Tyme's future revenue and financial condition and increase its costs and expenses.

Tyme's operations could be subject to equipment failures, labor shortages, labor strikes, earthquakes, power shortages, telecommunications failures, floods, hurricanes, typhoons, fires, extreme weather conditions, terrorist activities, medical epidemics, riots, crime, acts of foreign enemies, war, nationalization, government sanction, blockage, embargo, widespread public health crises, economic and political disruptions including the impacts of military conflict between Russia and Ukraine and other natural or human-caused disasters or business interruptions. The occurrence of any of these business disruptions could seriously harm Tyme's operations and financial condition and could increase its costs and expenses.

Tyme's current and future, third-party collaborators, future partners, supplies, CROs and investigational sites are or will be, located throughout the United States or internationally and may be located near major high-risk terrorist targets, earthquake faults, flood and fire zones. The ultimate impact on Tyme, its significant partners and suppliers as well as its and their general infrastructures being located near major high-risk terrorist targets, earthquake faults, flood and fire zones and being consolidated in certain geographical areas is unknown, but Tyme's operations and financial condition could suffer in the event of a major terrorist attack, earthquake, fire, flood or other natural or manmade disaster.

Tyme's business is also subject to risks associated with conducting international business. If Tyme conducts clinical trials outside of the United States, or pursue and/or obtain approval to commercialize any approved products outside of the United States, a variety of risks associated with international operations could materially adversely affect Tyme's business. Some of Tyme's third-party collaborators, future partners, suppliers, CROs and investigational sites could be located outside the United States. Obtaining foreign regulatory approvals and compliance with foreign regulatory requirements could result in significant difficulties and costs for Tyme and could delay or prevent the introduction of its products in certain countries. Tyme may not obtain foreign regulatory approvals for its product candidates on a timely basis, if at all. Accordingly, Tyme's future success could be harmed by a variety of factors, which include, but are not limited to:

- economic weakness, including inflation or political instability in particular non-U.S. economies and markets;
- differing regulatory requirements for drug approvals in non-U.S. countries;
- differing, and in some cases, more stringent data protection requirements in non-U.S. countries, such as the GDPR;
- potentially reduced protection for IP rights;
- difficulties in compliance with non-U.S. laws and regulations;

- changes in non-U.S. regulations and customs, tariffs and trade barriers;
- changes in non-U.S. currency exchange rates and currency controls;
- changes in a specific country's or region's political or economic environment;
- trade protection measures, import/export licensing requirements or other restrictive actions by U.S. or non-U.S. governments;
- negative consequences from changes in tax laws;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- difficulties associated with staffing and managing international operations, including differing labor relations;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geo-political actions, including war and terrorism, such as the current conflict between Ukraine and Russia, widespread public health crises or pandemics, such as COVID-19, and related government responses, or natural disasters including earthquakes, typhoons, floods and fires.

Tyme may seek approvals of its product candidates in the European Union and United Kingdom. On June 23, 2016, the electorate in the United Kingdom voted in favor of leaving the European Union, commonly referred to as Brexit. Pursuant to the formal withdrawal arrangements agreed between the United Kingdom and the European Union, the United Kingdom was subject to a transition period until December 31, 2020, or the Transition Period, during which EU rules continued to apply. A trade and cooperation agreement, or the Trade and Cooperation Agreement, which outlines the future trading relationship between the United Kingdom and the European Union, was agreed upon in December 2020.

The Trade and Cooperation Agreement provides details on how some aspects of the United Kingdom's and European Union's relationship will operate going forwards, however, there are still many uncertainties. Brexit has already and may continue to adversely affect European and/or worldwide regulatory conditions and increase regulatory complexities. Brexit could lead to legal uncertainty and potentially divergent national laws and regulations in Europe, including those related to the pricing of prescription pharmaceuticals, as the United Kingdom determines which EU laws to replicate or replace, which could impair Tyme's ability to transact business in the European Union and the United Kingdom in the future, if Tyme elects to seek regulatory approval and commercialize any of its products there, if approved. The impact of Brexit on the regulatory regime with respect to the approval of Tyme's product candidates in the United Kingdom or the European Union remains uncertain, and could prevent or delay Tyme from commercializing its product candidates in the United Kingdom or the European Union and restrict its ability to generate revenue and achieve and sustain profitability. If any of these outcomes occur, Tyme may be forced to restrict or delay efforts to seek regulatory approval in the United Kingdom and/or European Union for its product candidates.

Tyme may be party to legal proceedings that could have a material adverse effect on Tyme's liquidity, financial position, and results of operations, as well as its reputation.

Tyme has limited experience in litigation and other legal proceedings, but any lawsuit brought against Tyme or legal proceeding that Tyme may bring to enforce its rights could result in substantial costs, divert the time and attention of Tyme management, result in counterclaims (whether meritorious or as a litigation tactic), result in substantial monetary judgments or settlement costs and harm Tyme's reputation, any of which could seriously

harm Tyme's business. For example, during the fourth quarter of fiscal year 2019, Tyme, along with its Chief Executive Officer, or CEO, and Chief Financial Officer, or CFO, were named in a securities lawsuit by a purported stockholder, in which the plaintiff alleged to represent a class of stockholders and asserted claims under the Exchange Act. Though such complaint was voluntarily dismissed by the plaintiff, Tyme could be subject to lawsuits in the future and any litigation or claim against Tyme, even without merit, may cause Tyme to incur substantial costs, and could place a significant strain on Tyme's financial resources, divert the attention of management from Tyme's core business, and harm Tyme's reputation.

In addition, in the past, when the market price of a stock has been volatile, holders of that stock have instituted securities class action litigation against the company that issued the stock. The threat of these types of lawsuits is particularly pronounced in the biotechnology and pharmaceuticals industry. Any lawsuit brought against Tyme by one or more of its stockholders, could result in substantial costs to defend the lawsuit, divert the time and attention of Tyme management, result in substantial monetary judgments or settlement costs and harm Tyme's reputation, any of which could seriously harm Tyme's business.

Further, as Tyme continues to seek to expand, raise capital, and develop and commercialize products, Tyme has entered into, and expect to enter into in the future, agreements and instruments, such as Tyme's outstanding warrants and co-promotion agreement, which are subject to interpretation and the potential for dispute. If Tyme and the counterparty to any such agreements or holders of such instruments are unable to resolve such disagreements, the disagreements may result in lawsuits, other legal proceedings and/or protracted negotiations, including those whereby Tyme seeks to enforce its rights. Even if successful, litigation, other legal proceedings or protracted negotiations could be expensive and time consuming and could divert management's attention from managing Tyme's business and could result in significant adverse judgments or costs of settlement, amendments to agreements or adjustments to instruments, any of which may have a material adverse effect on Tyme's liquidity, financial position, business, reputation or prospects.

Tyme's internal computer systems or those of Tyme's CROs or other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of Tyme's drug development program.

Despite the implementation of security measures, Tyme's internal computer systems, and those of Tyme's CROs and other third parties on which Tyme relies, are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. If such an event were to occur and cause interruptions in Tyme's operations, it could result in a material disruption of Tyme's drug development programs. For example, the loss of clinical trial data from completed or ongoing or planned clinical trials could result in delays in Tyme's regulatory approval efforts and significantly increase Tyme's costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of or damage to Tyme's data or applications, or inappropriate disclosure of confidential or proprietary information, Tyme could incur liability and the further development of its product candidates could be delayed.

Cyber-attacks are increasing in their frequency, sophistication and intensity, and have become increasingly difficult to detect. Cybersecurity incidents resulting in the failure of Tyme's systems to operate effectively or to integrate with other systems, including those of third-parties with whom Tyme relies on for research, clinical trial services or other business and administrative services, or a breach in security or other unauthorized access of these systems, may affect Tyme's ability to manage and maintain its operations. A breach in security, unauthorized access resulting in misappropriation, theft, or sabotage with respect to Tyme's proprietary and confidential information, including research or clinical data, could require significant investments of capital and time to remediate and could adversely affect Tyme's business, financial condition and results of operations. For example, any such event that leads to unauthorized access, use or disclosure of personal information, including personal information regarding patients in Tyme's clinical trials or other studies or Tyme's employees, could harm Tyme's reputation, require Tyme to comply with federal and/or state breach notification laws, and otherwise subject Tyme to liability under laws and regulations that protect the privacy and security of personal information. Security breaches and other inappropriate access can be difficult to detect, and any delay in

identifying them may lead to increased harm of the type described above. Potential vulnerabilities can be exploited through inadvertent or intentional actions of Tyme's employees, third-party vendors, and business partners, or by malicious third parties. There can be no assurance that the security measures Tyme has implemented to protect its information technology systems and infrastructure will prevent service interruptions or security breaches that could adversely affect Tyme's business.

Use of social media could give rise to liability, breaches of data security, or reputational harm.

Tyme and its employees use social media to communicate externally. There is risk that the use of social media by Tyme or its employees to communicate about Tyme's product candidates or business may give rise to liability, lead to the loss of trade secrets or other IP, or result in public exposure of personal information of Tyme's employees, clinical trial patients, customers, and others. Furthermore, negative posts or comments about Tyme or its product candidates in social media could seriously damage Tyme's reputation, brand image, and goodwill. Any of these events could have a material adverse effect on Tyme's business, prospects, operating results, and financial condition and could adversely affect the price of Tyme's common stock.

Risks Related to IP

Tyme's ability to successfully commercialize its technology and drug candidate may be materially adversely affected if Tyme is unable to obtain and maintain effective IP.

Tyme's success is largely dependent on its ability to obtain and maintain patent and other IP protection in the United States and in other countries with respect to its proprietary technology and drug candidates. In some circumstances, Tyme may not have the right or ability to control the preparation, filing and prosecution of patent applications or to maintain or enforce the patents covering technology or products that Tyme licenses to third parties or, conversely, that Tyme may license from third parties. Therefore, if Tyme becomes aware of any patent infringement, Tyme cannot be certain that these patents and applications will be prosecuted and enforced in a manner consistent with the best interests of Tyme's business. In addition, if third parties who license patents to Tyme or from Tyme fail to maintain such patents or lose rights to those patents, licensing rights or the protection afforded by those patents may be reduced or eliminated.

Tyme has sought to protect its proprietary position by filing patent applications in the United States and abroad related to Tyme's novel technologies and products that are important to its business. This process is expensive and time-consuming and Tyme may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. In addition, Tyme may not pursue or obtain patent protection in all relevant markets. It is also possible that Tyme fails to identify patentable aspects of Tyme's research and development output before it is too late to obtain patent protection. Tyme's pending and future patent applications may be insufficient to protect its technology or products, completely or in part. In addition, existing and any future patents Tyme obtains may not be extensive enough to prevent others from using its technologies or from developing competing drugs and technologies.

The patent position of specialty pharmaceutical and biotechnology companies generally is highly uncertain and involves complex legal and factual questions for which many legal principles remain unresolved. In recent years, patent rights have been the subject of significant litigation and, as a result, the issuance, scope, validity, enforceability and commercial value of Tyme's patent rights are highly uncertain. Tyme's pending and future patent applications may result in patents not being issued to Tyme in the United States or in other countries. Changes in either the patent laws or interpretation of patent laws in the United States and other countries may diminish the value of Tyme's patents or narrow the scope of its patent protection. In addition, the laws of foreign countries may not protect Tyme's rights to the same extent as the laws of the United States. Publications of discoveries in scientific literature often lag behind the actual discoveries and patent applications in the United States and other countries are typically not published until 18 months after filing or in some cases not at all. Therefore, Tyme cannot be certain that Tyme was the first to make the inventions claimed in its patents or

pending patent applications or that Tyme was the first to file for patent protection of such inventions. In addition, the USPTO, might require that the term of a patent issuing from a pending patent application be disclaimed and limited to the term of another patent that is commonly owned or names a common inventor. As a result, the issuance, scope, validity, enforceability and commercial value of Tyme's patent rights is highly uncertain.

Recent or future patent reform legislation could increase the uncertainties and costs surrounding the prosecution of Tyme's patent applications and the enforcement or defense of Tyme's issued patents. Tyme may become involved in opposition, interference, derivation, *inter partes* review or other proceedings that challenge Tyme's patent rights or the patent rights of others and the outcome of any proceedings are highly uncertain. An adverse determination in any such proceeding could reduce the scope of or invalidate Tyme's patent rights, allowing third parties to commercialize Tyme's technology or drug products and compete directly with Tyme, without payment to Tyme or result in Tyme's inability to manufacture or commercialize products without infringing third-party patent rights.

Even if Tyme's patent applications issue as patents, they may not issue in a form that will provide Tyme with any meaningful protection, prevent competitors from competing with Tyme or otherwise provide Tyme any competitive advantage. Tyme's competitors may be able to circumvent Tyme's owned or licensed patents by developing similar or alternative technologies or drugs in a non-infringing manner. The issuance of a patent is not conclusive as to its scope, validity or enforceability and Tyme's owned and licensed patents may be challenged in the courts or patent offices in the United States and abroad. Such challenges may result in the patent claims of Tyme's owned or licensed patents being narrowed, invalidated or held unenforceable and may cost significant time and resources to defend. This could limit Tyme's ability to stop or prevent Tyme from stopping others from using or commercializing similar or identical technology and drugs or limit the duration of the patent protection of Tyme's technology and drugs. Given the amount of time required for the development, testing and regulatory review of new drug candidates, patents protecting use of Tyme's drug might expire before or shortly after any drug candidate is commercialized. As a result, Tyme's patent portfolio may not provide Tyme with sufficient rights to exclude others from commercializing products similar or identical to Tyme's drug products or otherwise provide Tyme with a competitive advantage. Furthermore, changes to patent laws could diminish the value of patents in general, thereby impairing Tyme's ability to protect Tyme's rights in its product candidates.

Tyme may not be able to protect its IP rights throughout the world.

Filing, prosecuting and defending patents for Tyme's drug candidates throughout the world would be prohibitively expensive. Competitors may use Tyme's technologies in countries where it has not obtained patent protection to develop their own drugs and, further, may export otherwise infringing products to territories where Tyme has patent protection but where enforcement is not as strong as in the United States. These products may compete with Tyme's drug products in countries where Tyme does not have any issued patents and Tyme's patent claims or other IP rights may not be effective or sufficient to prevent them from so competing. Many companies have encountered significant problems in protecting and defending IP rights in foreign countries. The legal systems of a number of countries, particularly a number of developing countries, do not favor the enforcement of patents and other IP protection, including those relating to biopharmaceuticals, which could make it difficult for Tyme to stop the infringement of Tyme's patents or marketing of competing products against third parties in violation of Tyme's proprietary rights. Even if Tyme does secure patents in foreign jurisdictions, the legal systems in certain of those countries might require Tyme, as examples, to do business through an entity that is partially owned by a local investor, or to grant license rights to local partners in a manner not required by the jurisdictions in which Tyme currently operates. Additionally, governmental actions, such as the potential waiver of IP protection or imposition of compulsory licenses related to COVID-19 vaccines, or other potential waivers of IP during emergencies, if applicable to any of Tyme's product candidates could harm Tyme's ability to successfully and profitably commercialize its product candidates. Requirements such as the foregoing could limit Tyme's ability to fully exploit and in the future monetize its product candidates and patents, as well as placing potential additional difficulties on Tyme's enforcement efforts in those jurisdictions. Further, the initiation of

proceedings to enforce or protect Tyme's patent rights in foreign countries could result in substantial cost and divert Tyme's efforts and attention from other aspects of its business.

Obtaining and maintaining Tyme's patent protection depends upon compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies. Tyme's patent protection could be reduced or eliminated for noncompliance with these requirements.

The USPTO and various non-U.S. patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during and following the patent prosecution process. Tyme's failure to comply with such requirements could result in abandonment or lapse of a patent or patent application, which would result in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, competitors might be able to enter the market earlier than would have been the case if Tyme's patents were in force.

Tyme may become involved in lawsuits or other proceedings to protect or enforce its patents or other IP, which could be expensive, time-consuming and unsuccessful.

Competitors or other third parties may infringe or otherwise violate Tyme's patents, trademarks, copyrights or other IP. To counter infringement or unauthorized use, Tyme or its licensees may be required to file infringement claims, which can be expensive and time-consuming. For example, if Tyme needs to file patent infringement lawsuits in the future against manufacturers of generic pharmaceuticals that have filed ANDAs with the FDA seeking approval to manufacture and sell generic versions of Tyme's drug candidates, Tyme anticipates that the prosecution of such lawsuits will require a significant amount of time and attention from Tyme's chief executive officer, chief science officer and other senior executives. In addition, in a patent infringement proceeding, a court may decide that Tyme's patent is invalid or unenforceable or may refuse to stop the other party from using the technology at issue on the grounds that Tyme's patents do not cover the technology in question. An adverse result in the litigation or proceeding could put one or more of Tyme's patents at risk of being invalidated or interpreted narrowly. Such a result could limit Tyme's ability to prevent others from using or commercializing similar or identical technology and drugs, limit Tyme's ability to prevent others from launching generic versions of Tyme's drug products and could limit the duration of patent protection for Tyme's products, all of which could have a material adverse effect on Tyme's business. A successful challenge to Tyme's patents could reduce or eliminate Tyme's right to receive royalties. Furthermore, because of the substantial amount of discovery required in connection with IP litigation, there is a risk that some of Tyme's confidential information could be compromised by disclosure during litigation.

Tyme's commercial success depends significantly on its ability to operate without infringing the patents and other proprietary rights of third parties.

Tyme's success will depend in part on its ability to operate without infringing the proprietary rights of third parties. Other entities may have or obtain patents or proprietary rights that could limit Tyme's ability to make, use, sell, offer for sale or import/export any approved drug candidate, or impair Tyme's competitive position.

Patents could be issued to third parties that Tyme may ultimately be found to infringe. Third parties may have or obtain valid and enforceable patents or proprietary rights that could block Tyme from developing product candidates using its technology. Tyme's failure to obtain a license to any technology that it requires or on commercially reasonable terms may materially harm Tyme's business, financial condition and results of operations. Moreover, Tyme's failure to maintain a license to any technology that it requires for its drug products or their manufacture may also materially harm Tyme's business, financial condition and results of operations. Furthermore, Tyme would be exposed to a threat of litigation.

In the pharmaceutical industry, significant litigation and other proceedings regarding patents, patent applications, trademarks and other IP rights have become commonplace. The types of situations in which Tyme may become a party to such litigation or proceedings include:

- Tyme or its collaborators may initiate litigation or other proceedings against third parties seeking to invalidate the patents held by those third parties or to obtain a judgment that Tyme's drugs or processes do not infringe those third parties' patents;
- if Tyme's competitors file patent applications that claim technology also claimed by Tyme or its licensors or collaborators, Tyme or its licensors or collaborators may be required to participate in interference or opposition proceedings to determine the priority of invention, which could jeopardize Tyme's patent rights and potentially provide a third-party with a dominant patent position;
- if third parties initiate litigation claiming that Tyme's processes or products infringe their patent or other IP rights, Tyme and its licensors or collaborators will need to defend against such proceedings; and
- if a license to necessary drug technology is terminated, the licensor may initiate litigation claiming that Tyme's processes or products infringe or misappropriate their patent or other IP rights and/or that Tyme breached Tyme's obligations under the license agreement and Tyme and Tyme's collaborators would need to defend against such proceedings.

These lawsuits would likely be costly and could affect Tyme's results of operations and divert the attention of its management and scientific personnel. There is a risk that a court would decide that Tyme or its collaborators are infringing the third party's patents and would order Tyme or its collaborators to stop the activities covered by the patents. In that event, Tyme or its collaborators may not have a viable alternative to the technology protected by the patent and may need to halt work on the affected product candidate or cease commercialization of an approved product. In addition, there is a risk that a court will order Tyme or its collaborators to pay the other party damages. An adverse outcome in any litigation or other proceeding could subject Tyme to significant liabilities to third parties and require Tyme to cease using the technology that is at issue or to license the technology from third parties. Tyme may not be able to obtain any required licenses on commercially acceptable terms or at all. Any of these outcomes could have a material adverse effect on Tyme's business.

The pharmaceutical and biotechnology industries have produced a significant number of patents and it may not always be clear to industry participants, including Tyme, which patents cover various types of products or methods of use. The coverage of patents is subject to interpretation by the courts and the interpretation is not always uniform or predictable. If Tyme is sued for patent infringement, it would need to demonstrate that Tyme's products or methods do not infringe the patent claims of the relevant patent or that the patent claims are invalid. Tyme may not be able to do this because proving invalidity is difficult. For example, in the United States, proving invalidity requires a showing of clear and convincing evidence to overcome the presumption of validity enjoyed by issued patents. Even if Tyme is successful in these proceedings, it may incur substantial costs and divert management's time and attention in pursuing these proceedings, which could have a material adverse effect on Tyme. If Tyme is unable to avoid infringing the patent rights of others, it may be required to seek a license, defend an infringement action or challenge the validity of the patents in court. Tyme may not have sufficient resources to bring these actions to a successful conclusion. In addition, if Tyme does not obtain a license, develop or obtain non-infringing technology, fail to defend an infringement action successfully or have infringed patents declared invalid, Tyme may incur substantial monetary damages, encounter significant delays in bringing Tyme's drug candidates to market and be precluded from manufacturing or selling one or more of Tyme's drug products.

As noted previously, the cost of any patent litigation or other proceeding, even if resolved in Tyme's favor, could be substantial. Some of Tyme's competitors may be able to sustain the cost of such litigation and proceedings more effectively than Tyme can because of their substantially greater resources. Uncertainties resulting from the

initiation and continuation of patent litigation or other proceedings could have a material adverse effect on Tyme's ability to compete in the marketplace. For example:

- patent litigation and other proceedings initiated by or against Tyme may also absorb significant management time;
- if proceedings are initiated by or against Tyme to determine the priority of invention, they could jeopardize Tyme's patent rights and potentially provide a third-party with a dominant patent position;
- if third parties initiate litigation claiming that Tyme's processes or products infringe their patent or other IP rights, Tyme and its licensors or collaborators will need to defend against such proceedings; and
- if a license to necessary drug technology is terminated, the licensor may initiate litigation claiming that Tyme's processes or products infringe or misappropriate their patent or other IP rights and/or that Tyme breached its obligations under the license agreement and Tyme and its collaborators would need to defend against such proceedings.

For example, Tyme may sometimes need to collaborate with U.S. andnon-U.S. academic institutions to accelerate Tyme's nonclinical research or development under written agreements with these institutions. Typically, these institutions could provide Tyme with an option to negotiate a license to any of the institution's rights in technology resulting from Tyme's collaboration. Regardless of such option, Tyme may be unable to negotiate a license within the specified timeframe or under terms that are acceptable to Tyme. If Tyme is unable to do so, the institution may offer the IP rights to other parties, potentially blocking Tyme's ability to pursue the applicable drug candidate or program.

In addition, companies that perceive Tyme to be a competitor may be unwilling to assign or license rights to Tyme. Tyme also may be unable to license or acquire third-party IP rights on terms that would allow Tyme to make an appropriate return on Tyme's investment. If Tyme is unable to successfully obtain a license to third-party IP rights necessary for the development of Tyme's drug products, Tyme may have to abandon its development and therefore, its business and financial condition could suffer.

Tyme may be unable to protect the confidentiality of its trade secrets, thus harming its business and competitive position.

In addition to Tyme's patented technology, Tyme relies upon trade secrets, including unpatentedknow-how, technology and other proprietary information to develop and maintain its competitive position, which Tyme seeks to protect, in part, by confidentiality agreements with its current and future employees, as well as its collaborators and consultants. Tyme also have agreements with its employees and selected consultants that obligate them to assign their inventions to Tyme. However, while it is Tyme's policy to require its employees and contractors who may be involved in the conception or development of IP to execute such agreements, Tyme may be unsuccessful in executing such an agreement with each party who in fact conceives or develops IP that Tyme regards as its own. In addition, it is possible that technology relevant to Tyme's business will be independently developed by a person that is not a party to such an agreement. While to Tyme's knowledge the confidentiality of its trade secrets has not been compromised, if the employees, consultants or collaborators that are parties to these agreements breach or violate the terms of these agreements, Tyme may not have adequate remedies for any such breach or violation and Tyme could lose its trade secrets through such breaches or violations. Further, Tyme's trade secrets could be disclosed, misappropriated or otherwise become known or be independently discovered by Tyme's competitors. In addition, IP laws in foreign countries may not protect Tyme's IP to the same extent as the laws of the United States. If Tyme's trade secrets are disclosed or misappropriated, it would harm Tyme's ability to protect its rights and adversely affect its business.

Tyme may be subject to claims that its employees and outside contractors have wrongfully used or disclosed IP from their former employers and clients. IP litigation or proceedings could cause Tyme to spend substantial resources and distract Tyme's personnel from their normal responsibilities.

Although Tyme will try to ensure that its employees and outside contractors do not use the proprietary information or the know-how of others in their work for Tyme and Tyme has no knowledge of any instances of wrongful use or disclosure by Tyme's employees and outside contractors to date, Tyme may be subject to claims that it or these employees and outside contractors have used or disclosed IP, including trade secrets or other proprietary information from their former employers or clients. Litigation may be necessary to defend Tyme against these claims. If Tyme fails in defending any such claims, in addition to paying monetary damages, Tyme may lose valuable IP rights, personnel or consulting services. Even if Tyme is successful in defending against such claims, litigation or other legal proceedings relating to IP claims may cause Tyme to incur significant expenses and could distract Tyme's scientific and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments. Should this occur and securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of Tyme's common stock. This type of litigation or proceeding could substantially increase Tyme's operating losses and reduce resources available to Tyme for development activities. Tyme may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of Tyme's competitors may be able to sustain the costs of such litigation or proceedings more effectively than Tyme can because of their substantially greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other IP-related proceedings could adversely affect Tyme's ability to compete in the marketplace.

If Tyme does not obtain protection under the Hatch-Waxman Amendments and similar non-U.S. legislation for extending the term of patents covering Tyme's drug candidates, its business may be materially harmed.

Depending upon the timing, duration and conditions of FDA marketing approval of SM-88 and any other drug product Tyme may develop in the future, one or more of Tyme's U.S. patents may be eligible for limited patent term extension under the the Hatch-Waxman Amendments and similar legislation in the European Union. The Hatch-Waxman Amendments permit a patent term extension of up to five years for a patent covering an approved drug as compensation for effective patent term lost during drug development and the FDA regulatory review process. However, Tyme may not receive an extension if it fails to apply within applicable deadlines, fail to apply prior to expiration of relevant patents or otherwise fail to satisfy applicable requirements. Moreover, the length of the extension could be less than Tyme requests. If Tyme is unable to obtain patent term extension or the term of any such extension is less than Tyme requests, the period during which Tyme can enforce its patent rights for that drug will be shortened and Tyme's competitors may obtain approval to market competing products sooner. As a result, Tyme's revenue could be materially reduced.

If Tyme's trademarks and trade names are not adequately protected, then Tyme may not be able to build name recognition in its markets of interest and its business may be adversely affected.

Tyme's registered or unregistered trademarks or trade names, to the extent Tyme obtains and uses them, may be challenged, infringed, circumvented, declared generic, unregisterable or determined to be infringing on other marks. Tyme may not be able to protect its rights to these trademarks and trade names, which Tyme needs to build name recognition among potential partners or customers in Tyme's markets of interest. At times, competitors may adopt trade names or trademarks similar to Tyme's, thereby impeding Tyme's ability to build brand identity and possibly leading to market confusion or trademark dilution. In addition, there could be potential trade name or trademark infringement claims brought by owners of other registered trademarks or trademarks that incorporate variations of Tyme's registered or unregistered trademarks or trade names. Over the long term, if Tyme is unable to establish name recognition based on Tyme's trademarks and trade names, then Tyme may not be able to compete effectively, and its business may be adversely affected. Tyme's efforts to enforce or protect its proprietary rights related to trademarks, trade secrets, domain names, copyrights or other IP

may be ineffective and could result in substantial costs and a diversion of resources and could adversely affect Tyme's financial condition or results of operations.

Risks Related to Government Regulations and Agencies

Health care reform measures could hinder or prevent the commercial success of Tyme's drug candidates.

In the United States, there has been, and Tyme expects there will continue to be, a number of legislative and regulatory changes to the healthcare system that could affect Tyme's future revenue and profitability and the future revenue and profitability of its potential customers. Federal and state lawmakers regularly propose and, at times, enact legislation that would result in significant changes to the healthcare system, some of which are intended to contain or reduce the costs of medical products and services. For example, the ACA contains a number of provisions, including those governing enrollments in federal healthcare programs, reimbursement changes and fraud and abuse measures, all of which have affected existing government healthcare programs and resulted in the development of new programs. Among the provisions of the ACA of importance to Tyme's current and potential product candidates are the following:

- an annual, nondeductible fee payable by any entity that manufactures or imports specified branded prescription drugs and biologic agents;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% and 13.0% of the average manufacturer price for branded and generic drugs, respectively;
- a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 70% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D;
- extension of manufacturers' Medicaid rebate liability to individuals enrolled in Medicaid managed care organizations;
- expansion of healthcare fraud and abuse laws, including the False Claims Act and the Anti-Kickback Statute, which include, among other things, new government investigative powers and enhanced penalties for non-compliance;
- expansion of eligibility criteria for Medicaid programs in certain states;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- a new requirement to annually report drug samples that manufacturers and distributors provide to physicians;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research; and
- an independent payment advisory board that will submit recommendations to Congress to reduce Medicare spending if projected Medicare spending exceeds a specified growth rate.

Additionally, various initiatives continue to increase pathways for patients to seek treatment of investigational products outside of clinical trials, including the Trickett Wendler, Frank Mongiello, Jordan McLinn, and Matthew Bellina Right to Try Act of 2017, state right to try laws, and the FDA's Expanded Access program. These initiatives could potentially impact patient enrollment in clinical trials. These pathways do not currently include any obligations for a manufacturer to make its investigational products available to patients. The future direction and impact of these initiatives is unknown.

There have been, and likely will continue to be, legislative and regulatory proposals at the foreign, federal and state levels directed at broadening the availability of healthcare and containing or lowering the cost of healthcare, including initiatives designed to control or influence product pricing. Tyme cannot predict the initiatives that may be adopted in the future. The continuing efforts of the government, insurance companies, managed care organizations and other payors of health care services to contain or reduce costs of health care may, among other things, adversely affect:

- Tyme's ability to set a price Tyme believes is fair for its drug products;
- Tyme's ability to generate revenue and achieve or maintain profitability; and
- the availability of capital.

Judicial challenges, executive orders and legislative repeal measures relating to the ACA may create regulatory uncertainty with respect to the pharmaceutical, biotechnology and other life sciences industries and may materially harm Tyme's business, financial condition and results of operations.

Since its enactment, there have been executive, judicial and Congressional challenges to certain aspects of the ACA.

Although Congress has not passed comprehensive repeal legislation, several bills affecting the implementation of certain taxes under the ACA have been signed into law. The Tax Act includes a provision that became effective on January 1, 2019 and repealed the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year, which payment is commonly referred to as the "individual mandate." In addition, the 2020 federal spending package permanently eliminated, effective January 1, 2020, the ACA-mandated "Cadillac" tax on high-cost employer-sponsored health coverage and medical device tax and, effective January 1, 2021, also eliminated the health insurer tax. The Bipartisan Budget Act of 2018, or the BBA, among other things, amended the ACA, effective January 1, 2019, to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole." On December 14, 2018, a Texas U.S. District Court judge ruled that the ACA is unconstitutional in its entirety because the individual mandate was repealed by Congress as part of the Tax Act. Additionally, on December 18, 2019, the U.S. Court of Appeals for the 5th Circuit upheld the District Court ruling that the individual mandate was unconstitutional and remanded the case back to the District Court to determine whether the remaining provisions of the ACA are also invalid. On June 17, 2021, the Supreme Court ruled that the plaintiffs (consisting of the state of Texas, as well as other states and individuals) did not have proper standing and accordingly vacated the Fifth Circuit's decision and instructed the district court to dismiss the case. As a result, the Affordable Care Act will remain in its current form for the foreseeable future, but Tyme cannot predict when, or whether, additional challenges may arise and what the outcome of such challenge may be. The Biden administration has also introduced various measures in 2021 focusing on healthcare and drug pricing. On January 28, 2021, President Biden issued an executive order to initiate a special enrollment period from February 15, 2021 through May 15, 2021 for purposes of obtaining health insurance coverage through the ACA marketplace. The executive order also instructs certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. On March 11, 2021, the American Rescue Plan Act of 2021 was signed into law, which, in relevant part, eliminates the statutory Medicaid drug rebate cap, currently set at 100% of a drug's average manufacturer price, for single source drugs and innovator multiple source drugs, beginning January 1, 2024. In July 2021, the Biden administration released an executive order entitled, "Promoting Competition in the American Economy," with multiple provisions aimed at prescription drugs. In response, HHS released a "Comprehensive Plan for Addressing High Drug Prices" that outlines principles for drug pricing reform and sets out a variety of potential legislative policies that Congress could pursue as well as potential administrative actions that HHS can take to advance these principles. In November 2021, President Biden announced the Prescription Drug Pricing Plan as part of the Build Back Better Act (H.R. 5376) passed by the House of

Representatives on November 19, 2021, which aims to lower prescription drug pricing by, among other things, allowing Medicare to negotiate prices for certain high-price prescription drugs covered under Medicare Part D and Part B after the drugs have been on the market for a certain number of years and imposing tax penalties on drug manufacturers that refuse to negotiate pricing with Medicare or increase drug prices "faster than inflation." If passed, this bill could have a substantial impact on Tyme's business, particularly when Tyme has commercially available products on the U.S. market, if ever.

Continued judicial challenges to the Health Care Reform Act and other executive action and legislation, could result in increased uncertainty with respect to the pharmaceutical, biotechnology and other life science industries and may materially harm Tyme's business, financial condition and results of operations. Further, Tyme can provide no assurance that the ACA, as currently enacted or as amended in the future, or other related laws will not adversely affect its business, financial condition or results of operations. Nor can Tyme predict how future federal or state legislative or administrative changes relating to health care reform will affect its business, financial condition or results of operations.

If Tyme fails to comply with healthcare and privacy laws and regulations, it could face substantial penalties and its business, operations and financial condition could be adversely affected.

Certain federal and state healthcare laws and regulations pertaining to fraud and abuse patients' rights are, and other healthcare issues and will be, applicable to Tyme's business. Tyme could be subject to healthcare fraud and abuse, privacy and security, and transparency regulation by both the federal government and the states in which Tyme conducts its business. The regulations that may affect Tyme's ability to operate include, but are not limited to:

- the federal healthcare program Anti-Kickback Statute, which prohibits knowingly and willfully offering, soliciting, receiving or providing any remuneration (including any kickback, bribe or rebate), directly or indirectly, overtly or covertly, in cash or in kind, in exchange for or to induce either the referral of an individual for or the purchase order, lease or recommendation of any good, facility, item or service for which payment may be made, in whole or in part, under federal healthcare programs, such as the Medicare and Medicaid programs;
- the federal false claims laws and civil monetary penalty laws, which prohibit, among other things, individuals or entities from knowingly presenting or causing to be presented, false or fraudulent claims for payment or approval or knowingly using false statements, to obtain payment from the federal government and which may apply to entities like Tyme which provide coding and billing advice to customers;
- HIPAA which created new federal criminal statutes that prohibit knowingly and willfully executing or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations or promises, any of the money or property owned by or under the custody or control of, any healthcare benefit program, regardless of the payor (e.g., public or private) and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false statements in connection with the delivery of or payment for, healthcare benefits, items or services relating to healthcare matters;
- the federal physician self-referral law, commonly known as the Stark Law, which prohibits a physician from making a referral to an entity for certain designated health services reimbursed by Medicare or Medicaid if the physician or a member of the physician's family has a financial relationship with the entity and which also prohibits the submission of any claims for reimbursement for designated health services furnished pursuant to a prohibited referral;
- the federal transparency requirements under the ACA, which require manufacturers of drugs, devices, biologicals and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report annually to the HHS

information related to physician payments and other transfers of value made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, as well as certain ownership and investment interests held by physicians and their immediate family members;

- HIPAA, the HITECH Act and their respective implementing regulations, which govern the conduct of certain electronic healthcare transactions and are designed to protect the security and privacy of individual identifiable health information; and
- state, local and foreign law equivalents of each of the above federal laws, such as anti-kickback, false claims and transparency laws, which may be broader in scope and apply to items or services reimbursed by any third-party payor, including commercial insurers; for example, California has recently passed the CCPA, which Tyme may become subject to in the future. The CCPA introduces strict compliance regulations on organizations doing business in California that collect personal information about California residents. The CCPA defines personal information broadly and allows for fines as well as a private right of action from individuals in relation to certain security breaches involving personal information. The CCPA is also prompting similar legislative developments in other U.S. states, which could lead to a series of overlapping but varying laws. These developments, as Tyme becomes subject to such laws, are likely to increase Tyme's compliance burden and its risk, including risks of regulatory fines, litigation and associated reputational harm. Further, as Tyme's operations expand, it may become subject to the GDPR. The GDPR, together with the national legislation of the EU member states governing the processing of personal data, impose strict obligations and restrictions on the ability to collect, analyze and transfer personal data, including health data from clinical trials and adverse event reporting. It is unclear whether the transfer of personal information from the European Union to the United Kingdom will continue to remain lawful under the GDPR in light of Brexit. Pursuant to a post-Brexit trade deal between the United Kingdom and the European Union, transfers of personal information from the EEA to the United Kingdom are not considered restricted transfers under the GDPR for a period of up to four months from January 1, 2021 with a potential two-month extension. However, unless the EU Commission makes an adequacy finding with respect to the United Kingdom before the end of that period, the United Kingdom will be considered a "third country" under the GDPR and transfers of European personal information to the United Kingdom will require an adequacy mechanism to render such transfers lawful under the GDPR. Additionally, although U.K. privacy, data protection and data security laws are designed to be consistent with the GDPR, uncertainty remains regarding how data transfers to and from the United Kingdom will be regulated notwithstanding Brexit.

The ACA, among other things, amended the intent standard of the federal Anti-Kickback Statute and criminal healthcare fraud statutes to a stricter standard such that a person or entity no longer needs to have actual knowledge of a violation of this statute or specific intent to violate it to be convicted. In addition, the ACA codified case law held that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal False Claims Act.

If Tyme's operations are found to be in violation of any of the laws described above or any other governmental regulations that apply to Tyme, it may be subject to penalties, including civil, criminal and/or administrative penalties, damages, fines, disgorgement and possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings and the curtailment or restructuring of Tyme's operations, any of which could adversely affect Tyme's ability to operate its business and its financial results. Any action against Tyme for violation of these or other laws, even if Tyme successfully defends against it, could cause Tyme to incur significant legal expenses and divert Tyme's management's attention from the operation of its business. Moreover, achieving and sustaining compliance with applicable federal and state privacy, security, fraud and abuse, and transparency laws may prove costly.

Changes in tax laws or regulations that are applied adversely to Tyme may have a material adverse effect on its business, financial condition or results of operations.

New tax laws or regulations could be enacted at any time, and existing tax laws or regulations could be interpreted, modified or applied in a manner that is adverse to Tyme, which could adversely affect its business and financial condition. For example, the Tax Act resulted in many significant changes to the U.S. tax laws, including changes in corporate tax rates, the utilization of Tyme's net operating loss carryforwards, or NOLs, and other deferred tax assets, the deductibility of expenses, and the taxation of foreign earnings. Future guidance from the Internal Revenue Service and other tax authorities with respect to the Tax Act may affect Tyme, and certain aspects of the Tax Act could be repealed or modified by future legislation. For example, The CARES Act modified certain provisions of the Tax Act. In addition, it is uncertain if and to what extent various states will conform to the Tax Act, the CARES Act, or any newly enacted federal tax legislation. The impact of changes under the Tax Act, the CARES Act, or future reform legislation could increase Tyme's future U.S. tax expense and could have a material adverse impact on its business and financial condition. Tyme urges its stockholders to consult with their legal and tax advisors with respect to these legislations and the potential tax consequences of investing in or holding Tyme common stock.

Tyme is subject to anti-corruption laws, as well as export control laws, customs laws, sanctions laws and other laws governing Tyme's operations. If Tyme fails to comply with these laws, it could be subject to civil or criminal penalties, other remedial measures and legal expenses, which could adversely affect its business, results of operations and financial condition.

Tyme's operations are subject to anti-corruption laws, including the FCPA and other anti-corruption laws that apply in countries where Tyme operates or may do business in the future. The FCPA and these other laws generally prohibit Tyme, Tyme's officers and Tyme's employees and intermediaries from bribing, being bribed or making other prohibited payments to government officials or other persons to obtain or retain business or gain some other business advantage. Tyme may in the future operate in jurisdictions that pose a high risk of potential FCPA violations, and Tyme may participate in collaborations and relationships with third parties whose actions could potentially subject Tyme to liability under the FCPA or local anti-corruption laws. In addition, Tyme cannot predict the nature, scope or effect of future regulatory requirements to which Tyme's international operations might be subject or the manner in which existing laws might be administered or interpreted.

Because Tyme's business is heavily regulated, it therefore involves significant interaction with public officials. Tyme has or will have direct or indirect interactions with officials and employees of government agencies or government-affiliated hospitals, universities and other organizations. Additionally, in many other countries, the healthcare providers who prescribe pharmaceuticals are employed by their government and the purchasers of pharmaceuticals are government entities; therefore, any dealings with these prescribers and purchasers are subject to regulation under the FCPA.

Tyme is also subject to other laws and regulations, including regulations administered by the governments of the United States, United Kingdom, and authorities in the EU, including applicable export control regulations, economic sanctions on countries and persons, customs requirements and currency exchange regulations, which Tyme collectively refers to as Trade Control Laws.

There is no assurance that Tyme will be completely effective in ensuring its compliance, or the compliance of its employees, agents, suppliers, manufacturers, contractors, or collaborators, with all applicable anti-corruption laws, including the FCPA or other legal requirements, including Trade Control Laws. If Tyme is not in compliance with the FCPA, the Bribery Act and other anti-corruption laws or Trade Control Laws, Tyme may be subject to criminal and civil penalties, disgorgement and other sanctions and remedial measures, and legal expenses. The SEC also may suspend or bar issuers from trading securities on U.S. exchanges for violations of the FCPA's accounting provisions. Any of the foregoing could have an adverse impact on Tyme's reputation in the industry as well as its business, financial condition, results of operations and liquidity.

Because Tyme and its suppliers are subject to environmental, health and safety laws and regulations, Tyme may become exposed to liability and substantial expenses in connection with environmental compliance or remediation activities, which may adversely affect Tyme's business and financial condition.

Tyme's operations, including Tyme's discovery, development, testing, research and manufacturing activities, are subject to numerous environmental, health and safety laws and regulations. These laws and regulations govern, among other things, the controlled use, handling, release and disposal of and the maintenance of a registry for, hazardous materials and biological materials, such as chemical solvents, human cells, carcinogenic compounds, mutagenic compounds and compounds that have a toxic effect on reproduction, laboratory procedures and exposure to blood-borne pathogens. If Tyme fails to comply with such laws and regulations, it could be subject to fines or other sanctions.

As with other companies engaged in activities similar to Tyme's, Tyme faces a risk of environmental liability inherent in Tyme's current and historical activities, including liability relating to release of or exposure to, hazardous or biological materials. Environmental, health and safety laws and regulations are becoming more stringent. Tyme may be required to incur substantial expenses in connection with future environmental compliance or remediation activities, in which case, Tyme's production and development efforts may be interrupted or delayed and its financial condition and results of operations may be materially adversely affected.

The third parties with whom Tyme contracts to manufacture Tyme's drug candidates are also subject to these and other environmental, health and safety laws and regulations. Liabilities they incur pursuant to these laws and regulations could result in significant costs or, in certain circumstances, an interruption in operations, any of which could adversely affect Tyme's business and financial condition if Tyme is unable to find an alternate supplier in a timely manner.

Changes in funding for the FDA, the SEC and other government agencies could hinder their ability to hire and retain key leadership and other personnel, prevent new products and services from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal functions on which the operation of Tyme's business may rely, which could negatively impact its business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept payment of user fees, and statutory, regulatory, and policy changes. Average review times at the agency have fluctuated in recent years as a result. FDA review time and communications with the FDA may be delayed, prolonged and otherwise negatively impacted by the FDA's response to the COVID-19 pandemic. With many FDA staff working on COVID-19 activities, it is possible the FDA may need to reprioritize work in order to appropriately address the ongoing pandemic. In addition, government funding of the SEC and other government agencies on which Tyme's operations may rely, including those that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA and other agencies may also slow the time necessary for new drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect Tyme's business. For example, over the last several years, including most recently beginning on December 22, 2018, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA and the SEC, have had to furlough critical government employees and stop critical activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process Tyme's regulatory submissions, which could have a material adverse effect on its business. Further, future government shutdowns could impact Tyme's ability to access the public markets and obtain necessary capital in order to properly capitalize and continue its operations.

Tyme's employees, consultants, collaborators and other third parties may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements.

Tyme is exposed to the risk of employee fraud or other misconduct. Misconduct by employees, consultants, collaborators and other third parties include intentional failures to comply with FDA or EMA regulations, to provide accurate information to the FDA or EMA or intentional failures to report financial information or data accurately or to disclose unauthorized activities to Tyme. Misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to Tyme's reputation and subjects. The precautions Tyme takes to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting Tyme from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any such actions are instituted against Tyme and it is not successful in defending itself or asserting its rights, those actions could have a significant impact on Tyme's business, including the imposition of significant fines or other sanctions.

If generic manufacturers use litigation and regulatory means to obtain approval for generic versions of products on which Tyme's future revenue depends, its business will suffer.

Under the FDCA, the FDA can approve an ANDA for a generic version of a branded drug without the ANDA applicant undertaking the clinical testing necessary to obtain approval to market a new drug. In place of such clinical trials, an ANDA applicant usually needs only to submit data demonstrating that its drug has the same active ingredient(s) and is bioequivalent to the branded product, in addition to any data necessary to establish that any difference in strength, dosage form, inactive ingredients or delivery mechanism does not result in different safety or efficacy profiles, as compared to the reference drug.

The FDCA requires that an applicant for approval of a generic form of a branded drug certify either that its generic drug does not infringe any of the patents listed by the owner of the branded drug in the Orange Book or that those patents are not enforceable. This process is known as a Paragraph IV Challenge. Upon receipt of the Paragraph IV notice, the owner has 45 days to bring a patent infringement suit in federal district court against the company seeking ANDA approval of a drug covered by one of the owner's patents. The discovery, trial and appeals process in such suits can take several years. If this type of suit is commenced, the FDCA provides a 30-month stay on the FDA's approval of the competitor's application. This type of litigation is often time-consuming, costly and may result in generic competition if the patents at issue are not upheld or if the generic competitor is found not to infringe upon the owner's patents. If the litigation is resolved in favor of the ANDA applicant or the challenged patent expires during the 30-month stay period, the stay is lifted and the FDA may thereafter approve the application based on the usual standards for approval of ANDAs.

For various strategic and commercial reasons, manufacturers of generic medications frequently file ANDAs shortly after FDA approval of a branded drug regardless of the perceived strength and validity of the patents associated with such products. Based on these past practices, Tyme believes it is likely that one or more such generic manufacturers will file ANDAs with respect to SM-88, if approved by the FDA, prior to the expiration of the patents related to those compounds.

The filing of an ANDA as described above with respect to any of Tyme's products could have an adverse impact on its stock price. Moreover, if any such ANDAs were to be approved and the patents covering the relevant products were not upheld in litigation or if a generic competitor were found not to infringe these patents, the resulting generic competition would negatively affect Tyme's business, financial condition and results of operations.

If approved, the marketing for SM-88 or other drug candidates will be limited to the specific approved cancer or antiviral indications, as applicable, and if Tyme wants to expand the indications for which these drug candidates may be marketed, additional regulatory approvals will need to be obtained, which may not be granted.

In addition to other areas of regulatory oversight, Tyme will also need to comply with a variety of laws and regulations concerning the advertising and promotion of Tyme's products. For instance, the FDA closely regulates the post-approval labeling, marketing and promotion of drugs, including standards and regulations for direct-to-consumer advertising, off-label promotion, product-specific REMS, industry-sponsored scientific and educational activities and promotional activities involving the internet. Drugs may be marketed only for the approved indications and in accordance with the provisions of the approved labeling. If Tyme desires to market additional indications for its drug candidates, Tyme will need to seek additional regulatory approvals requiring additional clinical trials to support the new indications, which would be time-consuming and expensive and may produce results that do not support regulatory approvals. If Tyme does not obtain additional regulatory approvals, Tyme's ability to expand its business will be limited.

While physicians may choose to prescribe drugs for uses that are not described in a product's labeling and for uses that differ from those tested in clinical studies and approved by the regulatory authorities, Tyme's ability to promote products is limited to those indications that are specifically approved by the FDA, or similar regulatory authorities outside the United States. These "off-label" uses are common across medical specialties and may constitute an appropriate treatment for some patients in certain circumstances. Regulatory authorities in the U.S. generally do not regulate the behavior of physicians in their choice of treatments. Regulatory authorities do, however, restrict promotion by pharmaceutical companies on the subject of off-label use. If Tyme is found to have promoted its products for off-label uses after FDA approval for the applicable indication(s) or to have engaged in inappropriate pre-approval promotion of any approved drug candidate, Tyme may receive untitled or warning letters and become subject to significant liability, which would materially harm its business. The federal government and states' attorneys general have levied large civil and criminal fines against companies for alleged improper promotion and has enjoined several companies from engaging in off-label promotion. If Tyme becomes the target of such an investigation or prosecution based on its marketing and promotional practices, Tyme could face similar sanctions, which would materially harm Tyme's business. In addition, management's attention could be diverted from Tyme's business operations, significant legal expenses could be incurred and its reputation could be damaged. The FDA has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed. If Tyme is deemed by the FDA to have engaged in the promotion of its products for off-label use or engage in improper pre-approval promotion, Tyme could be subject to FDA prohibitions on the sale or marketing of Tyme's products or significant fines and penalties and the imposition of these sanctions could also affect its reputation and position within the industry.

Being a public company is expensive and administratively burdensome.

As a public reporting company, Tyme is subject to the information and reporting requirements of the Securities Act, the Exchange Act and other federal securities laws, rules and regulations related thereto, including compliance with the Sarbanes-Oxley Act of 2002, or SOX. Complying with these laws and regulations requires the time and attention of the Tyme board of directors and management and increases Tyme's expenses. Among other things, Tyme must:

- maintain and evaluate a system of internal controls over financial reporting in compliance with the requirements of Section 404 of SOX and the related rules and regulations of the SEC and the Public Company Accounting Oversight Board;
- maintain policies relating to disclosure controls and procedures;
- prepare and distribute periodic reports, proxy statements, Forms 8-K and other reports and filings in compliance with Tyme's obligations under applicable federal securities laws;

- institute a more comprehensive compliance function, including with respect to corporate governance; and
- involve, to a greater degree, Tyme's outside legal counsel and accountants in the above activities and incur additional expenses relating to such involvement.

The cost of preparing and filing annual, quarterly and current reports, proxy statements and other information with the SEC and furnishing annual reports containing audited financial statements to stockholders is expensive and much greater than that of a privately-held company. Compliance with these rules and regulations may require Tyme to hire additional financial reporting, internal controls and other finance personnel and will involve significant regulatory, legal and accounting expenses and the attention of management, including as a result of changing laws, regulations and standards. There can be no assurance that Tyme will be able to comply with the applicable regulations in a timely manner, if at all. Furthermore, if Tyme is unable to satisfy its obligations as a public company, it could be subject to delisting of Tyme's common stock, fines, sanctions and other regulatory action and potentially civil litigation.

Additionally, there continues to be public interest and increased legislative pressure related to public companies' environmental, social and governance, or ESG, activities. Tyme risks negative stockholder reaction, including from proxy advisory services, as well as damage to Tyme's brand and reputation, if Tyme does not act responsibly in a number of key areas, including diversity and inclusion, environmental stewardship, support for local communities, corporate governance and transparency and employing ESG strategies in Tyme's operations. A growing number of states are requiring organizations to report their board composition and/or mandating gender diversity, including New York and California. Tyme has included consistent, transparent diversity statistics in the section titled "*Tyme Directors, Officers and Corporate Governance*" in this joint proxy statement/prospectus regarding Tyme's board of directors and, in subsequent years, Tyme will be required to have, or disclose why it does not have, a minimum of two diverse board members.

In addition, being a public company makes it more expensive for Tyme to obtain director and officer liability insurance. Premiums for director and officer insurance can vary substantially from year-to-year and have recently been increasing due to the growth in threatened and actual suits across public companies, which is even more pronounced in biotechnology. In the future, Tyme may be required to accept reduced coverage or incur substantially higher costs to obtain this coverage. These factors could also make it more difficult for Tyme to attract and retain qualified executives and members of Tyme's board of directors, particularly directors willing to serve on Tyme's audit committee.

Risks Related to Syros Common Stock

The price of Syros common stock is likely to be highly volatile, which could result in substantial losses for its stockholders.

Syros' stock price is likely to be highly volatile. The stock market in general and the market for smaller pharmaceutical and biotechnology companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, you may lose some or all of your investment. The market price for Syros common stock may be influenced by many factors, including:

- the timing and results of clinical trials of tamibarotene, SY-2101 and SY-5609;
- the success of existing or new competitive products or technologies;
- regulatory actions with respect to Syros' product candidates or its competitors' products and product candidates;
- announcements by Syros or its competitors of significant acquisitions, strategic partnerships, joint ventures, collaborations or capital commitments;

- commencement or termination of collaborations for Syros' research or development programs;
- failure or discontinuation of any of Syros' development programs;
- results of clinical trials of product candidates of Syros' competitors;
- regulatory or legal developments in the United States and other countries;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to any of Syros' product candidates or clinical development programs;
- the results of Syros' efforts to develop additional product candidates or products;
- actual or anticipated changes in estimates as to financial results or development timelines or recommendations by securities analysts;
- announcement or expectation of additional financing efforts;
- sales of Syros common stock by Syros, its insiders or other stockholders;
- variations in Syros' financial results or those of companies that are perceived to be similar to Syros;
- changes in estimates or recommendations by securities analysts, if any, that cover Syros' stock;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry and market conditions;
- actual or threatened public health emergencies and outbreaks of disease (including, for example, the COVID-19 pandemic); and
- the other factors described in this "*Risk Factors*" section and elsewhere in this joint proxy statement/prospectus.

In the past, companies that have experienced volatility in the market price of their stock have been subject to an increased incidence of securities class action litigation. This risk is especially relevant for Syros because pharmaceutical companies have experienced significant stock price volatility in recent years. If Syros faces such litigation, it could result in substantial costs and a diversion of management's attention and resources, which could harm its business. Syros may also face other material adverse consequences due to volatility or a sustained decrease in the price of Syros common stock, such as negative publicity, a decreased ability to obtain additional financing, diminished investor and/or employee confidence, and the loss of business development opportunities, some or all of which may contribute to a further decline in Syros' stock price.

Syros must maintain effective internal control over financial reporting, and if Syros is unable to do so, the accuracy and timeliness of its financial reporting may be adversely affected, which could have a material adverse effect on its business and stock price.

Syros must maintain effective internal control over financial reporting in order to accurately and timely report its results of operations and financial condition. In addition, as a public company, SOX requires, among other things, that Syros assess the effectiveness of its disclosure controls and procedures quarterly and the effectiveness of its internal control over financial reporting at the end of each fiscal year.

The rules governing the standards that must be met for Syros' management to assess its internal control over financial reporting pursuant to Section 404 of the SOX are complex and require significant documentation, testing and possible remediation. These standards require that Syros' audit committee be advised and regularly

updated on management's review of internal control over financial reporting. Syros' management may not be able to effectively and timely implement controls and procedures that comply with the increased regulatory compliance and reporting requirements that are applicable to Syros as a public company. If Syros fails to staff its accounting and finance function adequately or maintain internal control over financial reporting adequate to meet the demands that are placed upon Syros as a public company, including the requirements of the SOX, Syros' business and reputation may be harmed and its stock price may decline.

Syros might not be able to utilize a significant portion of its net operating loss carryforwards and research and development tax credit carryforwards.

As of December 31, 2021, Syros had federal and state net operating loss carryforwards of $398.9 million and $401.9 million, respectively, and federal and state research and development tax credit carryforwards of $19.7 million and $3.5 million, respectively. These carryforwards could expire unused and be unavailable to offset future income tax liabilities. Syros' net operating loss carryforwards generated prior to 2018 and research and development tax credit carryforwards will generally expire at various dates through 2037.

The Tax Act, as amended by the CARES Act, contains significant changes with respect to federal net operating loss carryforwards, including the limitation of the deduction for net operating loss carryforwards to 80% of current year taxable income and the elimination of net operating loss carrybacks, in each case, for losses arising in taxable years beginning after December 31, 2017 (though any such net operating losses may be carried forward indefinitely and such net operating losses arising in taxable years beginning before January 1, 2021 are generally eligible to be carried back up to five years). Regulatory guidance under the Tax Act and the CARES Act is and continues to be forthcoming, and such guidance could further impact Syros' ability to utilize its net operating loss carryforwards.

In addition, the net operating loss and tax credit carryforwards are subject to review and possible adjustment by the Internal Revenue Service and state tax authorities. Furthermore, under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, and corresponding provisions of state law, if a corporation undergoes an "ownership change," which is generally defined as a cumulative change in ownership of significant shareholders of greater than 50%, by value, over a three-year period, the corporation's ability to use its pre-change net operating loss carryforwards and research and development tax credit carryforwards to offset its post-change income may be limited. The merger and the PIPE Financing is expected to result in an ownership change for both Syros and Tyme for purposes of Section 382, and as a result, the post-closing combined company's ability to use Syros' and Tyme's historical net operating loss and tax credit carryforwards will be materially limited. Such limitation, or any adjustments to such carryforwards made by the Internal Revenue Service or state tax authorities, could harm the combined company's future operating results by effectively increasing its future tax obligations.

Syros does not anticipate paying any cash dividends on its capital stock in the foreseeable future. Accordingly, stockholders must rely on capital appreciation, if any, for any return on their investment.

Syros has never declared nor paid cash dividends on its capital stock. Syros currently plans to retain all of its future earnings, if any, to finance the operation, development and growth of its business. In addition, the terms of Syros' term loan facility with Oxford precludes Syros from paying cash dividends to its stockholders without Oxford's consent. As a result, capital appreciation, if any, of Syros common stock will be the sole source of gain for Syros' stockholders for the foreseeable future.

Concentration of ownership of Syros common stock among its existing executive officers, directors and principal stockholders may prevent new investors from influencing significant corporate decisions.

Syros' executive officers and directors, combined with its stockholders who own more than 5% of Syros' outstanding common stock and their affiliates, in the aggregate, beneficially own a significant portion of Syros common stock. As a result, if these stockholders were to choose to act together, they would be able to substantially influence all matters submitted to Syros' stockholders for approval, as well as its management and

affairs. For example, these persons, if they choose to act together, would substantially influence the election of directors and approval of any merger, consolidation or sale of all or substantially all of Syros' assets. This concentration of ownership control may:

- delay, defer or prevent a change in control;
- entrench Syros' management or the board of directors; or
- impede a merger, consolidation, takeover or other business combination involving Syros that other stockholders may desire.

Provisions in Syros' certificate of incorporation and bylaws and under Delaware law may prevent or frustrate attempts by Syros' stockholders to change its management or hinder efforts to acquire a controlling interest in Syros.

Provisions in Syros' certificate of incorporation and Syros' bylaws may discourage, delay or prevent a merger, acquisition or other change in control of Syros that stockholders may consider favorable, including transactions in which Syros' stockholders might otherwise receive a premium for their shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of Syros common stock, thereby depressing the market price of Syros common stock. In addition, because Syros' board of directors is responsible for appointing the members of its management team, these provisions may frustrate or prevent any attempts by Syros' stockholders to replace or remove its current management by making it more difficult for stockholders to replace members of Syros' board of directors. Among other things, these provisions:

- establish a classified board of directors such that all members of the board are not elected at one time;
- allow the authorized number of Syros' directors to be changed only by resolution of its board of directors;
- limit the manner in which stockholders can remove directors from the board;
- establish advance notice requirements for nominations for election to the board of directors or for proposing matters that can be acted on at stockholder meetings;
- require that stockholder actions must be effected at a duly called stockholder meeting and prohibit actions by Syros' stockholders by written consent;
- limit who may call a special meeting of stockholders;
- authorize Syros' board of directors to issue preferred stock without stockholder approval, which could be used to institute a "poison pill" that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by Syros' board of directors; and
- require the approval of the holders of at least 75% of the votes that all Syros' stockholders would be entitled to cast to amend or repeal certain provisions of Syros' certificate of incorporation or bylaws.

Moreover, because Syros is incorporated in Delaware, Syros is governed by the provisions of Section 203 of the DGCL, which prohibits a person who owns in excess of 15% of Syros' outstanding voting stock from merging or combining with Syros for a period of three years after the date of the transaction in which the person acquired in excess of 15% of Syros' outstanding voting stock, unless the merger or combination is approved in a prescribed manner. This could discourage, delay or prevent someone from acquiring Syros or merging with it, whether or not it is desired by, or beneficial to, Syros' stockholders. This could also have the effect of discouraging others from making tender offers for Syros common stock, including transactions that may be in stockholders' best interests. These provisions may also prevent changes in Syros' management or limit the price that investors are willing to pay for Syros' stock.

If securities or industry analysts do not publish research or publish inaccurate or unfavorable research about Syros' business, its share price and trading volume could decline.

The trading market for Syros common stock will likely depend in part on the research and reports that securities or industry analysts publish about Syros or its business. Syros does not have any control over these analysts. There can be no assurance that analysts will cover Syros, or provide favorable coverage. Securities or industry analysts may elect not to provide research coverage of Syros common stock, and such lack of research coverage may negatively impact the market price of Syros common stock. In the event Syros does have analyst coverage, if one or more analysts downgrade Syros' stock or change their opinion of Syros' stock, Syros' share price would likely decline. In addition, if one or more analysts cease coverage of Syros or fail to regularly publish reports on it, Syros could lose visibility in the financial markets, which could cause Syros' share price or trading volume to decline.

Risks Related to the Combined Company

The market price of the combined company's common stock is expected to be volatile, and the market price of the common stock may drop following the merger.

The market price of the combined company's common stock following the merger could be subject to significant fluctuations. Some of the factors that may cause the market price of the combined company's common stock to fluctuate include:

- results of clinical trials and preclinical studies of the combined company's product candidates, or those of the combined company's competitors or the combined company's existing or future collaborators;
- failure to meet or exceed financial and development projections the combined company may provide to the public;
- failure to meet or exceed the financial and development projections of the investment community;
- if the combined company does not achieve the perceived benefits of the merger as rapidly or to the extent anticipated by financial or industry analysts;
- announcements of significant acquisitions, strategic collaborations, joint ventures or capital commitments by the combined company or its competitors;
- actions taken by regulatory agencies with respect to the combined company's product candidates, clinical studies, manufacturing process or sales and marketing terms;
- disputes or other developments relating to proprietary rights, including patents, litigation matters, and the combined company's ability to obtain patent protection for its technologies;
- additions or departures of key personnel;
- significant lawsuits, including patent or stockholder litigation;
- if securities or industry analysts do not publish research or reports about the combined company's business, or if they issue adverse or misleading opinions regarding its business and stock;
- changes in the market valuations of similar companies;
- general market or macroeconomic conditions or market conditions in the pharmaceutical and biotechnology sectors;
- sales of securities by the combined company or its securityholders in the future;
- if the combined company fails to raise an adequate amount of capital to fund its operations and continued development of its product candidates;
- trading volume of the combined company's common stock;

- announcements by competitors of new commercial products, clinical progress or lack thereof, significant contracts, commercial relationships or capital commitments;
- adverse publicity relating to precision medicine product candidates, including with respect to other products in such markets;
- the introduction of technological innovations or new therapies that compete with the products and services of the combined company; and
- period-to-period fluctuations in the combined company's financial results.

Moreover, the stock markets in general have experienced substantial volatility that has often been unrelated to the operating performance of individual companies. These broad market fluctuations may also adversely affect the trading price of the combined company's common stock. In addition, a recession, depression or other sustained adverse market event resulting from the spread of COVID-19 or otherwise could materially and adversely affect the combined company's business and the value of its common stock. In the past, following periods of volatility in the market price of a company's securities, stockholders have often instituted class action securities litigation against such companies. Furthermore, market volatility may lead to increased shareholder activism if the combined company experiences a market valuation that activists believe is not reflective of its intrinsic value. Activist campaigns that contest or conflict with the combined company's strategic direction or seek changes in the composition of its board of directors could have an adverse effect on its operating results and financial condition.

Following the merger, the combined company may be unable to integrate successfully and realize the anticipated benefits of the merger.

The merger involves the combination of two companies which currently operate as independent companies. The combined company may fail to realize some or all of the anticipated benefits of the merger if the integration process takes longer than expected or is more costly than expected. In addition, Syros and Tyme have operated and, until the completion of the merger, will continue to operate, independently. It is possible that the integration process also could result in the diversion of each company's management's attention, the disruption or interruption of, or the loss of momentum in, each company's ongoing businesses or inconsistencies in standards, controls, procedures and policies, any of which could adversely affect the combined company's ability to maintain relationships with third parties or the ability to achieve the anticipated benefits of the merger, or could otherwise adversely affect the business and financial results of the combined company.

Once the combined company is no longer a smaller reporting company or otherwise no longer qualifies for applicable exemptions, the combined company will be subject to additional laws and regulations affecting public companies that will increase the combined company's costs and the demands on management and could harm the combined company's operating results.

The combined company will be subject to the reporting requirements of the Exchange Act, which requires, among other things, that the combined company file with the SEC, annual, quarterly and current reports with respect to the combined company's business and financial condition as well as other disclosure and corporate governance requirements. However, as a "smaller reporting company" the combined company may take advantage of some of exemptions from disclosure requirements including not being required to comply with the auditor attestation requirements of Section 404 of the SOX and reduced disclosure obligations regarding executive compensation in the combined company's periodic reports and proxy statements. Once the combined company is no longer a smaller reporting company or otherwise qualifies for these exemptions, the combined company will be required to comply with these additional legal and regulatory requirements applicable to public companies and will incur significant legal, accounting and other expenses to do so. If the combined company is not able to comply with the requirements in a timely manner or at all, the combined company's financial condition or the market price of the combined company's common stock may be harmed. For example, if the

combined company or its independent auditor identifies deficiencies in the combined company's internal control over financial reporting that are deemed to be material weaknesses the combined company could face additional costs to remedy those deficiencies, the market price of the combined company's stock could decline or the combined company could be subject to sanctions or investigations by the SEC or other regulatory authorities, which would require additional financial and management resources.

The unaudited pro forma condensed combined financial data for Syros and Tyme included in this joint proxy statement/prospectus is preliminary, and the combined company's actual financial position and operations after the merger may differ materially from the unaudited pro forma financial data included in this proxy statement/prospectus.

The unaudited pro forma financial data for Syros and Tyme included in this proxy statement/prospectus is presented for illustrative purposes only and is not necessarily indicative of the combined company's actual financial condition or results of operations of future periods, or the financial condition or results of operations that would have been realized had the entities been combined during the periods presented. The unaudited pro forma financial statements have been derived from the historical financial statements of Syros and Tyme and adjustments and assumptions have been made regarding the combined company after giving effect to the transaction. The information upon which these adjustments and assumptions have been made is preliminary, and these kinds of adjustments and assumptions are difficult to make with accuracy. Moreover, the unaudited pro forma financial statements do not reflect all costs that are expected to be incurred by the combined company in connection with the transactions or that have been incurred since the date of such unaudited pro forma financial statements. The assumptions used in preparing the unaudited pro forma financial information may not prove to be accurate, and other factors may affect the combined company's financial condition following the transaction. For more information see the section titled "*Unaudited Pro Forma Condensed Combined Financial Statements*" beginning on page 410 of this joint proxy statement/prospectus.

Syros and Tyme do not anticipate that the combined company will pay any cash dividends in the foreseeable future.

The current expectation is that the combined company will retain its future earnings, if any, to fund the growth of the combined company's business as opposed to paying dividends. As a result, capital appreciation, if any, of the common stock of the combined company will be the sole source of gain for Syros' and Tyme's stockholders, if any, for the foreseeable future.

Future sales of shares by existing stockholders could cause the combined company's stock price to decline.

If existing securityholders of Syros and Tyme sell, or indicate an intention to sell, substantial amounts of the combined company's common stock in the public market after legal restrictions on resale discussed in this joint proxy statement/prospectus lapse, the trading price of the common stock of the combined company could decline. Based on the number of shares of Syros common stock outstanding on June 30, 2022 and the number of shares of Syros common stock estimated to be issued in connection with the merger (assuming an exchange ratio of 0.4312) and the PIPE Financing, the combined company is expected to have outstanding a total of approximately 275,383,510 shares of common stock immediately following the completion of the merger and the PIPE Financing, which number assumes the exercise of the Pre-Funded PIPE Warrants, without giving effect to any beneficial ownership limitations applicable thereto. Syros and Tyme estimate that approximately 5,244,852 shares of common stock will be available for sale in the public market beginning 90 days after the closing of the merger as a result of the expiration of lock-up agreements between Syros and Tyme on the one hand and certain securityholders of Syros and Tyme on the other hand. All other outstanding shares of common stock, other than shares held by affiliates of the combined company, will be freely tradable, without restriction, in the public market. If these shares are sold, the trading price of the combined company's common stock could decline.

The combined company may be exposed to increased litigation, including stockholder litigation, which could have an adverse effect on the combined company's business and operations.

The combined company may be exposed to increased litigation from stockholders, customers, suppliers, consumers and other third parties due to the combination of Syros' business and Tyme's business following the merger. Such litigation may have an adverse impact on the combined company's business and results of operations or may cause disruptions to the combined company's operations. In addition, in the past, stockholders have initiated class action lawsuits against biotechnology companies following periods of volatility in the market prices of these companies' stock. Such litigation, if instituted against the combined company, could cause the combined company to incur substantial costs and divert management's attention and resources, which could have a material adverse effect on the combined company's business, financial condition and results of operations.

If equity research analysts do not publish research or reports, or publish unfavorable research or reports, about the combined company, its business or its market, its stock price and trading volume could decline.

The trading market for the combined company's common stock will be influenced by the research and reports that equity research analysts publish about it and its business. Equity research analysts may elect not to provide research coverage of the combined company's common stock after the completion of the merger, and such lack of research coverage may adversely affect the market price of its common stock. In the event it does have equity research analyst coverage, the combined company will not have any control over the analysts or the content and opinions included in their reports. The price of the combined company's common stock could decline if one or more equity research analysts downgrade its stock or issue other unfavorable commentary or research. If one or more equity research analysts ceases coverage of the combined company or fails to publish reports on it regularly, demand for its common stock could decrease, which in turn could cause its stock price or trading volume to decline.

The combined company will have broad discretion in the use of the cash and cash equivalents of the combined company and the proceeds from the PIPE Financing and may invest or spend the proceeds in ways with which you do not agree and in ways that may not increase the value of your investment.

The combined company will have broad discretion over the use of the cash and cash equivalents of the combined company and the proceeds from the PIPE Financing. You may not agree with the combined company's decisions, and its use of the proceeds may not yield any return on your investment. The combined company's failure to apply these resources effectively could compromise its ability to pursue its growth strategy and the combined company might not be able to yield a significant return, if any, on its investment of these net proceeds. You will not have the opportunity to influence its decisions on how to use the combined company's cash resources.

CAUTIONARY STATEMENT CONCERNING FORWARD-LOOKING STATEMENTS

This joint proxy statement/prospectus contains forward-looking statements relating to Syros, Tyme, the merger and the other proposed transactions contemplated thereby.

These forward-looking statements are based on current expectations and beliefs and involve numerous risks and uncertainties that could cause actual results to differ materially from expectations. These forward-looking statements should not be relied upon as predictions of future events as Syros and Tyme cannot assure you that the events or circumstances reflected in these statements will be achieved or will occur. You can identify forward-looking statements by the use of forward-looking terminology including "believes," "expects," "may," "will," "should," "seeks," "intends," "plans," "pro forma," "estimates" or "anticipates" or the negative of these words and phrases or other variations of these words and phrases or comparable terminology. All statements other than statements of historical fact are statements that could be deemed forward-looking statements. For example, forward-looking statements include any statements regarding the strategies, prospects, plans, expectations or objectives of management of Syros or Tyme for future operations of the combined company, the progress, scope or timing of the development of the combined company's product candidates, the benefits that may be derived from any future products or the commercial or market opportunity with respect to any future products of the combined company, the ability of the combined company to protect its IP rights, the anticipated operations, financial position, ability to raise capital to fund operations, revenues, costs or expenses of Syros, Tyme or the combined company, statements regarding future economic conditions or performance, statements of belief and any statement of assumptions underlying any of the foregoing. Forward-looking statements may also include any statements regarding the approval and closing of the merger, including the timing of the consummation of the merger, Syros' ability to solicit a sufficient number of proxies to approve the Syros proposals, Tyme's ability to solicit a sufficient number of proxies to approve the Tyme proposals, satisfaction of conditions to the completion of the merger, the expected benefits of the merger, the ability of Syros and Tyme to complete the merger, Syros' ability to complete the PIPE Financing immediately prior to the merger and any statement of assumptions underlying any of the foregoing.

For a discussion of the factors that may cause Syros, Tyme or the combined company's actual results, performance or achievements to differ materially from any future results, performance or achievements expressed or implied in such forward-looking statements, or for a discussion of risk associated with the ability of Syros and Tyme to complete the merger and the effect of the merger on the business of Syros, Tyme and the combined company, please see the section titled "*Risk Factors*" beginning on page 31 of this joint proxy statement/prospectus. Additional factors that could cause actual results to differ materially from those expressed in the forward-looking statements are discussed in reports filed with the SEC by Syros. Please see the section titled "*Where You Can Find More Information*" beginning on page 445 of this joint proxy statement/prospectus. There can be no assurance that the merger will be completed, or if it is completed, that it will be completed within the anticipated time period or that the expected benefits of the merger will be realized.

If any of these risks or uncertainties materialize or any of these assumptions prove incorrect, the results of Syros, Tyme or the combined company could differ materially from the forward-looking statements. All forward-looking statements in this joint proxy statement/prospectus are current only as of the date on which the statements were made. Syros and Tyme do not undertake any obligation to (and expressly disclaim any such obligation to) publicly update any forward-looking statement to reflect events or circumstances after the date on which any statement is made or to reflect the occurrence of unanticipated events.

Date, Time and Place

The Syros special meeting will be held on September 15, 2022, commencing at 10:00 A.M. Eastern Time, unless postponed or adjourned to a later date. The Syros special meeting will be held entirely online. Syros is sending this joint proxy statement/prospectus to its stockholders in connection with the solicitation of proxies by Syros' board of directors for use at the Syros special meeting and any adjournments or postponements of the Syros special meeting. This joint proxy statement/prospectus is first being furnished to Syros stockholders on or about August 10, 2022.

Purposes of the Syros Special Meeting

The purposes of the Syros special meeting are:

- Proposal No. 1: To approve, for purposes of Nasdaq Listing Rule 5635(a) and (d), the issuance of shares of Syros common stock pursuant to the terms of the Merger Agreement and the Securities Purchase Agreement.
- Proposal No. 2: To approve an amendment to the Syros restated certificate of incorporation to increase the number of authorized shares of Syros common stock from 200,000,000 shares to 700,000,000 shares.
- Proposal No. 3: To approve an amendment to the Syros restated certificate of incorporation to effect a reverse stock split of Syros common stock, by a ratio of not less than 1-for-5 and not more than 1-for-15, and a proportionate reduction in the number of authorized shares of Syros common stock, such ratio and the implementation and timing of the reverse stock split to be determined in the discretion of Syros' board of directors.
- Proposal No. 4. To approve the adoption of the Syros Pharmaceuticals, Inc. 2022 Equity Incentive Plan.
- Proposal No. 5: To consider and vote upon an adjournment of the Syros special meeting, if necessary, to solicit additional proxies if there are not sufficient votes in favor of Proposal Nos. 1, 2 and 3 or to ensure that any supplement or amendment to this joint proxy statement/prospectus is timely provided to holders of Syros common stock.

Proposal No. 1 is referred to herein as the Syros share issuance proposal and is a condition to the completion of the merger. Proposal No. 2 is referred to herein as the Syros share increase proposal and is not a condition to the completion of the merger, but is necessary for completion of the PIPE Financing. Proposal No 3. is referred to herein as the Syros reverse stock split proposal. Proposal No. 4 is referred to herein as the Syros equity plan proposal.

Recommendation of Syros' Board of Directors

Syros' board of directors has determined and believes that the issuance of shares of Syros common stock pursuant to the Merger Agreement and the Securities Purchase Agreement is fair to, in the best interests of, and advisable to, Syros and its stockholders and has approved such issuance. Syros' board of directors unanimously recommends that Syros stockholders vote "FOR" Proposal No. 1 to approve, for purposes of Nasdaq Listing Rule 5635(a) and (d), the issuance of shares of Syros common stock pursuant to the terms of the Merger Agreement and the Securities Purchase Agreement.

Syros' board of directors has determined and believes that it is fair to, in the best interests of, and advisable to, Syros and its stockholders to approve the amendment to the restated certificate of incorporation of Syros to effect the increase in authorized shares of Syros common stock, as described in this joint proxy statement/prospectus. Syros' board of directors unanimously recommends that Syros stockholders vote "FOR" Proposal No. 2 to approve the increase in authorized shares.

Syros' board of directors has determined and believes that it is fair to, in the best interests of, and advisable to, Syros and its stockholders to approve the amendment to the restated certificate of incorporation of Syros to effect the reverse stock split, as described in this joint proxy statement/prospectus. Syros' board of directors unanimously recommends that Syros stockholders vote "FOR" Proposal No. 3 to approve the reverse stock split of Syros common stock.

Syros' board of directors has determined and believes that it is fair to, in the best interests of, and advisable to, Syros and its stockholders to approve the adoption of the Syros Pharmaceuticals, Inc. 2022 Equity Incentive Plan, as described in this joint proxy statement/prospectus. Syros' board of directors unanimously recommends that Syros stockholders vote "FOR" Proposal No. 4 to approve the adoption of the Syros Pharmaceuticals, Inc. 2022 Equity Incentive Plan.

Syros' board of directors has determined and believes that adjourning the Syros special meeting, if necessary, to solicit additional proxies if there are not sufficient votes in favor of Proposal Nos. 1, 2 and 3 or to ensure that any supplement or amendment to this joint proxy statement/prospectus is timely provided to holders of Syros common stock is fair to, in the best interests of, and advisable to, Syros and its stockholders. Syros' board of directors unanimously recommends that Syros stockholders vote "FOR" Proposal No. 5 to adjourn the Syros special meeting, if necessary in the judgment of Syros management and subject to the Merger Agreement, to solicit additional proxies in such circumstances.

Record Date and Voting Power

Only holders of record of Syros common stock at the close of business on the record date August 8, 2022, are entitled to notice of, and to vote at, the Syros special meeting. At the close of business on the record date, there were 32 holders of record of Syros common stock and there were 63,005,295 shares of Syros common stock issued and outstanding. Each share of Syros common stock entitles the holder thereof to one vote on each matter submitted for stockholder approval.

Voting and Revocation of Proxies

The proxy accompanying this joint proxy statement/prospectus is solicited on behalf of Syros' board of directors for use at the Syros special meeting.

If, as of the record date referred to above, your shares were registered directly in your name with the transfer agent for Syros common stock, Computershare Trust Company, N.A., then you are a stockholder of record. Whether or not you plan to attend the Syros special meeting online, Syros urges you to fill out and return the proxy card or vote by proxy over the telephone or on the internet as instructed below to ensure your vote is counted.

The procedures for voting are as follows:

If you are a stockholder of record, you may vote at the Syros special meeting. Alternatively, you may vote by proxy by using the accompanying proxy card, over the internet or by telephone. Whether or not you plan to attend the Syros special meeting, Syros encourages you to vote by proxy to ensure your vote is counted. Even if you have submitted a proxy before the Syros special meeting, you may still attend the Syros special meeting and vote in person. In such case, your previously submitted proxy will be disregarded.

- To vote at the Syros special meeting, attend the Syros special meeting online and follow the instructions posted at meetnow.global/MYRZKZT.
- To vote using the proxy card by mail, simply complete, sign and date the accompanying proxy card and return it promptly in the envelope provided. If you return your signed proxy card before the Syros special meeting, Syros will vote your shares in accordance with the proxy card.

- To vote by proxy over the internet, follow the instructions provided on the Notice of Internet Availability or proxy card.
- To vote by telephone, you may vote by proxy by calling the toll free number found on the Notice of Internet Availability or proxy card.

If you are a beneficial owner of shares registered in the name of your broker, bank or other agent, you should have received a voting instruction card and voting instructions with these proxy materials from that organization rather than from us. Simply complete and mail the voting instruction card to ensure that your vote is counted. To vote in person at the Syros special meeting, you must obtain a valid proxy from your broker, bank or other agent. Follow the instructions from your broker, bank or other agent included with these proxy materials, or contact your broker, bank or other agent to request a proxy form.

Syros provides internet proxy voting to allow you to vote your shares online, with procedures designed to ensure the authenticity and correctness of your proxy vote instructions. However, please be aware that you must bear any costs associated with your internet access, such as usage charges from internet access providers and telephone companies.

Under applicable stock exchange rules, banks, brokers and other nominees may use their discretion to vote "uninstructed" shares (i.e., shares of record held by banks, brokers or other nominees, but with respect to which the beneficial owner of such shares has not provided instructions on how to vote on a particular proposal) with respect to matters that are considered to be "routine," but not with respect to "non-routine" matters. With respect to non-routine items for which you do not give your broker instructions, your shares will be treated as broker non-votes. At the Syros special meeting, it is anticipated that Syros Proposal Nos. 1, 2, 4 and 5 will be non-routine, and that Syros Proposal No. 3 will be routine.

All properly executed proxies that are not revoked will be voted at the Syros special meeting and at any adjournments or postponements of the Syros special meeting in accordance with the instructions contained in the proxy. **If a holder of Syros common stock executes and returns a proxy and does not specify otherwise, the shares represented by that proxy will be voted "FOR" all of the proposals in accordance with the recommendation of Syros' board of directors.**

If you are a stockholder of record of Syros, you may change your vote at any time before your proxy is voted at the Syros special meeting in any one of the following ways (subject to the terms of the support agreement, to the extent that you have executed a support agreement):

- You may submit another properly completed proxy with a later date by mail or via the internet.
- You can provide your proxy instructions via telephone at a later date.
- You may send a written notice that you are revoking your proxy to Syros' Corporate Secretary at 35 CambridgePark Drive, 4th Floor, Cambridge MA 02140, attention: Corporate Secretary.
- You may attend the Syros special meeting online and vote by following the instructions at meetnow.global/MYRZKZT. Simply attending the Syros special meeting will not, by itself, revoke your proxy.

If your shares are held by your broker, bank or other agent, you should follow the instructions provided by them.

Required Vote

The presence, in person or represented by proxy, at the Syros special meeting of the holders of a majority of the shares of Syros common stock outstanding and entitled to vote at the Syros special meeting is necessary to constitute a quorum at the meeting. The affirmative vote of a majority of the total votes cast by the holders of

Syros common stock entitled to vote on the matter at the Syros special meeting is required for approval of Syros Proposal Nos. 1, 4 and 5. Abstentions and broker non-votes will have no effect on such proposals. The affirmative vote of the holders of a majority of the outstanding shares of Syros common stock entitled to vote at the Syros special meeting is required for approval of Syros Proposal Nos. 2 and 3. Abstentions and broker non-votes will have the same effect as "AGAINST" votes on such proposals.

Votes will be counted by the inspector of election appointed for the meeting, who will separately count "FOR" and "AGAINST" votes, abstentions and broker non-votes. Abstentions and broker non-votes will also be treated as shares present for the purpose of determining the presence of a quorum for the transaction of business at the special meeting.

As of June 30, 2022, the directors and certain executive officers of Syros owned or controlled approximately 8% of the outstanding shares of Syros common stock entitled to vote at the Syros special meeting. As of June 30, 2022, the Syros stockholders that are party to a support agreement, including the directors and executive officers of Syros and certain other stockholders, owned an aggregate of 17,460,552 shares of Syros common stock representing approximately 28% of the outstanding shares of Syros common stock. Each stockholder that entered into a support agreement, including the directors and executive officers of Syros and certain other stockholders, has agreed to vote all shares of Syros common stock owned by him or her as of the record date in favor of Proposal Nos. 1, 2 and 3, and against any competing "Acquisition Proposal" (as defined in the Merger Agreement).

Solicitation of Proxies

In addition to solicitation by mail, the directors, officers, employees and agents of Syros may solicit proxies from Syros stockholders by personal interview, telephone, email, fax or otherwise. Syros will bear the costs of printing and mailing this joint proxy statement/prospectus and its proxy card to Syros stockholders and Tyme will bear the costs of printing and mailing this joint proxy statement/prospectus and its proxy card to Tyme stockholders. Arrangements will also be made with brokerage firms and other custodians, nominees and fiduciaries who are record holders of Syros common stock for the forwarding of solicitation materials to the beneficial owners of Syros common stock. Syros will reimburse these brokers, custodians, nominees and fiduciaries for the reasonable out of pocket expenses they incur in connection with the forwarding of solicitation materials. Syros has retained Morrow Sodali to assist it in soliciting proxies using the means referred to above. Syros will pay the fees of Morrow Sodali, which Syros expects to be approximately $15,000, plus reimbursement of out-of-pocket expenses.

Other Matters

As of the date of this joint proxy statement/prospectus, Syros' board of directors does not know of any business to be presented at the Syros special meeting other than as set forth in the notice accompanying this joint proxy statement/prospectus. If any other matters should properly come before the Syros special meeting, it is intended that the shares represented by proxies will be voted with respect to such matters in accordance with the judgment of the persons voting the proxies.

THE SPECIAL MEETING OF TYME STOCKHOLDERS

Date, Time and Place

The special meeting of holders of common stock, par value $0.0001, of Tyme Technologies, Inc. will be held on September 15, 2022, commencing at 11:00 A.M. Eastern Time, unless postponed or adjourned to a later date. The Tyme special meeting will be held entirely online. Tyme is sending this joint proxy statement/prospectus to its stockholders in connection with the solicitation of proxies by Tyme's board of directors for use at the Tyme special meeting and any adjournments or postponements of the Tyme special meeting. The joint proxy statement/prospectus is first being mailed to Tyme stockholders on or about August 10, 2022.

Tyme stockholders may attend, vote and submit questions during or in advance of the Tyme special meeting via the Internet at https://www.cstproxy.com/tymeinc/2022 in accordance with the rules of conduct for the meeting. Tyme has designed the format of the Tyme special meeting to provide Tyme stockholders the same rights and opportunities to participate as they would at an in-person meeting, allowing for active participation by all Tyme stockholders at no cost, regardless of their geographic location, using online tools to ensure access and participation. Tyme believes that a virtual meeting will provide meaningful stockholder access and participation and also protect the health and safety of our stockholders, directors, officers and employees.

Purposes of the Tyme Special Meeting

The purposes of the Tyme special meeting are to:

1. Adopt the Merger Agreement, or the Tyme Merger Proposal;
2. Conduct an advisory, non-binding vote to approve merger-related executive compensation;
3. Approve an amendment to Tyme's amended and restated certificate of incorporation to effect a reverse stock split of Tyme common stock, by a ratio of not less than 1-for-15 and not more than 1-for-75, such ratio and the implementation and timing of the reverse stock split to be determined in the discretion of Tyme's board of directors;
4. Consider and vote upon an adjournment of the Tyme special meeting, if necessary, to solicit additional proxies if there are not sufficient votes in favor of Proposal Nos. 1, 2 and 3 or to ensure that any supplement or amendment to this joint proxy statement/prospectus is timely provided to holders of Tyme common stock; and
5. Transact any other business as may properly come before the meeting or any adjournment or postponement thereof

Recommendation of Tyme's Board of Directors

- The Tyme board of directors has determined that the adoption of the Merger Agreement is fair to, and in the best interests of, Tyme and the Tyme stockholders and has approved and declared advisable the adoption of the Merger Agreement. The Tyme board of directors recommends that Tyme stockholders vote "FOR" Tyme Proposal No. 1 to approve the adoption of the Merger Agreement.
- The Tyme board of directors recommends that Tyme stockholders vote "FOR" Tyme Proposal No. 2 to approve, on a non-binding advisory basis, the merger-related executive compensation that will or may become payable by Tyme to the Tyme Named Executive Officers in connection with the consummation of the merger as disclosed pursuant to Item 402(t) of Regulation S-K in the "*The Merger—Tyme Golden Parachute Compensation*" and "*The Merger—Tyme Golden Parachute Compensation Table*" sections of this joint proxy statement/prospectus.
- The Tyme board of directors recommends that Tyme stockholders vote "FOR" Tyme Proposal No. 3 to approve an amendment to the Tyme Certificate of Incorporation effecting the reverse stock split.

- The Tyme board of directors has determined and believes that considering and voting on the adjournment of the Tyme special meeting, if necessary, to solicit additional proxies if there are not sufficient votes in favor of the Tyme Proposals Nos. 1, 2 and 3 or to ensure that any supplement or amendment to this joint proxy statement/prospectus is timely provided to holders of Tyme common stock is fair to, and in the best interests of, Tyme and Tyme Stockholders and has approved and declared advisable the solicitation of additional proxies if there are not sufficient votes in favor of such proposals. The Tyme board of directors recommends that Tyme stockholders vote "FOR" Tyme Proposal No. 4 to adjourn the Tyme special meeting, if necessary in the judgment of Tyme management and subject to the Merger Agreement, in such circumstances.

Tyme stockholders should understand, however, that Tyme's Board intends to consider the implementation of the reverse stock split pursuant to Tyme Proposal No. 3 only if the Tyme Merger Proposal is not approved by the Tyme stockholders or if the merger is not completed for any other reason.

Record Date and Voting Power

Holders of Tyme common stock as of the close of business on August 8, 2022, the record date, may vote at the Tyme special meeting. As of the record date, there were 172,206,894 shares of Tyme common stock outstanding. Each share of Common Stock is entitled to one vote.

Voting and Revocation of Proxies

The proxy accompanying this joint proxy statement/prospectus is solicited on behalf of Tyme's board of directors for use at the Tyme special meeting.

Tyme stockholders of record may vote their shares by proxy over the Internet or by mail. Regardless of whether you plan to attend the virtual Tyme Stockholder Meeting, Tyme urges you to vote by proxy before the meeting to ensure your vote is counted. You may choose one of the following voting methods to cast your vote:

1. **BY INTERNET**: To vote by Internet, follow the instructions on the Notice of Internet Availability of Proxy Materials or proxy card. Internet voting before the Tyme special meeting is available 24 hours a day, 7 days a week, until 11:59 P.M., Eastern Time, on September 14, 2022. Your Internet vote authorizes the named proxies below to vote your shares in the same manner as if you marked, signed, dated and returned your proxy card.
2. **BY MAIL**: To vote by mail, simply mark your proxy, date and sign it, and return it to Tyme in the postage-paid envelope provided. If you return your signed proxy card before the Tyme special meeting, Tyme will vote your shares as you direct.

The method by which you vote now will in no way limit your right to vote electronically at the virtual Tyme special meeting if you later decide to attend. As discussed above, if you are a beneficial owner, you may not vote your shares at the meeting unless you obtain a legal proxy from your broker, bank or other nominee.

When proxies are properly signed, dated and returned, the shares represented by the proxies will be voted in accordance with the instructions of the stockholder. If no specific instructions are given, you give authority to Richard Cunningham and/or James Biehl to vote the shares in accordance with the recommendations of the Tyme board of directors as described above. If any director nominee is not able to serve, proxies will be voted in favor of the other nominee and may be voted for a substitute nominee, unless the Tyme board of directors chooses to reduce the number of directors serving on the Tyme board of directors. If any matters not described in this joint proxy statement/prospectus are properly presented at the Tyme special meeting, then the proxy holders will use their own judgment to determine how to vote the shares. If the Tyme special meeting is adjourned, the proxy holders can vote your shares on the new meeting date as well, unless you have revoked your proxy

If you are a stockholder of record of Tyme, unless you are a party to a voting agreement or a support agreement, you can change your vote or revoke your proxy before it is exercised by:

- written notice to Tyme's Corporate Secretary at Tyme Technologies, Inc., 1 Pluckemin Way, Suite 103, Bedminster, NJ 07921; however, if you intend to revoke your proxy by providing such a written notice, Tyme advises that you also send a copy via email to investorrelations@Tymeinc.com;
- timely delivery of a valid, later-dated proxy;
- entering a new vote online before the cutoff time (11:59 P.M., EST, on September 14, 2022); or
- attending and voting online during the Tyme special meeting (although attendance at the Tyme special meeting will not, by itself, revoke a proxy).

Your latest proxy submitted before the Tyme special meeting is the one that will be counted, unless you are admitted to attend the Tyme special meeting and vote your shares online during the meeting.

If you are the beneficial owner of your shares of Tyme common stock, you must contact the broker, bank or other nominee holding your shares and follow their instructions to change your vote or revoke your proxy. You may also vote online during the Tyme special meeting if you have obtained a legal proxy as described above.

Required Vote

The presence, by attendance at the Tyme special meeting or by proxy, of the holders of at leastone-third (1/3) in voting power of the shares of Tyme common stock issued and outstanding and entitled to vote at the Tyme special meeting must be present or represented to conduct business at the Tyme special meeting. You will be considered part of the quorum if you are represented by proxy or if you attend the virtual Tyme special meeting.

Abstentions and withhold votes are counted as "shares present" at the Tyme special meeting for purposes of determining whether a quorum exists. Proxies submitted by banks, brokers or other holders of record holding shares for you as a beneficial owner that do not indicate a vote for some or all of the proposals because that holder does not have voting authority and has not received voting instructions from you (so-called "broker non-votes") are also considered "shares present" for purposes of determining whether a quorum exists. If you are a beneficial owner, these holders are permitted to vote your shares on the ratification of the appointment of Tyme's independent registered public accounting firm, even if they do not receive voting instructions from you.

The following table summarizes the vote threshold required for approval of each item of business to be transacted at the Tyme special meeting, provided that there is a quorum. In addition, the table shows the effect on the outcome of the vote of: (i) abstentions; (ii) uninstructed shares held by brokers (which result in broker non-votes when a beneficial owner of shares held in "street name" does not provide voting instructions and, as a result, the nominee is prohibited from voting those shares on certain proposals); and (iii) signed but unmarked proxy cards.

Proposal	Vote Required for Approval	Effect of Abstentions(1)	Uninstructed Shares/ Effect of Broker Non-Votes(1)	Signed but Unmarked Proxy Cards(2)
1. Tyme Merger Proposal	Majority of outstanding shares of Tyme common stock	Same effect as a vote "Against"	Same effect as a vote "Against"	Voted "For"
2. Advisory Vote on Merger-related Executive Compensation	Majority of shares present at the Tyme special meeting or represented by proxy and entitled to vote thereon	Same effect as a vote "Against"	Not voted / no effect	Voted "For"

Proposal	Vote Required for Approval	Effect of Abstentions(1)	Uninstructed Shares/ Effect of Broker Non-Votes(1)	Signed but Unmarked Proxy Cards(2)
3. Amendment to Tyme's amended and restated certificate of incorporation to effect the Tyme Reverse Stock Split	Majority of outstanding shares of Tyme common stock	Same effect as a vote "Against"	Discretionary vote by broker	Voted "For"
4. Tyme Adjournment Proposal	Majority of shares present at the Tyme special meeting or represented by proxy and entitled to vote thereon	Same effect as a vote "Against"	Not voted / no effect	Voted "For"

(1) Abstentions and broker non-votes are included for purposes of determining whether a quorum is present, however, abstentions are considered "entitled to vote" whereas broker non-votes are not.

(2) If you sign and return your proxy card properly, but do not provide instructions on your proxy card as to how to vote your shares, your shares will be voted as shown in this column and in accordance with the judgment of the individuals named as proxies on the proxy card as to any other matter properly brought before the Tyme special meeting.

Under the applicable stock exchange rules, banks, brokers and other nominees may use their discretion to vote "uninstructed" shares (i.e., shares of record held by banks, brokers or other nominees, but with respect to which the beneficial owner of such shares has not provided instructions on how to vote on a particular proposal) with respect to matters that are considered to be "routine," but not with respect to "non-routine" matters. Tyme Proposal Nos. 1, 2 and 4 are non-routine matters, however, Tyme Proposal No. 3 is a routine matter and therefore, a broker is entitled to vote shares held for a beneficial owner on Tyme Proposal No. 3 without instructions from the beneficial owner of those shares.

Solicitation of Proxies

Syros will bear the costs of printing and mailing this joint proxy statement/prospectus and its proxy card to Syros stockholders and Tyme will bear the costs of printing and mailing this joint proxy statement/prospectus and its proxy card to Tyme stockholders. Tyme has retained MacKenzie Partners, Inc., or MacKenzie, to assist in the solicitation of proxies for the Tyme special meeting, and Tyme expects that the remuneration to MacKenzie for its services will not exceed $18,500 plus reimbursement for out-of-pocket expenses. Tyme will ask brokers, banks, voting trustees and other nominees and fiduciaries to forward any proxy materials to the beneficial owners of Tyme common stock and to obtain the authority to execute proxies. Tyme will reimburse them for their reasonable expenses upon request. In addition to mailing proxy materials, Tyme's directors, officers and employees may solicit proxies in person, by telephone or otherwise. These individuals will not be specially compensated.

Instructions for Participation in the Tyme Special Meeting

Registered Stockholders: Shares Registered in Own Name

For Tyme stockholders with shares are registered in their name with Tyme's transfer agent, Continental Stock Transfer and Trust Company, or Continental, who wish to attend the virtual Tyme special meeting, should go to https://www.cstproxy.com/tymeinc/2022, enter the 12-digit control number received on such stockholder's proxy card and click on the "Click here to preregister for the online meeting" link at the top of the page. Just before the start of the meeting, the Tyme stockholder will need to log back into the meeting site using control number. Pre-registration, which opens on September 12, 2022 at 5:00 P.M. (Eastern Time), is recommended, but not required, to attend.

Stockholders who do not have or misplace their control numbers may contact Continental at (917)262-2373 or proxy@continentalstock.com.

Registered stockholders may also dial in to listen to the meeting. Stockholders within the United States or Canada may call toll-free 1 800-450-7155 and those outside the United States and Canada may call +1 857-999-9155 (standard rates apply), and enter the passcode that will be posted at https://www.cstproxy.com/tymeinc/2022. Tyme stockholders will need their 12-digit control number to enter https://www.cstproxy.com/tymeinc/2022. By dialing in, stockholders will not be able to vote or participate during the meeting.

Beneficial Owner: Shares Registered in the Name of a Broker, Bank or Other Nominee

Tyme stockholders whose shares held in a stock brokerage account or by a bank or other nominee are considered the "beneficial owner" of shares held in street name. The Tyme joint proxy statement/prospectus was forwarded to you by your broker, bank or other nominee who is considered, with respect to those shares, the stockholder of record.

Beneficial owners who wish to attend the virtual Tyme special meeting must obtain a legal proxy by contacting their account representative at the bank, broker, or other nominee that holds their shares and e-mail a copy (a legible photograph is sufficient) of their legal proxy to Continental, proxy@continentalstock.com. Beneficial owners who e-mail a valid legal proxy will be issued a meeting control number that will allow them to register to attend and participate in the online-only meeting. After contacting Continental, a beneficial holder will receive an e-mail before the meeting with a link and instructions for entering the virtual meeting. Beneficial owners should contact Continental at least five (5) business days before the meeting date.

Beneficial owners who do not obtain a legal proxy will still be able to attend the virtual Tyme special meeting by (1) requesting a guest control number from Continental (email proxy@continentalstock.com) and then (2) visiting https://www.cstproxy.com/tymeinc/2022. or dialing-in to the meeting and entering the passcode that will be posted at https://www.cstproxy.com/tymeinc/2022. Stockholders within the U.S. and Canada may call toll-free 1 800-450-7155 and stockholders outside the U.S. and Canada may call +1 857-999-9155 (standard rates apply). However, in either case, such Tyme Stockholder will not be able to vote or participate during the meeting. Beneficial owners may be also required to provide proof of beneficial ownership.

All owners: By following the instructions above, a Tyme stockholder may log into the Tyme special meeting beginning at 10:45 A.M. (Eastern Time) on September 15, 2022, and the Tyme special meeting will begin promptly at 11:00 A.M. (Eastern Time).

Asking Questions at the Virtual Tyme Special Meeting

Stockholders have multiple opportunities to submit questions to Tyme for the virtual Tyme special meeting in accordance with the rules of conduct for the meeting (which rules will be available on the meeting site). Stockholders who wish to submit a question in advance may do so at https://www.cstproxy.com/tymeinc/2022 beginning on September 12, 2022 at 5:00 P.M. (Eastern Time), the day pre-registration opens. Stockholders may also submit questions online during the meeting at https://www.cstproxy.com/tymeinc/2022. Tyme intends to answer as many questions that are germane to the business of the meeting as time allows, but given time constraints, some questions may not be addressed during the virtual Tyme special meeting.

Technical Difficulties or Trouble Accessing the Live Webcast of the Tyme Special Meeting

Tyme will have technicians ready to assist stockholders with any technical difficulties they may have accessing the virtual Tyme special meeting. A phone number where stockholders can obtain technical assistance will be made available on the day of the Tyme special meeting.

Other Business

Tyme's board of directors does not know of any other matters to be presented at the Tyme special meeting. If any additional matters are properly presented at the Tyme special meeting, the persons named in the proxy card will have discretion to vote the shares of Tyme common stock represented by proxy in accordance with their own judgment on such matters.

It is important that your shares be represented at the Tyme special meeting, regardless of the number of shares of Tyme common stock that you hold. Tyme urges you to vote by proxy at your earliest convenience or by attending the virtual Tyme special meeting.

This section and the section titled "The Merger Agreement" beginning on page 203 of this joint proxy statement/prospectus describe the material aspects of the merger and the Merger Agreement. While Syros and Tyme believe that this description covers the material terms of the merger and the Merger Agreement, it may not contain all of the information that is important to you. You should read carefully this entire joint proxy statement/prospectus for a more complete understanding of the merger and the Merger Agreement and the other documents to which you are referred in this joint proxy statement/prospectus. See the section titled "Where You Can Find More Information" beginning on page 445 of this joint proxy statement/prospectus.

Background of the Merger

In an effort to enhance stockholder value, Tyme's board of directors, led primarily by its Strategic Planning Committee, and executive management regularly review and discuss Tyme's near and long-term operating and strategic priorities. Among other things, these reviews and discussions focus on the opportunities and risks associated with Tyme's clinical pipeline, development programs, financial condition and its potential long-term strategic options.

Similarly, the Syros board of directors and its executive management team regularly review and discuss Syros' near and long-term operating and strategic priorities, focusing on the opportunities and risks associated with Syros' clinical pipeline, development programs, financial condition and its potential long-term strategic options.

On November 23, 2020, Tyme's board of directors appointed Richie Cunningham as the new Chief Executive Officer of Tyme. In connection therewith, during the fourth quarter of calendar year 2020, Tyme's executive management team initiated a strategic review of Tyme's development strategy and product candidate portfolio with the goal of maximizing opportunities, improving operational efficiencies and minimizing risk to focus on creating value for all shareholders. The strategic review process encompassed an extensive review of internal and external resources, the design of and results from Tyme's preclinical and clinical trials, the likelihood of approval by the FDA or similar regulatory authorities outside the United States, the potential market for pipeline candidates, the costs and complexities of manufacturing to ensure a safe and sustainable supply of investigational compounds can be delivered to patients, the potential of competing products, the likelihood of any challenges to its IP, regardless of merit, the ongoing and potential effects of COVID-19 or any future pandemics, and industry and market conditions generally.

At this time, Tyme's lead product candidate was being evaluated for pancreatic cancer in two ongoing trials: (i) Precision Promise, the PanCAN-sponsored Phase 2/3 trial evaluating SM-88 as a second-line therapy, and (ii) TYME-88-Panc (Part 2), sponsored by Tyme's clinical trial evaluating SM-88 as a third-line therapy in metastatic pancreatic cancer.

At the conclusion of this review, Tyme announced on June 10, 2021 that it would be discontinuing its TYME-88-Panc trial and focusing its efforts in pancreatic cancer on the Precision Promise trial conducted by PanCAN. Enrollment rates for its TYME-88-Panc trial had progressed more slowly than anticipated, due in large part to the COVID-19 pandemic and had experienced higher-than-expected drop-out rates in patients randomized to the chemotherapy control arm, which could have potentially impacted the interpretive and regulatory utility of the data. At the same time, Tyme also announced the launch of the Phase II OASIS trial in certain breast cancers as well as a biomarker initiative and other preclinical research work on SM-88, based, in part, on the early clinical results of SM-88 in breast cancers and support of Georgetown University for the trial, in an effort to pursue pipeline diversification.

On December 22, 2021, Tyme received notice from The Nasdaq Stock Market that the closing bid price for its common stock had been below $1.00 per share for the previous 30 consecutive business days, and that Tyme was therefore not in compliance with the minimum bid price requirement for continued inclusion on The Nasdaq Capital Market under Nasdaq Listing Rule 5550(a)(2). The Nasdaq Stock Market notice started a 180-day

compliance period in which Tyme would need to regain compliance if the closing price of its common stock was at least $1.00 per share for a minimum of ten consecutive business days. On June 21, 2022, Tyme received a second notice from The Nasdaq Stock Market granting an additional 180-day compliance period, through December 19, 2022.

On January 26, 2022, Tyme announced that it had received notice from PanCAN that SM-88 was being discontinued in the Precision Promise trial due to futility compared to the standard of care control group.

On February 7, 2022, Tyme's board of directors held a meeting by teleconference. Tyme's acting Chief Medical Officer joined the meeting and provided an update on the recent PanCAN announcement, Tyme's remaining ongoing clinical trials and preclinical studies and when additional data might become available. Tyme's board of directors asked questions regarding the cost and feasibility of initiating trials in additional indications. Management believed that beginning trials in a new indication at that time would be time consuming and costly. In particular, designing and initiating a trial before receipt of the biomarker initiative and other preclinical data could present difficulties in targeting optimal patient populations.

After reviewing the information received from PanCAN, discussions with Tyme's board of directors, and a review of ongoing trials and finances, Tyme management believed that additional opportunities existed that could enhance value for Tyme stockholders, notwithstanding the discontinuation of its most advanced clinical trial, and began to explore a process to evaluate strategic alternatives. The process was intended to be comprehensive, exploring all possible value-maximizing alternatives—including ways to improve execution and maximize the potential for success of Tyme's strategies to advance SM-88, possible strategic partnerships to enhance Tyme's ability to execute such strategies, and a broad range of transformational strategic transactions.

In February and March 2022, Tyme management met with representatives from eight investment banks, including Moelis, to discuss strategy and planning for exploring possible transactions and strategic alternatives for Tyme and to assess each bank's qualifications and fit for a potential engagement to assist with the strategic review process.

On March 9, 2022, the Strategic Planning Committee held a meeting by teleconference at which members of Tyme management, representatives of Moelis and certain external advisors were present. At the meeting, Tyme management gave the committee an update on Tyme's clinical trials and its efforts to diversify its assets, including its discussions with investment banking advisors. After such update, the representatives of Moelis suggested that Tyme's board of directors engage in a parallel review of multiple potential strategic alternatives in addition to further development of SM-88, including potential in-licensing transactions, acquisitions and other business combination transactions, for the committee to consider. At the end of such meeting, the Strategic Planning Committee, after considering the discussion with Moelis and the recommendation of management based upon its meetings with multiple investment banks, directed management to negotiate an engagement letter with Moelis. Tyme's board of directors selected Moelis as its financial advisor in connection with this process primarily because Moelis had substantial experience in similar transactions. Moelis is regularly engaged in the valuation of businesses and their securities in connection with mergers and acquisitions, strategic transactions, corporate restructurings, and valuations for corporate and other purposes.

Beginning in March 2022, Tyme met with and engaged a drug development and regulatory consultant and a suite of other consultants with relevant experience in scientific, development, commercial, regulatory, and biotech investment experience to assist in its analysis of potential strategic alternatives and to advise Tyme on counterparty diligence related to such parties' operations and assets. These external advisors were consulted throughout the bid and negotiation process discussed herein and assisted Tyme in evaluating potential opportunities and strategic alternatives. During this time, Tyme also began coordinating diligence processes and plans with Tyme's outside counsel, Faegre Drinker Biddle & Reath LLP, or Faegre Drinker, and Morgan, Lewis & Bockius LLP, or Morgan Lewis, its patent and IP counsel.

On March 14, 2022, Moelis provided an initial draft of an engagement letter to Tyme management. Tyme management, with the assistance of Faegre Drinker and in consultation with the chair of the Strategic Planning Committee, proceeded to negotiate the terms of such engagement letter.

On March 21, 2022, Tyme's board of directors met in a special meeting to discuss the strategic review process. Tyme's board of directors approved the engagement of Moelis as Tyme's financial advisor, subject to management finalizing the engagement letter within certain constraints discussed at the meeting, and appointed the Strategic Planning Committee as the transaction committee for any such transaction.

On March 25, 2022, Tyme signed the engagement letter with Moelis to engage Moelis as its financial advisor for this process. On March 29, 2022, Tyme publicly announced that it had commenced a formal process to explore potential strategic options.

On April 6, 2022, Tyme's board of directors held a meeting by teleconference, which was also attended by Tyme management, Moelis and Faegre Drinker. Tyme management provided a brief update on the process being initiated to explore potential strategic options. The representatives from Faegre Drinker provided an overview of director fiduciary duties, including in connection with the evaluation of strategic transactions. Tyme's board of directors also noted the fact that Eagle is an existing investor in Tyme with prior interest in SM-88, and discussed potential outreach to Eagle regarding SM-88 and Eagle's possible inclusion in the process. Eagle was subsequently engaged in the process but later declined to proceed.

From late March through May 2022, under the oversight and direction of the Strategic Planning Committee, Moelis engaged with at least 94 potential counterparties to gauge their interest in a potential strategic transaction with Tyme. This included 50 potential counterparties who contacted Tyme or Moelis (in response to Tyme's announcement regarding the strategic review process or otherwise on their own initiative) and 44 potential counterparties who responded to outreach by Moelis. 42 of these potential counterparties engaged in interactions with Tyme and Moelis, executed confidentiality agreements, or NDAs, and received access to limited information in a virtual data room prepared by Tyme. During this time, members of Tyme management and representatives of Moelis engaged in preliminary introductory discussions, information exchange, and limited due diligence calls and related activities with multiple potential counterparties to explore interest in a potential transaction with Tyme. In addition, Tyme, through Moelis, shared a process letter and requested non-binding proposals from potential counterparties under NDAs with a May 4th proposal deadline. Ultimately, indications of interest were received from 34 of the 42 potential counterparties under NDAs. Of these 34 total bids, 26 proposed an all-stock reverse merger, four concerned an in-licensing transaction, and four involved an all-stock merger with another public company. None of the interested parties offered a cash transaction to acquire Tyme outright. Of the proposed counterparties, 19 were oncology companies, whereas 15 were not oncology-focused. Four of the counterparties were public companies compared to 30 private entities.

As described below, Tyme proceeded to focus on possible transactions with three counterparties who advanced through the final stages of the process: Syros and two private biotech companies that are referred to as "Party B" and "Party C."

Initial Syros Contacts

From June 2021 through early March 2022, Syros' board of directors and senior management engaged in efforts to explore various alternatives to raise financing to provide Syros with sufficient funding to continue the research and development of its product candidates through anticipated value inflection points. These efforts included consideration of a private placement equity financing, pursuit of a structured financing, efforts to identify a strategic transaction and efforts to identify and pursue other business development and licensing initiatives.

On March 30, 2022, as part of these efforts, representatives of Syros contacted Moelis and indicated that Syros might be interested in a transaction with Tyme. At the direction of Tyme's board of directors, Moelis provided a "teaser" document approved by Tyme and Tyme's NDA. On April 4, 2022, Moelis had an introductory call with Syros management and Syros signed the NDA on April 11, 2022. Between April 17 and April 29, Syros was granted access to the limited virtual data room prepared by Tyme and conducted preliminary due diligence calls with Tyme management and Moelis.

On April 29, 2022, Syros' board of directors held a meeting at which members of Syros management, representatives of Cowen and Company LLC, a financial advisor to Syros, or Cowen, and a representative of Wilmer Cutler Pickering Hale and Dorr LLP, or WilmerHale, were present. At this meeting, Nancy Simonian, M.D., Syros' Chief Executive Officer and a Syros director, reviewed the financing alternatives pursued by Syros to date and, after discussion, Syros' board of directors authorized Syros management to pursue a financing through a private placement of Syros' securities, or the Proposed Financing, and formed a committee of Syros' board of directors comprising Mark J. Alles, Marsha H. Fanucci and Peter Wirth to facilitate the Proposed Financing, or the Syros Pricing Committee. Following this meeting, on April 29, 2022, Syros indicated to Moelis that it did not at that time anticipate moving forward in a transaction with Tyme.

From April 29, 2022 through May 12, 2022, Syros and Cowen engaged in efforts to market the Proposed Financing to investors. During this period, no lead investor emerged to offer a set of terms for the Proposed Financing that would satisfy Syros' funding requirements. During this period, representatives of Syros, Tyme and Moelis engaged in a series of discussions regarding the terms on which Syros might be willing to explore an acquisition of Tyme in an all-stock merger. Representatives of Syros also engaged in discussions with Oxford regarding an extension of the amortization period and maturity date on Syros' term loan, which would be contingent on Syros' successful completion of the Proposed Financing.

On May 12, 2022, the Syros Pricing Committee held a meeting at which members of Syros management were present. At the meeting, Dr. Simonian updated the Syros Pricing Committee regarding the activities related to the Proposed Financing, including Syros' difficulty, prior to that time, in securing indications of interest for the Proposed Financing for a sufficient quantum of capital to satisfy Syros' funding requirements. Jason Haas, Syros' Chief Financial Officer, then reviewed the possibility of facilitating a smaller Proposed Financing in combination with an acquisition of Tyme (including its cash) and reviewed the terms of a potential proposal for Syros to acquire Tyme in an all-stock merger. Following discussion, the Syros Pricing Committee authorized management to submit a non-binding indication of interest for Syros to acquire Tyme in anall-stock merger that would result in pro forma ownership of the combined company being held 60% by Syros stockholders and 40% by Tyme stockholders, based on estimated cash balances at the time and before taking into account a contemplated $75 million concurrent financing via the Proposed Financing, which indication of interest Syros submitted to Tyme on May 13, 2022.

Initial Party B Contacts

On April 4, 2022, representatives from an investment banking firm contacted Moelis and shared a corporate presentation of a private clinical-stage oncology company, or Party B, that was interested in exploring a transaction with Tyme. After introductory discussions between Moelis and the investment banking firm between April 4 and 6, 2022, Party B executed the NDA on April 10, 2022. Party B was granted access to Tyme's limited virtual data room on April 17, 2022. The Chief Executive Officer of Party B then requested to schedule management calls, which were held with Moelis on April 26, 2022 and Tyme management on April 29, 2022. On these calls, representatives of Party B provided details on their corporate overview, clinical programs, upcoming inflection points and financing needs.

Tyme and Moelis then held a call on May 4, 2022 to discuss Party B's proposal for a potential transaction made on May 3, 2022 in a preliminary indication of interest submitted to Moelis. The indication of interest contemplated a reverse merger – that is, Tyme would acquire Party B in an all-stock merger that would result in the stockholders of Party B owning a majority of Tyme. Party B was primarily interested in acquiring Tyme's public company designation and Nasdaq stock listing and its net cash. The proposed transaction would have valued Tyme at $20 million plus its net cash, but would have valued Party B at $345 million. Party B's indication of interest estimated that this would result in pro forma ownership of the combined company being held approximately 80% by Party B stockholders and 20% by Tyme stockholders, in each case before taking into account a contemplated $45 to $65 million concurrent financing via private placement of Party B stock. Party B attributed $5 million of its proposed Tyme valuation to SM-88 and suggested willingness to include a mechanic

to allow pre-closing Tyme holders to realize a portion of further value from certain future developments with respect to SM-88.

Initial Party C Contacts

On March 30, 2022, Moelis contacted the head of corporate development of a private clinical-stage biopharmaceutical company, or Party C, to gauge interest in a potential transaction. Moelis conducted an initial call and follow up discussion with representatives from Party C on April 1, 2022, and Party C executed the Transaction NDA on April 5, 2022.

On April 13, 2022, Tyme management held a call with representatives from Party C and discussed Party C's corporate overview, clinical programs, upcoming inflection points and financing needs. Party C was granted access to Tyme's limited virtual data room on April 17, 2022 and conducted a call to discuss the proposed valuation of Party C in a potential transaction with Moelis and Tyme representatives on April 18, 2022.

On May 4, 2022, Party C submitted a preliminary indication of interest for a transaction with Tyme. Party C also proposed a reverse merger transaction, contemplating an all-stock transaction that would have valued Tyme at $12.5 million plus its net cash and valued Party C at approximately $119 million. Party C's indication of interest estimated that this would result in pro forma ownership of the combined company being held approximately 60% by Party C stockholders and 40% by Tyme stockholders. Party C indicated that its proposal valued Tyme's SM-88 at $3 million, but suggested willingness to also consider a contingent value right for Tyme's current pipeline. Party C also indicated that it was considering a concurrent financing of up to $125 million through the private placement of Party C stock.

* * *

At a meeting on May 9, 2022, Tyme's board of directors reviewed the preliminary bid information from the 34 counterparties, including Syros, Party B and Party C. In examining the bids received, Tyme's board of directors, with input from advisors present at the meeting, considered the totality of each offer with a view toward maximizing value for Tyme stockholders. Given that the bids received involved all-stock transactions, Tyme's board of directors paid special attention to factors that would affect the long-term value to be received by Tyme stockholders. Tyme's board of directors discussed in particular the following factors:

- the valuation ascribed to the counterparty and the valuation ascribed to Tyme (generally viewed as a premium applied over Tyme's expected closing net cash) and the resulting proposed ownership split;
- history and quality of the counterparty's clinical pipeline and clinical data to date;
- potential and timeline to commercialization and attractiveness of the target market opportunity;
- pro forma cash runway and projected timeline for achievement of multiple clinical milestones;
- perceived ability of the surviving company to achieve its milestones;
- potential liabilities and encumbrances on key assets;
- existing potential public company infrastructure and readiness (which could affect the timing and certainty of closing and potential value leakage due to the consumption of Tyme's net cash during the pendency of the merger);
- historical funding and concurrent financing considerations (including the inclusion of new external investors in a concurrent financing to validate the proposed valuation of any private company counterparties); and
- quality of counterparty management, board and investor base.

After such discussions, Tyme's board of directors selected seven parties, including Syros, Party B and Party C, forin-depth, in-person meetings with Moelis, Tyme management and members of Tyme's board of directors. At the direction of Tyme's board of directors, Moelis then informed the other potential counterparties that they had not advanced to the next stage of discussions.

Meetings with seven parties occurred over the course of May 2022 with fivein-person meetings, including Party B and Party C, held between May 12 and May 13, 2022, and two additional meetings through videoconference, including Syros held on May 18, 2022, at which meeting Syros management provided certain financial information regarding its long-term plans, and another party on May 31, 2022. Following six of the seven meetings and consultation with members of Tyme's Strategic Planning Committee, on May 18, 2022 all parties except Syros, Party B, and Party C were informed that they would not be moving forward in the process. Following the seventh meeting on May 31, 2022 the seventh party was also informed it would not be moving forward in the process.

Tyme's board of directors met on May 23, 2022 by videoconference and was joined by representatives of Tyme management and Moelis. At the meeting, Tyme's board of directors reviewed the potential counterparties and respective transaction proposals to date, taking into account criteria that Tyme's board of directors, with advice from Tyme management and Moelis, considered relevant for its evaluation. Following these discussions, Tyme's board of directors confirmed the three parties to advance to term sheet negotiations and preliminary due diligence: Syros, Party B and Party C. As part of that process, Tyme, together with its external consultants and advisors, engaged in a number of diligence calls with each of Syros, Party B and Party C between May 26, 2022 and June 17, 2022 on operational, commercial, supply chain, clinical, regulatory, legal and intellectual property matters for each company. Tyme also granted certain parties, including Syros, Party B, and Party C, with access to an expanded data room during this time. Based on the preliminary bids submitted by Syros, Party B and Party C and any additional discussions, Tyme, with the assistance of Faegre Drinker and Moelis, prepared draft non-binding term sheets for each of Syros, Party B and Party C and distributed the drafts to such parties on June 1, 2022. Syros, Party B and Party C responded with revised term sheets on June 13, June 11, and June 9, 2022, respectively. Thereafter, at the direction of Tyme's board of directors, Moelis and Faegre Drinker engaged with such parties and their counsel in an effort to clarify or negotiate the terms of their proposals.

On May 24, 2022, Syros' board of directors held a meeting at which members of Syros management, representatives of Cowen and representatives of Piper Sandler, were present. At the meeting, Dr. Simonian reviewed Syros' efforts to pursue an acquisition of Tyme through an all-stock merger and the Proposed Financing in a contemporaneous transaction. Dr. Simonian advised Syros' board of directors that due to challenging market conditions, there was uncertainty surrounding Syros' ability to raise sufficient funds through the Proposed Financing alone, noting that the proposed acquisition of Tyme was being contemplated as a complement to the Proposed Financing to increase the likelihood that Syros raise sufficient capital to fund its research and development activities through anticipated value inflection points. Following discussion, Syros' board of directors authorized Syros management to continue efforts to pursue the acquisition of Tyme and the Proposed Financing. In addition, Mr. Haas reviewed with Syros' board of directors the terms of an engagement letter proposed to be entered into by Syros and Piper Sandler for Piper Sandler to act as Syros' financial advisor in connection with Syros' proposed acquisition of Tyme. Thereafter, based on, among other attributes, Piper Sandler's qualifications, knowledge of the industry and reputation, Syros' board of directors authorized the engagement of Piper Sandler on the terms described by Mr. Haas.

During this period, Syros engaged with prospective investors to identify a lead investor in the Proposed Financing, which ultimately resulted in the receipt of investment terms for the Proposed Financing from a lead investor on June 7, 2022. Between June 7, 2022 and July 3, 2022, members of Syros management conducted meetings with prospective investors and engaged in negotiations regarding the final terms of the Securities Purchase Agreement, the Warrants and the Pre-Funded Warrants in connection with the Proposed Financing.

On June 15, 2022, Tyme's Strategic Planning Committee met by videoconference and was joined by representatives of Moelis who provided an update on counterparty discussions, term sheets, and financing updates from each counterparty. In particular, the committee discussed the progress that Syros had made on its private placement transaction, which appeared to be moving faster than other counterparties. The committee reviewed the latest proposed terms and financial details, including the warrant coverage to be issued in the private placement, and potential timing for finalizing the financing arrangements.

On June 17, 2022, Tyme's board of directors met by videoconference to discuss the process, including the status of negotiations and diligence with Syros, Party B and Party C. Members of Tyme management and representatives of Moelis and certain external advisors were present. At the meeting, Tyme's management reviewed the due diligence conducted to date on each of the potential counterparties, including their respective science and technology, their respective management teams, their respective upcoming value inflection points and their respective public company readiness. Representatives from Moelis reviewed the non-binding term sheets most recently exchanged with the three remaining potential counterparties, which reflected the following proposals:

- Syros proposed an all-stock merger that would value Syros based on recent market prices (which represented a discount to Syros' net cash), rather than at its net cash balance (as originally proposed) and that would provide some premium to Tyme above its net cash balance. Moelis noted that Tyme was pushing to increase the premium to $7.5 million, with an implied ownership interest in the combined company of approximately 30% for existing Tyme stockholders (after taking into account dilution from a contemplated private placement financing). Syros would also obtain at least $100 million in a private placement (an increase from the $75 million financing as originally proposed), which would fund Syros' pipeline into 2025. The term sheet contemplated a mutual termination fee in certain situations in an amount equal to 3.5% of the implied valuation of each party and included a "force the vote" provision that prohibited either party from terminating the Merger Agreement to accept a superior proposal before such party's stockholder vote.
- Party B continued to propose an all-stock merger, with Tyme as the surviving entity. Despite negotiation efforts by Tyme management and Moelis, Party B expressed an unwillingness to consider soliciting new, external parties as part of its concurrent financing and their proposed valuation remained the same as their initial proposal. The term sheet provided a mutual termination fee in certain situations in an amount equal to 4% of the implied valuation of Tyme. Party B's term sheet contemplated a $50 million financing from only existing investors.
- Party C continued to propose an all-stock merger, with Tyme as the surviving entity. The term sheet provided a mutual termination fee in certain situations in an amount equal to 4.5% of the implied valuation of Tyme. Party C's term sheet contemplated a financing between $75-100 million, with up to $30 million from new investors.

Tyme's board of directors reviewed and considered the proposed valuations of Tyme and the respective counterparties, each counterparty's clinical history, clinical pipeline and commercialization potential, financial projections and cash runways, the percentage of ownership that current Tyme stockholders would have in the combined entity, the counterparty's analysis of Tyme's clinical pipeline and future development plans, existing investor makeup, willingness and ability to complete the transaction efficiently, any existing collaborations or encumbrances on valuations and the experience of the counterparty's management team. Tyme's board of directors considered the viability of continuing as a standalone company, including the cash requirements that such strategy would entail, the potential value that could be obtained if Tyme's clinical pipeline could be successfully commercialized, and the risks and uncertainties associated with such strategy. Tyme's board of directors also discussed the possibility that Tyme's operations could be wound down, its assets liquidated, the company dissolved, and any remaining value distributed to stockholders. Finally, Tyme's board of directors also considered the possibility that there may be other alternative transactions not yet identified, despite the effort conducted by Tyme (with the assistance of Moelis) to identify the range of strategic alternatives.

Following discussion and consideration, Tyme's board of directors concluded that the Syros transaction likely represented the highest possible value under the circumstances for Tyme stockholders, if it could be completed on the currently contemplated terms and if Syros were able to obtain definitive commitments from investors in a concurrent private placement to fund Syros into 2025. However, Tyme's board of directors requested further analysis by Tyme management (with Moelis' assistance) regarding Tyme's standalone prospects and regarding the potential value that Tyme stockholders would receive in a dissolution. Furthermore, given the uncertainty

around Syros' ability to obtain the necessary commitments for the concurrent private placement, and the associated investment terms, Tyme's board of directors directed management to continue negotiations and diligence with each of Syros, Party B and Party C, while prioritizing negotiations and diligence with Syros and Party C. Tyme's board of directors also directed Moelis to advise Syros that to be considered Tyme's board of directors preferred transaction counterparty, that additional concessions and a fully committed financing of at least $100 million would be needed for Tyme to move forward toward a transaction with Syros.

Tyme's board of directors also directed Moelis to advise Party C that to be considered Tyme's board of directors preferred transaction counterparty, that additional concessions and a fully committed financing of at least $100 million, of which a portion needed to be from new, external parties, would be needed for Tyme to move forward toward a transaction with Party C.

On June 18, 2022, Faegre Drinker and Moelis communicated with representatives of Syros' outside counsel, WilmerHale and Piper Sandler, regarding the term sheet, diligence matters, the transaction timeline and drafting of definitive agreements. The parties agreed to continue to negotiate key business terms in the term sheet while also drafting the definitive merger agreement.

On June 19, 2022, Faegre Drinker sent a revised draft of the term sheet to WilmerHale. Among other things, Faegre Drinker's draft of the term sheet (i) increased the premium ascribed to Tyme's valuation from $5 million to $7.5 million, (ii) included a covenant that Syros would commit at least $2.5 million toward the continued development of SM-88, (iii) provided Tyme the right to pursue a sale of certainnon-cash assets prior to closing, with any such proceeds included in the calculation of Tyme net cash, (iv) provided for a right of Tyme to terminate the Merger Agreement to accept a "superior proposal" in certain circumstances, (v) proposed modifications to the definition of "net cash" that would result in additional value for Tyme holders, and (vi) provided that all existing Tyme equity awards and warrants would be assumed by Syros. Additionally, representatives of Piper and Syros informed representatives of Moelis that they had made substantive progress in securing commitments for their concurrent financing and they believed they would be able to secure at least $100 million over the course of the week.

On June 21, 2022, Piper Sandler sent a revised draft of the term sheet to Moelis. The revised term sheet draft (i) rejected the increase to the premium payable to Tyme holders, restoring it back to Syros' prior position of $5 million, (ii) rejected the covenant related to SM-88's development, (iii) accepted the provision that Tyme could pursue value maximizing transactions for non-cash assets prior to closing, but imposed a limit on the amount of value that could be included in Tyme net cash, (iv) included a "force the vote" provision, and (v) modified the definition of Tyme net cash. Representatives of Piper Sandler also indicated that Syros expected exclusivity as a condition of further negotiations, and provided a draft of an exclusivity agreement that would provide for an exclusivity period through July 11, 2022.

Later in the day on June 21, 2022, Faegre Drinker responded with preliminary comments on the exclusivity agreement, noting that Tyme's board of directors had not yet determined whether to accept any exclusivity agreement. WilmerHale later responded that the comments were acceptable.

On June 22, 2022, WilmerHale sent a draft merger agreement to Faegre Drinker, noting several business points were still being negotiated in the term sheet document. Faegre Drinker began reviewing and circulated to Tyme management and Moelis for input. Additionally, Moelis and Tyme continued to hold diligence calls with Party B and Party C.

Also on June 22, 2022, Tyme directed Moelis to deliver a revised term sheet to Piper Sandler that reinserted a covenant to continue developingSM-88 (but without any commitment for specific expenditures), reverted to Tyme's earlier proposed premium for Tyme of $7.5 million, and modified certain portions of the definition of Tyme's net cash, among other things. The following day, representatives from Tyme, Moelis, Faegre Drinker, Syros, Piper Sandler and WilmerHale had a conference call to discuss and negotiate the remaining issues in the

term sheet, including the potential tax treatment of the transaction for Tyme stockholders, the definition of net cash, the calculation of the exchange ratio, certain covenants of each party, the treatment of Tyme options and warrants and the amount of the termination fees.

On June 24, 2022, WilmerHale circulated a revised term sheet reflecting the discussion on the previous day. The term sheet accepted key components of Tyme's prior proposal, including a $7.5 million premium for Tyme, a commitment to explore value-enhancing paths for SM-88, and a definition of Tyme net cash that would exclude certain costs and thereby increase value received by Tyme stockholders. WilmerHale and Faegre Drinker discussed certain issues in the term sheet or to be addressed in definitive agreements. Additionally, representatives of Piper Sandler and Syros indicated they had secured commitments in excess of $100 million, and shared details of the composition and order indications of the existing and new investors that comprised the external financing. Tyme's management reviewed the terms of the term sheet and exclusivity agreement with members of Tyme's Strategic Planning Committee, who directed management to finalize and execute them.

Also on June 24, 2022, Syros' board of directors held a meeting at which members of Syros management and representatives of Cowen, Piper Sandler and WilmerHale were present. At this meeting, Dr. Simonian and Mr. Haas updated Syros' board of directors on Syros' efforts to pursue an acquisition of Tyme and the Proposed Financing, and Mr. Haas reviewed the term sheet circulated by WilmerHale on June 24, 2022. Following discussion, Syros' board of directors authorized Syros to sign the term sheet and to enter into with Tyme an exclusivity letter with an exclusivity period that prohibited Syros and Tyme from engaging in discussions regarding alternative transactions with third parties through July 11, 2022.

On June 25, 2022, Tyme and Syros executed the term sheet and exclusivity letter. Upon execution of the term sheet and exclusivity letter, Moelis informed Party B and Party C that Tyme was terminating negotiations to pursue a transaction with another party.

On June 26, 2022, Faegre Drinker circulated a revised draft of the Merger Agreement to WilmerHale, reflecting the updated term sheet and additional changes.

During the period of June 26 to July 2, 2022 representatives of Tyme and representatives of Syros completed confirmatory due diligence on the other company and representatives of Faegre Drinker and WilmerHale negotiated the remaining terms of the Merger Agreement, including the representations and warranties and interim and post-closing covenants of each party, the mechanics and final treatment of Tyme warrants, the closing of the PIPE Financing as a closing condition to the merger, the definitions of a "Superior Proposal" and "Intervening Event," the procedures around each party's respective stockholder vote and the terms of the forms of support agreement and the form of lock-up agreement. The parties also negotiated the final treatment and process for the assumption of certain outstanding Tyme options, including an extension of the exercise period for Tyme options with an exercise price of under $2.00 per share held by individuals providing services as of the closing in exchange for such holders entering into cooperation agreements prior to closing.

On June 30, 2022, Tyme's board of directors held a meeting at which members of Tyme management and representatives of Moelis, Faegre Drinker and certain external advisors were present. During the meeting, the representatives of Faegre Drinker reviewed the fiduciary duties of Tyme's board of directors in connection with the proposed transaction with Syros and the terms of the Merger Agreement and forms of support agreement and form of lock-up agreement, and answered questions from Tyme's board of directors. Representatives of Moelis then reviewed the process conducted to solicit potential interest in a strategic transaction involving Tyme and reviewed preliminary financial information and other data relating to a potential transaction with Syros. Tyme's board of directors also reviewed and considered the alternative financial forecasts of Tyme management regarding the execution of a standalone strategy and a dissolution of Tyme. Tyme's board of directors also reviewed sensitivity analyses that indicated how various assumptions, including as to the amount of Tyme net cash at closing, would affect the value to be received by Tyme stockholders. Moelis noted that its discussion was preliminary and would be updated for the final closing price of Syros common stock the following day. Tyme's board of directors then discussed various considerations with respect to the proposed transaction, including those summarized under "*—Tyme Reasons for the Merger*." At the conclusion of the meeting, Tyme's board of

directors directed Tyme's management and advisors to continue to progress the transaction and agreed to convene again the following afternoon.

Also on June 30, 2022, the Syros Board held a meeting at which members of Syros management and representatives of Cowen, Piper Sandler and WilmerHale were present. During the meeting, Mr. Haas updated Syros' board of directors on Syros' efforts to pursue an acquisition of Tyme and the Proposed Financing, as well as the terms of the Proposed Financing. Representatives of Piper Sandler then reviewed the economic terms of Syros' proposed acquisition of Tyme and the financial analyses that had been performed by Piper Sandler in connection therewith. Thereafter, representatives of WilmerHale reviewed the fiduciary duties of the Syros directors in connection with the proposed acquisition of Tyme and the Proposed Financing and reviewed the material terms of the proposed merger agreement with Tyme. The Syros Board then discussed various considerations related to the merger and the Proposed Financing, including those described in "*—Syros Reasons for the Merger*". Following discussion, it was the consensus of Syros' board of directors that Syros should continue to pursue an acquisition of Tyme and the Proposed Financing on the terms described to Syros' board of directors.

Tyme's board of directors met again on July 1, 2022 to review changes in the Merger Agreement documentation and updated financial analysis regarding the proposed transaction, based upon the final market closing price per share of Syros common stock that had been calculated that afternoon.

Also on July 1, 2022, Syros' board of directors held a meeting at which members of Syros management and representatives of Cowen, Piper Sandler and WilmerHale were present. At the meeting, a representative of Piper Sandler reviewed the final economic terms of the merger and conveyed the oral opinion of Piper Sandler, which was confirmed by delivery of a written opinion, dated July 1, 2022, addressed to Syros' board of directors to the effect that, as of the date of the opinion and based upon and subject to the assumptions made, procedures followed, matters considered and limitations on the review undertaken in connection with the opinion, the Exchange Ratio provided in the merger pursuant to the Merger Agreement was fair, from a financial point of view, to Syros. Thereafter, Dr. Simonian noted an investor in the Proposed Financing had indicated a requirement to nominate a director as condition to its investment and another investor had indicated a requirement to nominate a director to Syros' board of directors or, in the alternative, an observer on the board, as condition to its investment. Members of Syros management also described the interests of certain of Syros directors and stockholders in the merger and the Proposed Financing, as described in "*—Interests of Syros Directors and Executive Officers in the Merger*". Following discussion, the Syros Board (with Dr. Simonian recusing herself and Srinivas Akkaraju, M.D., Ph.D., absent) approved the Merger Agreement and the Proposed Financing and authorized Syros Management to enter into the Merger Agreement and the Securities Purchase Agreement.

On July 2, 2022, Tyme's board of directors met again and received an update from Faegre Drinker regarding the finalization of the transaction documents and developments since the last meeting, including the implications that the final terms of the merger (including the proposed PIPE Financing of approximately $130 million) would have on the pro forma capitalization of the surviving company and on the tax treatment for the transaction. Representatives of Moelis also presented an update on Moelis' preliminary financial analysis, including with respect to Tyme, Syros and the proposed merger. After answering questions for members of Tyme's board of directors, representatives of Moelis delivered to Tyme's board of directors an oral opinion, which was confirmed by delivery of a written opinion, dated July 2, 2022, addressed to Tyme's board of directors to the effect that, as of the date of the opinion and based upon and subject to the assumptions made, procedures followed, matters considered and limitations on the review undertaken in connection with the opinion, the Exchange Ratio provided in the merger pursuant to the Merger Agreement was fair, from a financial point of view, to the holders of Tyme common stock. Tyme's board of directors briefly recessed so that the Strategic Planning Committee and Compensation Committee could each convene and consider resolutions relating to the transaction. The members of the Strategic Planning Committee of Tyme's board of directors unanimously recommended that Tyme's board of directors approve the Merger Agreement and the transactions contemplated therein. The Compensation

Committee of Tyme's board of directors unanimously approved the contemplated treatment of Tyme's equity incentive plans and outstanding stock options in the merger. Tyme's board of directors then reconvened and, taking into account the recommendation of the Strategic Planning Committee and other factors described in "*—Tyme Reasons for the Merger,"* unanimously approved the Merger Agreement and the transactions contemplated by the Merger Agreement and authorized Tyme management to execute the Merger Agreement on behalf of Tyme. Before the meeting adjourned, Faegre Drinker outlined remaining steps before the Merger Agreement would be executed and the expectations regarding the announcement of the transaction.

On July 3, 2022, Tyme and Syros entered into the Merger Agreement and Syros and the investors in the Proposed Financing entered into the Securities Purchase Agreement. The transaction was announced on July 5, 2022, prior to the open of trading on Nasdaq.

Syros Reasons for the Merger

During the course of its evaluation of the Merger Agreement, the PIPE Financing and the transactions contemplated by the Merger Agreement, Syros' board of directors held numerous meetings, consulted with Syros' senior management, legal counsel and financial advisor, and reviewed and assessed a significant amount of information. In reaching its decision to approve the Merger Agreement and the transactions contemplated by the Merger Agreement, Syros' board of directors considered a number of factors that it viewed as supporting its decision to approve the Merger Agreement, including:

- that the Syros board of directors and its financial advisors undertook a comprehensive and thorough process of reviewing and analyzing potential sources of capital to identify the opportunity that would, in the view of the Syros board of directors, create the most value for Syros stockholders;
- Syros' board of directors' belief, after initial fundraising discussions with prospective investors in a PIPE Financing and discussions with Syros' senior management, financial advisors and legal counsel, that it would be necessary to complete the merger, in combination with the PIPE Financing, to raise a sufficient quantum of capital to progress Syros' product candidates to significant value inflection points;
- the Syros board of directors' belief, after a thorough review of potential alternatives and discussions with Syros' senior management, financial advisors and legal counsel, that the merger is more favorable to Syros stockholders than alternative sources of capital available to Syros, including raising additional capital through the PIPE Financing;
- the Syros board of directors' consideration of the expected cash balances of the combined company as of the closing of the merger resulting from the approximately $62.3 million of net cash expected to be held by Tyme upon completion of the merger together with the cash Syros currently holds and the $130 million of expected gross proceeds from the PIPE Financing;
- the Syros board of directors' belief that, as a result of arm's length negotiations with Tyme, Syros and its representatives negotiated the lowest exchange ratio to which Tyme was willing to agree, and that the other terms of the Merger Agreement, taken as a whole, include the most favorable terms to Syros in the aggregate to which Tyme was willing to agree;
- the Syros board of directors' view, based on the scientific, regulatory and technical due diligence conducted by Syros management, of the regulatory pathway for, and market opportunity of, Syros' product candidates, including tamibarotene, SY-2101 and SY-5609;
- the Syros board of directors' view, following a review with Syros' management of Syros' and Tyme's current development and clinical trial plans, of the likelihood that the combined company, after giving effect to the amendment to Syros' debt facility, would possess sufficient cash resources at the closing of the merger to fund development of Syros' product candidates through upcoming value inflection points;

- the ability of Syros stockholders to participate in the growth and value creation of the combined company following the closing of the merger by virtue of their continued ownership of Syros common stock;
- the Syros board of directors' view that the combined company will be led by an experienced senior management team from Syros, and a board of directors comprised of Syros' current board of directors, a board member nominated by Tyme and up to two board members nominated by investors in the PIPE Financing, effective as of the closing of the merger;
- the current financial market conditions and historical market prices, volatility and trading information with respect to Syros common stock; and
- the Syros board of directors' consideration of the financial analyses of Piper Sandler & Co., including its opinion to the Syros board of directors as to the fairness, from a financial point of view and as of the date of the opinion, to Syros of the Exchange Ratio to be paid by Syros pursuant to the terms of the Merger Agreement, as more fully described below under the caption "*The Merger—Opinion of Piper Sandler & Co.*," beginning on page 165 of this joint proxy statement/prospectus.

The Syros board of directors also reviewed the terms of the Merger Agreement and related transaction documents, including those described below, and concluded that the terms of the Merger Agreement and related transaction documents, in the aggregate, were reasonable under the circumstances:

- the calculation of the Exchange Ratio, estimated closing net cash of Tyme expected to be held by Tyme upon completion of the merger and the estimated number of shares of Syros common stock to be issued in the merger;
- the number and nature of the conditions to Tyme's and Syros' respective obligations to complete the merger and the likelihood that the merger will be completed on a timely basis, including the fact that Syros' obligation to complete the merger would be conditioned on Tyme having at least $50 million of closing net cash and the fact that Tyme's obligation to complete the merger would be conditioned on all conditions precedent to the PIPE Financing having been completed, as more fully described below under the caption "*The Merger Agreement—Conditions to the Completion of the Merger*," beginning on page 215 of this joint proxy statement/prospectus;
- the respective rights of, and limitations on, Syros and Tyme under the Merger Agreement to consider and engage in discussions regarding unsolicited acquisition proposals under certain circumstances, and the limitations on the board of directors of each party to change its recommendation in favor of the merger, as more fully described below under the caption "*The Merger Agreement—Non-Solicitation*," beginning on page 210 of this joint proxy statement/prospectus;
- the potential termination fee of $2.07 million, in the case of the fee payable by Syros, or $2.44 million, in the case of the fee payable by Tyme, which could become payable by either Syros or Tyme to the other party if the Merger Agreement is terminated in certain circumstances, as more fully described below under the captions "*The Merger Agreement—Termination*" and "*The Merger Agreement—Termination Fees*," beginning on pages 219 and 221, respectively, of this joint proxy statement/prospectus;
- the lock-up agreements, pursuant to which certain Tyme stockholders have, subject to certain exceptions, agreed not to transfer their shares of Syros common stock during the period of 90 days following the completion of the merger, as more fully described below under the caption "*Agreements Related to the Merger—Lock-Up Agreements*," beginning on page 223 of this joint proxy statement/prospectus;
- the support agreements, pursuant to which certain stockholders of Syros and Tyme, respectively, have agreed, solely in their capacities as stockholders, to vote all of their shares of Syros common stock or Tyme common stock in favor of the proposals submitted to them in connection with the merger and against any alternative acquisition proposals, as more fully described below under the caption

"*Agreements Related to the Merger—Support Agreements*," beginning on page 222 of this joint proxy statement/prospectus; and

- the expectation that the merger will qualify as either a tax-free contribution pursuant to Section 351 of the Code, or will constitute a "reorganization" within the meaning of Section 368(a) of the Code, with the result that a U.S. Holder of Tyme common stock generally will not recognize any gain or loss for U.S. federal income tax purposes on the exchange of shares of Tyme common stock for shares of Syros common stock in the merger, except with respect to cash received by such U.S. Holder of Tyme common stock in lieu of a fractional share of Syros common stock, as more fully described below under the caption "*The Merger—Material U.S. Federal Income Tax Consequences of the Merger—Tax Characterization of the Merger*," beginning on page 199 of this joint proxy statement/prospectus.

In the course of its deliberations, the Syros board of directors also considered a variety of risks and other countervailing factors related to entering into the merger, including:

- alternative sources of capital available to Syros, including raising capital through the PIPE Financing alone;
- the potential effect of the $2.07 million termination fee payable by Syros upon the occurrence of certain events in deterring other potential acquirors from proposing an alternative acquisition proposal that may be more advantageous to Syros stockholders;
- the possibility that Tyme's board of directors could in certain circumstances change its recommendation in favor of the Tyme Proposal, which could result in the merger not being completed, and the fact that the $2.44 million termination fee payable by Tyme in such circumstances would not fully compensate Syros for its transaction expenses and lost opportunities;
- the prohibition on Syros to solicit alternative acquisition proposals during the pendency of the merger;
- the substantial expenses to be incurred by Syros in connection with the merger;
- wind-down costs and resource requirements associated with Tyme's operations and administration, including those associated with terminating Tyme's existing product candidates and clinical activities;
- the possible volatility of the trading price of Syros common stock resulting from the announcement, pendency or completion of the merger;
- the risk that the merger might not be consummated in a timely manner or at all, including as a result of an inability to complete the PIPE Financing in a timely manner;
- the scientific, technical, regulatory and other risks and uncertainties associated with development and commercialization of Syros' product candidates;
- the risk that the combined company may not have available sources of financing necessary to fund development of Syros' product candidates through upcoming value inflection points;
- the risk that the combined company may not be able to continue Tyme's work of evaluating the best path forward for Tyme's SM-88 program; and
- the various other risks associated with the combined company and the transaction, including those described in the sections entitled "*Risk Factors*" and "*Cautionary Statement Concerning Forward-Looking Statements*" in this joint proxy statement/prospectus.

The foregoing information and factors considered by the Syros board of directors are not intended to be exhaustive but are believed to include all of the material factors considered by the Syros board of directors. In view of the wide variety of factors considered in connection with its evaluation of the merger and the complexity of these matters, the Syros board of directors did not find it useful, and did not attempt, to quantify, rank or otherwise assign relative weights to these factors. In considering the factors described above, individual members

of the Syros board of directors may have given different weight to different factors. The Syros board of directors conducted an overall analysis of the factors described above, including thorough discussions with, and questioning of, the Syros management team and the legal and financial advisors of Syros, and considered the factors overall to be favorable to, and to support, its determination.

Tyme Reasons for the Merger

During the course of its evaluation of the Merger Agreement and the transactions contemplated by the Merger Agreement, Tyme's board of directors and the Strategic Planning Committee held numerous meetings, consulted with Tyme's senior management, legal counsel and its financial advisor, and reviewed and assessed a significant amount of information. In reaching its decision to approve the Merger Agreement and the transactions contemplated by the Merger Agreement, Tyme's board of directors considered a number of factors that it viewed as supporting its decision to approve the Merger Agreement, including:

- the financial condition and prospects of Tyme and the risks associated with continuing to operate Tyme on a stand-alone basis, particularly in light of the discontinuation of SM-88 in the Precision Promise trial in metastatic pancreatic cancer in January 2022 and internal estimates that Tyme could face substantial doubt in its ability to continue as a going concern by the end of 2024 without additional fundraising;
- the ability of Tyme's board of directors to continue to explore opportunities to obtain value for current Tyme stockholders from the potential sale or out-licensing of SM-88 assets prior to closing of the merger, the ability of Tyme's board of directors to change its recommendation in favor of the merger in response to certain Intervening Events (which could include positive developments in its SM-88 assets) and the commitment by Syros to explore and consider in good faith the viability of continued development of (or other value-maximizing opportunity for) assets related to SM-88 for the surviving corporation's stockholders (including former Tyme holders) after the closing;
- that Tyme's board of directors (with the assistance of its financial advisor) undertook a comprehensive and thorough process of reviewing and analyzing potential strategic alternatives, in-licensing opportunities and merger candidates to identify the opportunity that would, in Tyme's board of directors' view, create the most value for Tyme stockholders;
- Tyme's board of directors' belief, after a thorough review of strategic alternatives and discussions with Tyme's senior management, financial advisors and legal counsel, that the merger is more favorable to Tyme stockholders than the potential value that might have resulted from other strategic alternatives available to Tyme, including a liquidation of Tyme and the distribution of any available cash after wind down;
- Tyme's board of directors' belief that, as a result of arm's length negotiations with Syros, Tyme and its representatives negotiated the highest exchange ratio to which Syros was willing to agree, and that the other terms of the Merger Agreement, taken as a whole, include the most favorable terms to Tyme in the aggregate to which Syros was willing to agree;
- Tyme's board of directors' view, based on the clinical, regulatory and technical due diligence conducted by Tyme management and its outside advisors, of the regulatory pathway for, and market opportunity of, Syros' product candidates, both in and of itself and relative to the product candidates of other potential transaction counterparties;
- Tyme's board of directors' consideration of the anticipated cash available as of the closing of the merger and the PIPE Financing to fund the combined company, including Tyme's net cash, Syros' net cash and the proceeds of the PIPE Financing;
- Tyme's board of directors' view, following a review with Tyme's management of Syros' current development and clinical trial plans, of the likelihood that the combined company would possess sufficient cash resources at the closing of the merger to fund development of Syros' product candidates through upcoming value inflection points;

- Tyme board of directors' belief that the then-current market price of Syros common stock (upon which the Exchange Ratio would be based) was less than the intrinsic value of Syros common stock, due in part to general market conditions and Syros' financing overhang, which overhang would be addressed by the merger and concurrent private placement;
- the prospects of and risks associated with the other strategic candidates that had made proposals for a strategic transaction with Tyme based on the scientific, technical, financial and other due diligence conducted by Tyme management;
- progress made by Tyme throughout the negotiation process with Syros on each party's relative valuation, including a decrease in the implied valuation ascribed to Syros from the $85 million in Syros' initial indication of interest to less than $60 million in the Merger Agreement and an increase in the value ascribed to Tyme from no premium in Syros' initial indication of interest to $7.5 million in the Merger Agreement;
- Tyme's inability to obtain meaningful concessions on valuation from Party B or Party C and Tyme board of directors' belief that the relative valuations proposed by Party B and Party C, which were not based upon any public market, overvalued each such party and would have resulted in pro forma capitalization of the surviving corporation that would be less favorable to current Tyme stockholders, notwithstanding the fact that the stated value ascribed to Tyme by such parties may appear higher out of context;
- the ability of Tyme stockholders to participate in the growth and value creation of the combined company following the closing of the merger by virtue of their ownership of Syros common stock;
- Tyme board of directors' view that the combined company will be led by an experienced senior management team from Syros and a board of directors with representation from each of the current boards of directors of Tyme and Syros;
- the current financial market conditions and historical market prices, volatility and trading information with respect to Tyme common stock, the additional actions likely required for Tyme to regain compliance with Nasdaq listing requirements, and the potential for Tyme to secure funding for its clinical operations on acceptable terms in the future; and
- the financial analyses of Moelis reviewed with Tyme board of directors on July 2, 2022, and the opinion of Moelis, dated July 2, 2022, addressed to Tyme board of directors as to the fairness, from a financial point of view and as of the date of such opinion, to the holders of Tyme common stock of the Exchange Ratio provided in the Merger pursuant to the Merger Agreement, as more fully described below under the caption "*—Opinion of Moelis & Company LLC*."

The Tyme Board also reviewed the terms of the Merger Agreement and related transaction documents, including those described below, and concluded that the terms of the Merger Agreement and related transaction documents, in the aggregate, were reasonable under the circumstances:

- the calculation of the Exchange Ratio, including the definition of net cash, taking into consideration estimates of the resulting Exchange Ratio based upon the estimated closing net cash of Tyme expected to be held by Tyme upon completion of the merger and the estimated number of shares of Syros common stock to be issued in the merger;
- the number and nature of the conditions to Syros' and Tyme's respective obligations to complete the merger and the likelihood that the merger will be completed on a timely basis, including the fact that Syros' obligation to complete the merger would be conditioned on Tyme having at least $50 million of closing net cash and the fact that Tyme's obligation to complete the merger would be conditioned on all conditions precedent to the PIPE Financing having been completed, as more fully described below under the caption "*The Merger Agreement—Conditions to the Completion of the Merger*," beginning on page 215 of this joint proxy statement/prospectus;
- the respective rights of, and limitations on, Tyme and Syros under the Merger Agreement to consider and engage in discussions regarding unsolicited acquisition proposals under certain circumstances, and

the limitations on the board of directors of each party to change its recommendation in favor of the merger, as more fully described below under the caption "*The Merger Agreement—Non-Solicitation*," beginning on page 210 of this joint proxy statement/prospectus;

- the potential termination fee of $2.44 million, in the case of the fee payable by Tyme, or $2.07 million, in the case of the fee payable by Syros, which could become payable by either Tyme or Syros to the other party if the Merger Agreement is terminated in certain circumstances, as more fully described below under the captions "*The Merger Agreement—Termination*" and "*The Merger Agreement—Termination Fees*," beginning on pages 219 and 221, respectively, of this joint proxy statement/prospectus;
- lock-up agreements, pursuant to which certain Syros and Tyme stockholders have, subject to certain exceptions, agreed not to transfer their shares of Syros Common Stock during the period of 90 days following the completion of the merger, as more fully described below under the caption "*Agreements Related to the Merger—Lock-Up Agreements*," beginning on page 223 of this joint proxy statement/prospectus;
- the support agreements, pursuant to which certain stockholders of Tyme and Syros, respectively, have agreed, solely in their capacities as stockholders, to vote all of their shares of common stock in Tyme or Syros, respectively, in favor of the proposals submitted to them in connection with the merger and against any alternative acquisition proposals, as more fully described below under the caption "*Agreements Related to the Merger—Support Agreements*," beginning on page 222 of this joint proxy statement/prospectus; and
- the expectation that the merger will qualify as either a tax-free contribution pursuant to Section 351 of the Internal Revenue Code of 1986, as amended, or the Code, or will constitute a "reorganization" within the meaning of Section 368(a) of the Code, with the result that a U.S. Holder of Tyme common stock generally will not recognize any gain or loss for U.S. federal income tax purposes on the exchange of shares of Tyme common stock for shares of Syros common stock in the merger, except with respect to cash received by such U.S. Holder of Tyme common stock in lieu of a fractional share of Syros common stock, as more fully described below under the caption "*The Merger—Material U.S. Federal Income Tax Consequences of the Merger—Tax Characterization of the Merger*," beginning on page 199 of this joint proxy statement/prospectus.

In the course of its deliberations, Tyme's board of directors also considered a variety of risks and other countervailing factors related to entering into the merger, including

- the potential effect of the $2.44 million termination fee payable by Tyme upon the occurrence of certain events in deterring other potential acquirors from proposing an alternative acquisition proposal that may be more advantageous to Tyme stockholders;
- the possibility that Syros' board of directors could in certain circumstances change its recommendation in favor of the Syros Proposal, which could result in the merger not being completed, and the fact that the $2.07 million termination fee payable by Syros in such circumstances would not fully compensate Tyme for its transaction expenses and lost opportunities;
- the prohibition on Tyme to solicit alternative acquisition proposals during the pendency of the merger;
- the likelihood that Tyme will be unable to realize cash proceeds from a transaction involvingSM-88 prior to closing, notwithstanding the provisions of the Merger Agreement that would permit current Tyme holders to benefit from any such transaction;
- the possibility that Syros will be unable or unwilling to continue the development of, or otherwise realize value from,SM-88, despite the provisions of the Merger Agreement obligating Syros to explore alternatives for SM-88;
- the fact that the final Exchange Ratio will depend upon the amount of Tyme net cash as of closing, and the possibility that such amount could be materially different than the estimates considered by the Tyme board of directors;

- the substantial expenses to be incurred by Tyme in connection with the merger;
- the possible volatility of the trading price of Tyme common stock resulting from the announcement, pendency or completion of the merger;
- the risk that the merger might not be consummated in a timely manner or at all, including as a result of an inability to complete the PIPE Financing in a timely manner;
- the scientific, technical, regulatory and other risks and uncertainties associated with development and commercialization of Syros' product candidates;
- the fact that Tyme's cash will continue to deplete during the pendency of the merger, which will reduce the potential value that would be available to Tyme holders should the merger not be completed for any reason;
- the risk that the combined company may not have available sources of financing necessary to fund development of Syros' product candidates through upcoming value inflection points; and
- the various other risks associated with the combined company and the transaction, including those described in the sections entitled "*Risk Factors*" and "*Cautionary Statement Concerning Forward-Looking Statements*" in this joint proxy statement/prospectus.

The foregoing information and factors considered by Tyme's board of directors are not intended to be exhaustive but are believed to include all of the material factors considered by Tyme's board of directors. In view of the wide variety of factors considered in connection with its evaluation of the merger and the complexity of these matters, Tyme's board of directors did not find it useful, and did not attempt, to quantify, rank or otherwise assign relative weights to these factors. In considering the factors described above, individual members of Tyme's board of directors may have given different weight to different factors. Tyme's board of directors conducted an overall analysis of the factors described above, including thorough discussions with, and questioning of, the Tyme management team and the legal and financial advisors of Tyme, and considered the factors overall to be favorable to, and to support, its determination.

Opinion of Piper Sandler & Co.

On July 1, 2022, Piper Sandler rendered its oral opinion to Syros' board of directors (which was subsequently confirmed in writing by delivery of Piper Sandler's written opinion, dated the same date) to the effect that, as of July 1, 2022, and based upon and subject to the various assumptions and limitations set forth therein, the Exchange Ratio pursuant to the Merger Agreement was fair to Syros from a financial point of view.

The full text of the Piper Sandler written opinion dated July 1, 2022, which sets forth, among other things, the assumptions made, procedures followed, matters considered and limitations on the scope of the review undertaken by Piper Sandler in rendering its opinion, is attached as *Annex B* to this proxy statement. The Piper Sandler opinion addresses only the fairness, from a financial point of view, to Syros, of the Exchange Ratio pursuant to the Merger Agreement. Piper Sandler's opinion was directed to Syros' board of directors in connection with its consideration of the merger and was not intended to be, and does not constitute, a recommendation to any stockholder of Syros as to how such stockholder should act or vote with respect to the merger or any other matter. Piper Sandler's opinion was approved for issuance by the Piper Sandler opinion committee.

In connection with rendering the opinion described above and performing its related financial analyses, Piper Sandler, among other things:

- reviewed and analyzed the financial terms of a draft of the Merger Agreement dated June 29, 2022;
- reviewed and analyzed certain financial and other data with respect to Syros and Tyme which was publicly available;

- reviewed and analyzed certain information, including financial forecasts relating to the business, earnings, cash flow, assets, liabilities and prospects of Syros and Tyme, on a stand-alone basis, that were publicly available, as well as those that were furnished to Piper Sandler by Syros;
- conducted discussions with members of senior management and representatives of Syros and Tyme concerning the matters described in the preceding three bullets, as well as their respective business and prospects before and after giving effect to the merger;
- reviewed the current and historical reported prices and trading activity of Syros common stock and similar information for certain other companies deemed by Piper Sandler to be comparable to Syros;
- compared the financial performance of Syros with that of certain other publicly-traded companies that Piper Sandler deemed relevant;
- performed a discounted cash flow analysis with respect to Syros' projections; and
- reviewed the financial terms, to the extent publicly available, of certain business combination transactions that Piper Sandler deemed relevant.

In addition, Piper Sandler conducted such other analyses, examinations and inquiries and considered such other financial, economic and market criteria as Piper Sandler deemed necessary in arriving at its opinion.

The following is a summary of the material financial analyses performed by Piper Sandler in connection with the preparation of its fairness opinion and reviewed with Syros' board of directors at a meeting held on June 30, 2022. Piper Sandler subsequently rendered its oral opinion to Syros' board of directors on July 1, 2022 and provided Syros' board of directors with updated written materials reflecting market data as of the close of business on July 1, 2022, which is the basis for this summary.

This summary includes information presented in tabular format, which tables must be read together with the text of each analysis summary and considered as a whole in order to fully understand the financial analyses presented by Piper Sandler. The tables alone do not constitute a complete summary of the financial analyses. The order in which these analyses are presented below, and the results of those analyses, should not be taken as any indication of the relative importance or weight given to these analyses by Piper Sandler or Syros' board of directors. Except as otherwise noted, the following quantitative information, to the extent that it is based on market data, is based on market data as it existed on or before July 1, 2022, and is not necessarily indicative of current market conditions.

Unless the context indicates otherwise, for purposes of the financial analyses described below, Piper Sandler calculated (a) the market capitalization for each company based on the market value of the relevant company's fully diluted common equity using closing stock prices on July 1, 2022, (b) the net cash for each company based on cash and cash equivalents (excluding restricted cash), less short and long term investments plus debt (based on principal value of debt) plus capital leases, in each case based on such company's most recently reported quarter end (in the case of Syros, as of June 30, 2022), (c) the enterprise value for each company based on the market capitalization less net cash, each as calculated per the immediately preceding clauses (a) and (b), (d) the implied per share value for Syros based on (I) fully diluted shares outstanding, calculated using the treasury stock method, of Syros common stock (including options, warrants, pre-funded warrants and restricted stock units); or, based on the 5-day average closing prices of Syros common stock from June 27, 2022 through July 1, 2022 in order to calculate the estimated proposed exchange ratio of the merger, and (II) net cash as of June 30, 2022, (e) the implied exchange ratio of Syros common stock for each share of Tyme common stock based on (I) an implied share price for Syros common stock based on the fully diluted share and balance sheet information for Syros described in the immediately preceding clause and (II) the implied share price for Tyme common stock based on the sum of (A) $62.3 million, representing the estimated net cash of Tyme at the closing of the merger plus (B) $7.5 million, representing the premium to cash attributable to Tyme divided by (C) basic shares of Tyme outstanding.

Selected Public Companies Analysis

Piper Sandler reviewed certain public financial information for Syros and compared such data to corresponding public financial information of selected public companies in the biopharmaceutical industry that Piper Sandler considered to be comparable to Syros based on certain criteria, including, among other things, companies (i) with public market capitalizations near or below current cash holdings, (ii) in which their most advanced program is currently undergoing Phase 3 clinical trials, and (iii) in which such Phase 3 clinical trial data is not expected until at or after current cash runway ends.

Piper Sandler selected the following companies:

- Fulcrum Therapeutics, Inc.
- Ambrx Biopharma, Inc.
- MEI Pharma, Inc.
- Zynerba Pharmaceuticals, Inc.
- X4 Pharmaceuticals, Inc.
- Corbus Pharmaceuticals Holdings, Inc.
- Aravive, Inc.
- GlycoMimetics, Inc.
- Galmed Pharmaceuticals Ltd.

For this selected biopharmaceutical public companies analysis, Piper Sandler compared, among other things, the market capitalization, net cash, enterprise value and certain historical trading information of Syros to the selected companies based on information publicly available as of July 1, 2022.

The analysis indicated the following:

	Market Cap	Enterprise Value
75th Percentile	$ 77	($ 14)
Median	$ 34	($ 33)
25th Percentile	$ 32	($ 47)
Syros as of July 1, 2022	**$ 62**	**$ 18**

Piper Sandler then derived a range of implied exchange ratios of Syros common stock for each share of Tyme common stock utilizing the market capitalizations from the 25th and 75th percentile range of the selected biopharmaceutical public companies and based on the fully diluted share and balance sheet information for Syros and the basic shares outstanding and balance sheet information for Tyme described above. Piper Sandler observed that the implied exchange ratio range resulting from this analysis, as compared to the estimated proposed exchange ratio of 0.4312 in the merger, was 0.3614 to 0.8792.

Selected Reverse Merger Transactions Analysis

Piper Sandler reviewed selected M&A transactions in the biotechnology industry announced since January 1, 2017 and which have closed, involving a reverse merger between a public shell target and a buyer.

Based on these criteria, the following 33 transactions were selected:

Target	Acquiror	Date of Transaction Announcement	Date of Transaction Closing
Aprea Therapeutics, Inc.	Atrin Pharmaceuticals Inc.	05/16/2022	05/16/2022
Aerpio Pharmaceuticals, Inc.	Aadi Bioscience, Inc.	05/17/2021	08/26/2021

Target	Acquiror	Date of Transaction Announcement	Date of Transaction Closing
Millendo Therapeutics, Inc.	Tempest Therapeutics, Inc.	03/29/2021	06/25/2021
Cellect Biotechnology Ltd.	Quoin Pharmaceuticals Inc.	03/24/2021	10/28/2021
Seneca Biopharma, Inc.	Leading BioSciences, Inc.	12/17/2020	04/27/2021
Anchiano Therapeutics Ltd.	Chemomab Ltd.	12/15/2020	03/16/2021
Sunesis Pharmaceuticals, Inc.	Viracta Therapeutics, Inc.	11/30/2020	02/24/2021
Cleveland BioLabs, Inc.	Cytocom, Inc.	10/19/2020	07/27/2021
Cancer Genetics, Inc.	StemoniX, Inc.	08/24/2020	03/30/2021
Proteostasis Therapeutics, Inc.	Yumanity Therapeutics	08/24/2020	12/22/2020
Spring Bank Pharmaceuticals, Inc.	F-star Therapeutics, Limited	07/29/2020	11/20/2020
Rexahn Pharmaceuticals, Inc.	Ocuphire Pharma, Inc.	06/18/2020	11/05/2020
resTORbio, Inc.	Adicet Bio, Inc.	04/29/2020	09/15/2020
Tocagen Inc.	Forte Biosciences, Inc.	02/19/2020	06/15/2020
Conatus Pharmaceuticals Inc.	Histogen Inc.	01/28/2020	05/26/2020
Ritter Pharmaceuticals, Inc.	Qualigen, Inc.	01/21/2020	05/22/2020
Zafgen, Inc.	Chondrial Therapeutics, Inc.	12/18/2019	05/28/2020
Proteon Therapeutics, Inc.	ArTara Therapeutics, Inc.	09/23/2019	01/09/2020
OpGen, Inc.	Curetis N.V.	09/04/2019	04/01/2020
Gemphire Therapeutics Inc.	NeuroBo Pharmaceuticals, Inc.	07/24/2019	12/30/2019
Vical Incorporated	Brickell Biotech, Inc.	06/03/2019	08/31/2019
Vital Therapies, Inc.	Immunic AG	01/07/2019	04/12/2019
Flex Pharma, Inc.	Salarius Pharmaceuticals, LLC	01/04/2019	07/19/2019
Arsanis, Inc.	X4 Pharmaceuticals, Inc.	11/27/2018	03/13/2019
Edge Therapeutics, Inc.	PDS Biotechnology Corporation	11/26/2018	03/15/2019
Apricus Biosciences, Inc.	Seelos Therapeutics, Inc.	07/30/2018	01/24/2019
Aviragen Therapeutics, Inc.	Vaxart, Inc.	10/30/2017	02/13/2018
Neothetics, Inc.	Evofem Biosciences, Inc.	10/17/2017	01/17/2018
Inotek Pharmaceuticals Corporation	Rocket Pharmaceuticals, Ltd.	09/12/2017	01/04/2018
Mirna Therapeutics, Inc.	Synlogic, Inc.	05/16/2017	08/28/2017
Nivalis Therapeutics, Inc.	Alpine Immune Sciences, Inc.	04/18/2017	07/24/2017
Mast Therapeutics, Inc.	Savara Inc.	01/07/2017	04/27/2017
OncoGenex Pharmaceuticals, Inc.	Achieve Life Science, Inc.	01/05/2017	08/01/2017

For this selected biotechnology reverse merger transactions analysis, Piper Sandler calculated, among other things, (i) the pro forma ownership of the combined company immediately following the merger (without giving effect to any private placements), (ii) the aggregate value of the combined company used to determine the exchange ratio of the merger, (iii) the value of the target's ownership of the combined company based on the target's pro forma ownership, (iv) the amount of cash held by the target at the time of the announcement of the merger, (v) the additional value attributable to the target represented by the difference between the value of the target's ownership of the combined company and the amount of cash held by the target at the time of the announcement of the merger and (vi) the premium/(discount) to cash, calculated by dividing (A) the additional value attributable to the target by (B) the cash held by the target at the time of the announcement of the merger.

Piper Sandler then derived a range of implied exchange ratios of Syros common stock for each share of Tyme common stock utilizing the premium/(discount) to cash from the 25th and 75th percentile range of the selected biotechnology reverse merger M&A transactions and based on the fully diluted share and balance sheet information for Syros and the basic shares outstanding and balance sheet information for Tyme described above. Piper Sandler observed that the implied exchange ratio range resulting from this analysis, as compared to the estimated proposed exchange ratio of 0.4312 in the merger, was 0.4076 to 0.9749.

Piper Sandler also compared the implied premium/(discount) to cash from the 25th and 75th percentile range of the analysis of selected biotechnology reverse mergers and acquisitions, or M&A, transactions to the implied premium/(discount) to cash in the merger. Piper Sandler observed that the implied premium/(discount) range resulting from this analysis, as compared to the 12% implied premium in the merger, was 6% to 153%.

This analysis indicated the following:

	Premium /(Disc.) To Cash	Implied (Premium)/Disc. To Buyer Currency	Implied Exchange Ratio
75th Percentile	153%	61%	0.9749
Median	76%	43%	0.6776
25th Percentile	6%	6%	0.4076
Proposed Merger	**12%**	**11%**	**0.4312**

Discounted Cash Flow Analysis

Piper Sandler performed a discounted cash flow analysis of Syros by calculating an estimated present value of the standalone unlevered, after-tax free cash flows that Syros was forecasted to generate during the fiscal years ending December 31, 2022 through December 31, 2037 based on probability-weighted and tax-affected forecasts (inclusive of Syros' net operating loss carryforwards). The after-tax free cash flows for each year were calculated based on estimates provided to Piper Sandler by Syros management (see "*Summary of Certain Syros Unaudited Prospective Financial Information*") to which Piper Sandler applied probability-of-success factors per the "Clinical Development Success Rates and Contributing Factors 2011-2020 Handbook" published by BIO, PharmaIntelligence, Quantitative Life Sciences, or the "CDSR Handbook, as is customary with drugs in development and with Syros management's consent solely for purposes of Piper Sandler's discounted cash flow analysis. Per the CDSR Handbook, probabilities of success of 4.6%, 15.0% and 54.0% were assigned to Syros' Phase 1, Phase 2 and Phase 3 programs, respectively, based on historical data for solid tumor and hematological oncology clinical trials as appropriate at each program's stage of development.

The implied terminal value of Syros was derived by applying a selected range of perpetuity growth rates of (1.0%) to 1.0% to Syros' unlevered after-tax free cash flow for the fiscal year ending December 31, 2037. The present values (as of July 1, 2022) of the cash flows and terminal values were then calculated using a selected discount rate range of 15.5% to 17.5%, based on Piper Sandler's estimation of Syros' weighted average cost of capital using the capital asset pricing model. Piper Sandler then derived a range of implied equity values for Syros using estimated net cash as of June 30, 2022 and then subtracted the $234.0 million in cash needed to achieve Syros management's revenue projections, per Syros management.

Piper Sandler then derived a range of implied exchange ratios of Syros common stock for each share of Tyme common stock based on the fully diluted share and balance sheet information for Syros and the basic shares outstanding and balance sheet information for Tyme described above. Piper Sandler observed that the implied exchange ratio range resulting from this analysis, as compared to the estimated proposed exchange ratio of 0.4312 in the Merger, was 0.3062 to 3.2597.

Other Information

Piper Sandler also noted for Syros' board of directors the following additional information that was not relied upon in rendering its opinion, but was provided for informational purposes:

- *Historical Trading Analysis*. Piper Sandler reviewed the historical closing prices and trading volumes for Syros common stock over the one-year period ended July 1, 2022, which reflected low and high closing prices during such period ranging from $0.69 to $5.66 per share, as compared to the July 1, 2022 closing price of $0.91 per share.

Miscellaneous

The summary set forth above does not contain a complete description of the analysis performed by Piper Sandler and reviewed with Syros' board of directors. The preparation of a fairness opinion is not necessarily susceptible to partial analysis or summary description. Piper Sandler believes that its analyses and the summary set forth above must be considered as a whole and that selecting portions of its analyses or of the summary, without considering the analyses as a whole or all of the factors included in its analyses, would create an incomplete view of the processes underlying the analyses set forth in the Piper Sandler opinion. In arriving at its opinion, Piper Sandler considered the results of all of its analyses and did not attribute any particular weight to any factor or analysis. Instead, Piper Sandler made its determination as to fairness on the basis of its experience and financial judgment after considering the results of all of its analyses. In addition, the ranges of valuations resulting from any particular analysis described above should not be taken to be Piper Sandler's view of the actual value of Syros.

No company or transaction used in the analyses above is identical to Syros or the merger. Accordingly, an analysis of the results of the comparisons is not mathematical; rather, it involves complex considerations and judgments about differences in the companies and transactions to which Syros and the merger were compared and other factors that could affect the public trading value or transaction value of the companies.

Piper Sandler performed its analyses for purposes of providing its opinion to Syros' board of directors. Certain of the analyses performed by Piper Sandler were based upon financial projections of future results furnished to Piper Sandler by Syros management, which are not necessarily indicative of actual future results and may be significantly more or less favorable than actual future results. These financial projections are inherently subject to uncertainty because, among other things, they are based upon numerous factors or events beyond the control of the parties or their respective advisors. Piper Sandler does not assume responsibility if future results are materially different from projected financial results.

Piper Sandler's opinion was one of many factors taken into consideration by Syros' board of directors in making the determination to approve the Merger Agreement. While Piper Sandler provided advice to Syros' board of directors during Syros' negotiations with Tyme, Piper Sandler did not recommend any specific amount or type of consideration.

Piper Sandler relied upon and assumed, without assuming liability or responsibility for independent verification, the accuracy and completeness of all information that was publicly available or was furnished, or otherwise made available, to Piper Sandler or discussed with or reviewed by Piper Sandler. Piper Sandler further relied upon the assurances of the management of Syros that the financial information provided to Piper Sandler was prepared on a reasonable basis in accordance with industry practice, and that management of Syros was not aware of any information or facts that would make any information provided to Piper Sandler incomplete or misleading. Without limiting the generality of the foregoing, for the purpose of its fairness opinion, Piper Sandler assumed that with respect to financial forecasts, estimates and other forward-looking information reviewed by Piper Sandler, that such information was reasonably prepared based on assumptions reflecting the best currently available estimates and judgments of the management of Syros and Tyme as to the expected future results of operations and financial condition of Syros and Tyme, respectively. Piper Sandler expressed no opinion as to any such financial forecasts, estimates or forward-looking information or the assumptions on which they were based. Piper Sandler further assumed that the merger will have the tax consequences described in this proxy statement. Piper Sandler relied, with the consent of Syros' board of directors, on advice of the outside counsel and the independent accountants to Syros, and on the assumptions of the management of Syros as to all accounting, legal, tax and financial reporting matters with respect to Syros, Tyme and the Merger Agreement.

In arriving at its opinion, Piper Sandler assumed that the executed Merger Agreement would be in all material respects identical to the last draft reviewed by Piper Sandler. Piper Sandler relied upon and assumed, without independent verification, that (i) the representations and warranties of all parties to the Merger Agreement and all

other related documents and instruments that are referred to therein were true and correct, (ii) each party to such agreements will fully and timely perform all of the covenants and agreements required to be performed by such party, (iii) the merger will be consummated pursuant to the terms of the Merger Agreement without amendments thereto, including the Merger Partner Net Cash (as defined in the Merger Agreement) closing condition, and (iv) all conditions to the consummation of the merger will be satisfied without waiver by any party of any conditions or obligations thereunder. Additionally, Piper Sandler assumed that all the necessary regulatory approvals and consents required for the merger will be obtained in a manner that will not adversely affect Syros, Tyme or the contemplated benefits of the merger.

In arriving at its opinion, Piper Sandler did not perform any appraisals or valuations of any specific assets or liabilities (fixed, contingent or other) of Syros or Tyme, and was not furnished or provided with any such appraisals or valuations, nor did Piper Sandler evaluate the solvency of Syros or Tyme under any state or federal law relating to bankruptcy, insolvency or similar matters. The analyses performed by Piper Sandler in connection with its opinion were going concern analyses, subject to the assumption to which Syros' board of directors consented that Tyme's assets are substantially cash deposits. Piper Sandler expressed no opinion regarding the liquidation value of Syros, Tyme or any other entity. Without limiting the generality of the foregoing, Piper Sandler undertook no independent analysis of any pending or threatened litigation, regulatory action, possible unasserted claims or other contingent liabilities, to which Syros or Tyme or any of their affiliates is a party or may be subject, and at the direction of Syros and with its consent, Piper Sandler's opinion made no assumption concerning, and therefore did not consider, the possible assertion of claims, outcomes or damages arising out of any such matters. Piper Sandler also assumed that neither Syros nor Tyme was party to any material pending transaction, including without limitation any financing (other than the private placement of Syros common stock expected to occur concurrently with the merger), recapitalization, acquisition or merger, divestiture or spin-off, other than the merger.

Piper Sandler's opinion was necessarily based upon the information available to it and facts and circumstances as they existed and were subject to evaluation on the date of its opinion. Events occurring after the date of Piper Sandler's opinion could materially affect the assumptions used in preparing its opinion. Piper Sandler expressed no opinion as to the price at which shares of Syros common stock or Tyme common stock may trade following announcement of the merger or at any future time. Piper Sandler did not undertake to reaffirm or revise its opinion or otherwise comment upon any events occurring after the date of its opinion and does not have any obligation to update, revise or reaffirm its opinion.

Piper Sandler's opinion addressed solely the fairness, from a financial point of view, to Syros of the proposed Exchange Ratio set forth in the Merger Agreement and did not address any other terms or agreement relating to the merger or any other terms of the Merger Agreement. Piper Sandler was not requested to opine as to, and its opinion did not address: (i) the basic business decision to proceed with or effect the merger; (ii) the merits of the merger relative to any alternative transaction or business strategy that may be available to Syros; (iii) any other terms contemplated by the Merger Agreement or the fairness of the merger to, or any consideration received in connection therewith by, any creditor or other constituency of Syros: or (iv) the solvency or financial viability of Syros or Tyme at the date of its opinion, upon consummation of the merger, or at any future time. Furthermore, Piper Sandler expressed no opinion with respect to the amount or nature of compensation to any officer, director or employee of any party to the merger, or any class of such persons, to be paid by Syros in the merger or with respect to the fairness of any such compensation.

Information about Piper Sandler

As a part of its investment banking business, Piper Sandler is regularly engaged in the valuation of businesses in the biopharmaceutical, biotechnology and other industries and their securities in connection with mergers and acquisitions, underwritings, secondary distributions of listed and unlisted securities, private placements, and valuations for corporate and other purposes. Syros' board of directors selected Piper Sandler to be its financial advisor and render its fairness opinion in connection with the merger on the basis of such experience and its familiarity with Syros.

Piper Sandler acted as exclusive financial advisor to Syros in connection with the merger and will receive a fee from Syros for providing its services, contingent upon the consummation of a merger, of $2,250,000. Piper Sandler also received a fee of $750,000 for rendering its opinion, which is creditable against Piper Sandler's fee due at the consummation of the merger. Piper Sandler's opinion fee is not contingent upon the consummation of the merger or the conclusions reached in its opinion. In addition, Piper Sandler acted as co-agent to Syros in connection with the private placement of Syros common stock that is expected to occur concurrently with the merger, for which Piper Sandler will receive a fee. In connection with Piper Sandler's roles as financial advisor and co-agent, Syros has agreed to indemnify Piper Sandler against certain liabilities and reimburse Piper Sandler for certain expenses in connection with its services. Piper Sandler has, in the past, provided financing services to Syros; more specifically, Piper Sandler acted as an underwriter on Syros' (i) June 2016 initial public offering, (ii) January 2018 follow-on offering, (iii) March 2019 follow-on offering, and (iv) January 2021 follow-on offering. Moreover, Piper Sandler may continue to provide investment banking or brokerage services to Syros and its affiliates, for which Piper Sandler would expect to receive fees. In the ordinary course of its business, Piper Sandler and its affiliates may actively trade securities of Syros and Tyme for their own account or the account of their customers and, accordingly, may at any time hold a long or short position in such securities. Piper Sandler may also, in the future, provide investment banking and financial advisory services to Syros, Tyme or entities that are affiliated with Syros or Tyme, for which Piper Sandler would expect to receive compensation.

Summary of Certain Syros Unaudited Prospective Financial Information

Syros does not as a matter of course make public long-term forecasts or internal projections as to future performance, revenues, production, earnings, or other results due to, among other reasons, the uncertainty of the underlying assumptions and estimates. As a result, Syros does not endorse the unaudited prospective financial information as a reliable indication of future results. Please see the risk factor "*The financial analyses, estimates and forecasts presented herein and considered by Syros and Tyme in connection with the merger may not be realized*." in the section entitled "*Risk Factors*" beginning on page 31 of this joint proxy statement/prospectus. Syros has prepared this unaudited prospective financial information on a different basis than the selected unaudited pro forma condensed combined financial information included in this joint proxy statement/prospectus and is including certain unaudited prospective financial information in this joint proxy statement/prospectus because they were among the financial information made available to the Syros board of directors and Syros' financial advisor, and without probability adjustments to Tyme and Tyme's financial advisor, in connection with their respective evaluations of the merger. The unaudited prospective financial information is not being included in this joint proxy statement/prospectus to influence any Syros or Tyme stockholder to make an investment decision with respect to the merger or to influence any Syros or Tyme stockholder as to whether or how such stockholder should vote with respect to the Syros proposals, the Tyme proposals, the merger or the other transactions contemplated by the Merger Agreement or any other matter. The unaudited prospective financial information presented below was prepared by Syros' management for internal planning purposes prior to and during April, May, and June 2022, was modeled as of June 8, 2022, and is the responsibility of Syros management. The unaudited prospective financial information was based solely upon information available to Syros' management at the time of its preparation. The unaudited prospective financial information was based on estimates and assumptions made by Syros' management prior to and during April/May/June 2022 and spoke only as of June 8, 2022.

The unaudited prospective financial information included in this document has been prepared by, and is the responsibility of, Syros' management. Ernst & Young LLP, has not audited, reviewed, examined, compiled nor applied agreed-upon procedures with respect to the accompanying unaudited prospective financial information and, accordingly, Ernst & Young LLP does not express an opinion or any other form of assurance with respect thereto. The Ernst & Young LLP report contained in Syros' Annual Report on Form 10-K for the year ended December 31, 2021, which is included elsewhere in this joint proxy statement/prospectus, relates to Syros' previously issued financial statements. It does not extend to the unaudited prospective financial information and should not be read to do so.

The inclusion of the unaudited prospective financial information in this joint proxy statement/prospectus should not be regarded as an indication that any of Syros, Tyme, any of their respective affiliates, any of their respective

financial advisors or any other person considered, or now considers, this information (including any probability adjustments) to be necessarily predictive of actual future results or events, and it should not be relied upon as such. There can be no assurance that the prospective results will be realized or that actual results will not be significantly higher or lower than estimated.

Because the unaudited prospective financial information covers multiple years, such information by its nature becomes less predictive with each successive year. Syros and Tyme stockholders are urged to review the description of risk factors with respect to the business of Syros contained elsewhere in this joint proxy statement/prospectus and in the SEC filings of Syros incorporated by reference into this joint proxy statement/prospectus. See "*Risk Factors*", "*Cautionary Statement Concerning Forward-Looking Statements*" and "*References to Additional Information*". The unaudited prospective financial information of Syros was not prepared with a view toward public disclosure, and the unaudited prospective financial information was not prepared with a view toward compliance with published guidelines of the SEC or the guidelines established by the American Institute of Certified Public Accountants for preparation and presentation of prospective financial information. Furthermore, the unaudited prospective financial information does not necessarily reflect Syros' current estimates and does not take into account any circumstances or events occurring after the date it was prepared, and some or all of the assumptions that have been made regarding, among other things, the timing of certain occurrences or impacts, may have changed since such date. In particular, the unaudited prospective financial information set forth below assumes the completion of the merger and the PIPE Financing, but it does not take into account the effect of any failure of the merger or the PIPE Financing to occur, and so it should not be viewed as accurate in that context.

The inclusion of the unaudited prospective financial information herein should not be deemed an admission or representation by Syros, Tyme or any of their respective affiliates that it is or they view it as material information of Syros, and in fact, none of the foregoing view the unaudited prospective financial information as material because of the inherent risks and uncertainties associated with such long-term projections. The unaudited prospective financial information should be evaluated in conjunction with the historical financial statements and other information regarding Syros contained in this joint proxy statement/prospectus and Syros' public filings with the SEC.

Financial measures included in forecasts provided to a financial advisor and a board of directors in connection with a business combination transaction, such as the forecasts provided by Syros, are excluded from the definition of "non-GAAP financial measures" under the rules of the SEC, and therefore such forecasts are not subject to SEC rules regarding disclosures of non-GAAP financial measures, which would otherwise require a reconciliation of a non-GAAP financial measure to a GAAP financial measure. Reconciliations of non-GAAP financial measures were not provided to or relied upon by the Tyme board of directors or the Syros board of directors or their respective financial advisors in connection with the merger. Accordingly, no reconciliation of the financial measures included in the forecasts is provided in this joint proxy statement/prospectus.

Certain Projections of Syros

On an ongoing basis, in the normal course of business planning, Syros' management prepares, for internal use, certain unaudited prospective financial information with respect to Syros' business plans and operating plan for future periods. The preparation of these Syros forecasts is part of the Company's internal financial planning processes and is discussed with and reviewed by the Syros board of directors from time to time.

In April 2022, Syros initiated a private placement process with the goal of raising funds to address financing required for development of its lead product candidate, tamibarotene, as well as its development of a pipeline of additional oncology programs. Also in April 2022, Syros realigned its product development priorities in order to reduce cash burn and considered an acquisition of Tyme concurrent with a private placement. In connection with these activities, Syros management updated its internal forecasts and prepared a forecast, the Initial Syros Management Forecast, which included the Company's anticipated U.S. revenue forecasts for sales of

tamibarotene in MDS and anticipated operating expenses related to the product candidate and certain of its other pipeline projects. The Initial Syros Management Forecast, concerning Syros on a standalone basis, was discussed with and reviewed by the Syros board of directors in April 2022, and then, after subsequent input from management and members of the Syros board of directors, was shared in May 2022 with Tyme and Moelis & Company, Tyme's financial advisor.

Following further negotiations related to the merger and the PIPE Financing, Syros management prepared an updated forecast, the Syros Management Forecast, which was derived from the Initial Syros Management Forecast and incorporated certain adjustments to estimated revenues and costs in future years for tamibarotene in MDS. Revenue estimates for tamibarotene in MDS were increased after further refinement of Gross to Net assumptions. Operational costs associated with developing and commercializing tamibarotene in MDS were also adjusted upon further assessment. Finally, revenue projections for SY-2101 in APL were added to the total revenue projection, as well as operating expenses related to the program. The Syros Management Forecast was shared by Syros management with Piper Sandler & Co., or Piper Sandler, for use in connection with its financial analyses. The Syros Management Forecast, concerning Syros on a standalone basis, was presented to the Syros board of directors for purposes of its consideration and evaluation of the merger and reviewed, together with the Syros Probability-Adjusted Forecast (as described below), in a meeting on June 30, 2022. The Syros Management Forecast was also subsequently shared by Syros with Tyme and Moelis.

Syros management directed Piper Sandler to use the Syros Probability-Adjusted Forecast, solely for purposes of a discounted cash flow analysis presented at the meeting of the Syros board of directors on June 30, 2022, as described in the section of this proxy statement entitled "*The Merger—Opinion of Piper Sandler & Co.*" Piper Sandler performed a discounted cash flow analysis of Syros by calculating an estimated present value of the standalone unlevered, after-tax free cash flows that Syros was forecasted to generate during the fiscal years ending December 31, 2022 through December 31, 2037 based on probability-weighted and tax-affected forecasts (inclusive of Syros' net operating loss carryforwards). The after-tax free cash flows for each year were calculated based on the Syros Management Forecast to which Piper Sandler, at the direction of Syros management, applied probability-of-success factors per the "Clinical Development Success Rates and Contributing Factors 2011-2020 Handbook" published by BIO, PharmaIntelligence, Quantitative Life Sciences, or the "CDSR Handbook," as is customary with drugs in development. Per the CDSR Handbook, probabilities of success of 4.6%, 15.0% and 54.0% were assigned to Syros' Phase 1, Phase 2 and Phase 3 programs, respectively, based on historical data for solid tumor and hematological oncology clinical trials as appropriate at each program's stage of development.

The internally prepared Initial Syros Management Forecast, the Syros Management Forecast and the Syros Probability-Adjusted Forecast summarized below were based on information available to Syros management and estimates, assumptions and judgments made by Syros management at the time of their preparation and spoke only as of such time.

The Initial Syros Management Forecast is summarized below:

Fiscal year ended December 31 $ in millions	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E	2032E	2033E	2034E	2035E	2036E	2037E
Revenue(1)	$ 14.4	$ 3.2	$ 0.0	$ 15.0	$118.0	$286.0	$396.0	$419.0	$405.0	$394.0	$401.0	$419.0	$438.0	$458.0	$479.0	$499.0
EBIT(2)(4)	($107.0)	($85.0)	($79.7)	($51.8)	$ 47.5	$206.2	$310.2	$331.5	$317.7	$306.8	$312.9	$329.5	$347.0	$365.4	$384.8	$403.2
Unlevered Free Cash Flow(3)(4)	($112.1)	($87.9)	($92.7)	($73.2)	$ 45.0	$206.2	$248.2	$265.2	$254.2	$245.4	$250.3	$263.6	$277.6	$292.3	$307.8	$322.6

(1) Reflects US-only tamibarotene in MDS revenue
(2) Earnings before interest and taxes.
(3) Unlevered Free Cash Flow is defined as EBIT less income tax expenses, plus depreciation and amortization, less changes in net working capital, less capital expenditures.
(4) EBIT and Unlevered Free Cash Flow are non-GAAP measures and should not be considered as an alternative to operating income or net income as a measure of operating performance or cash flow or as a measure of liquidity.

The Syros Management Forecast is summarized below:

Fiscal year ended December 31 $ in millions

	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E	2032E	2033E	2034E	2035E	2036E	2037E
Revenue(1)	$ 14.4	$ 3.2	$ 0.0	$ 16.0	$124.0	$337.0	$490.0	$530.0	$521.0	$514.0	$525.0	$549.0	$515.0	$495.0	$516.0	$539.0
EBIT(2)(4)	($105.8)	($78.2)	($88.1)	($88.5)	$ 25.3	$242.1	$393.6	$431.0	$421.9	$414.6	$424.4	$446.6	$413.6	$394.0	$413.2	$434.4
Unlevered Free Cash Flow(3)(4)	($ 96.1)	($83.3)	($86.4)	($90.2)	$ 26.1	$242.1	$314.9	$344.8	$337.5	$331.7	$339.5	$357.3	$330.9	$315.2	$330.6	$347.5

(1) Reflects US-only revenue for tamibarotene in MDS and SY-2101 in APL
(2) Earnings before interest and taxes.
(3) Unlevered Free Cash Flow is defined as EBIT less income tax expenses, plus depreciation and amortization, less changes in net working capital, less capital expenditures.
(4) EBIT and Unlevered Free Cash Flow are non-GAAP measures and should not be considered as an alternative to operating income or net income as a measure of operating performance or cash flow or as a measure of liquidity.

The Syros Probability-Adjusted Forecast is summarized below:

Fiscal year ended December 31 $ in millions

	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E	2032E	2033E	2034E	2035E	2036E	2037E
Revenue(1)	$ 14.4	$ 3.2	$ 0.0	$ 8.6	$ 67.0	$167.9	$235.7	$251.5	$244.3	$239.0	$243.3	$254.3	$257.0	$262.6	$274.0	$286.0
EBIT(2)(4)	($ 72.4)	($ 55.5)	($ 58.7)	($ 62.1)	($ 4.2)	$ 90.0	$150.7	$163.9	$156.7	$151.2	$154.5	$163.8	$167.6	$173.7	$183.4	$193.7
Unlevered Free Cash Flow(3)(4)	$ (71.7)	$ (60.6)	$ (57.0)	$ (63.8)	$ (3.4)	$ 90.0	$ 72.0	$ 77.7	$ 72.3	$ 68.3	$ 69.6	$ 74.5	$ 84.9	$ 94.9	$100.8	$106.8

(1) Reflects US-only revenue for tamibarotene in MDS and SY-2101 in APL
(2) Earnings before interest and taxes.
(3) Unlevered Free Cash Flow is defined as EBIT less income tax expenses, plus depreciation and amortization, less changes in net working capital, less capital expenditures.
(4) EBIT and Unlevered Free Cash Flow are non-GAAP measures and should not be considered as an alternative to operating income or net income as a measure of operating performance or cash flow or as a measure of liquidity.

Though presented with numerical specificity, the unaudited prospective financial information described reflect numerous assumptions and estimates as to future events made by the management of Syros. In preparing the unaudited prospective financial information, Syros made certain assumptions and estimates regarding, among other things, as applicable, the commercial launch of Syros future product candidates, third-party payor reimbursement for Syros product candidates, the completion of and favorable outcomes of clinical trials, the potential market size of treatments for any diseases, interest rates, corporate financing activities, including the amount and timing of the issuance of debt, the timing and amount of equity issuances or repurchases, the effective tax rate, the regulatory and legal environment in which Syros operates and the amount of general and administrative costs. At the time such unaudited prospective financial information was prepared, Syros' management believed such assumptions and estimates were reasonable.

The unaudited prospective financial information constitutes forward-looking statements and no assurances can be given that the assumptions made in preparing the unaudited prospective financial information will accurately reflect future conditions. The estimates and assumptions underlying the unaudited prospective financial information involve judgments with respect to, among other things, future economic, competitive, regulatory and financial market conditions, future tax rates and future business decisions which may not be realized and that are inherently subject to significant business, economic, competitive and regulatory uncertainties and contingencies, including, among others, risks and uncertainties described under "*Risk Factors*" and "*Cautionary Statement Concerning Forward-Looking Statements*", all of which are difficult to predict and many of which are beyond the control of Syros and/or Tyme and will be beyond the control of the combined company. In addition, the unaudited prospective financial information will be affected by Syros' or the combined company's, as applicable, ability to achieve strategic goals, objectives and targets over the applicable periods. As a result, there can be no assurance that the underlying assumptions will prove to be accurate or that the projected results will be realized,

and actual results likely will differ, and may differ materially, from those reflected in the unaudited prospective financial information, whether or not the merger is completed.

Syros and Tyme stockholders are urged to review Syros' most recent SEC filings for a description of Syros' results of operations and financial condition and capital resources during 2019, 2020 and 2021, including *"Management's Discussion and Analysis of Financial Condition and Results of Operations"* in Syros' Annual Report on Form 10-K for the year ended December 31, 2021, along with the unaudited condensed consolidated financial statements of Syros contained in Syros' Quarterly Report on Form 10-Q for the three month period ended March 31, 2022, which are incorporated by reference into this joint proxy statement/prospectus.

In light of, among other matters, the foregoing factors and the uncertainties inherent in the unaudited prospective financial information, readers of this joint proxy statement/prospectus are cautioned not to place undue, if any, reliance on the unaudited prospective financial information included in this joint proxy statement/prospectus. No representation is made by Syros, Tyme, any of their respective affiliates, any of their respective financial advisors or any other person to any Syros or Tyme stockholder regarding the ultimate performance of Syros or the combined company compared to the information included in the unaudited prospective financial information. In particular, Syros has made no representation to Tyme or any other party to the Merger Agreement concerning the unaudited prospective financial information. None of Syros, Tyme, any of their respective affiliates or any of their respective financial advisors can provide assurance of the validity, reasonableness, accuracy, or completeness of the unaudited prospective financial information included in this joint proxy statement/prospectus. The inclusion of unaudited prospective financial information in this joint proxy statement/prospectus should not be regarded as an indication that such unaudited prospective financial information will be an accurate prediction of future events, and such information should not be relied on as such.

SYROS DOES NOT INTEND TO, AND DISCLAIMS ANY OBLIGATION TO, UPDATE, CORRECT OR OTHERWISE REVISE THE UNAUDITED PROSPECTIVE FINANCIAL INFORMATION TO REFLECT CIRCUMSTANCES EXISTING AFTER THE DATE WHEN MADE OR TO REFLECT THE OCCURRENCE OF FUTURE EVENTS, EVEN IN THE EVENT THAT ANY OR ALL OF THE ASSUMPTIONS UNDERLYING SUCH UNAUDITED PROSPECTIVE FINANCIAL INFORMATION ARE NO LONGER APPROPRIATE (EVEN IN THE SHORT TERM).

Opinion of Moelis & Company LLC

At the meeting of Tyme's board of directors on July 2, 2022 to evaluate and approve the merger, Moelis delivered an oral opinion, which was confirmed by delivery of a written opinion, dated July 2, 2022, addressed to Tyme's board of directors to the effect that, as of the date of the opinion and based upon and subject to the assumptions made, procedures followed, matters considered and limitations on the review undertaken in connection with the opinion, the Exchange Ratio provided in the merger pursuant to the Merger Agreement was fair, from a financial point of view, to the holders of Tyme common stock.

The full text of Moelis' written opinion dated July 2, 2022, which sets forth the assumptions made, procedures followed, matters considered and limitations on the review undertaken in connection with the opinion, is attached as *Annex C* to this joint proxy statement/prospectus and is incorporated herein by reference. Moelis' opinion was provided for the use and benefit of Tyme's board of directors (solely in its capacity as such) in its evaluation of the merger. Moelis' opinion is limited solely to the fairness, from a financial point of view, to the holders of Tyme common stock of the Exchange Ratio provided in the merger pursuant to the Merger Agreement, and does not address Tyme's underlying business decision to effect the merger or the relative merits of the merger as compared to any alternative business strategies or transactions that might be available with respect to Tyme. Moelis' opinion does not constitute a recommendation to any stockholder of Tyme as to how such stockholder should vote or act with respect to the merger or any other matter. Moelis' opinion was approved by a Moelis fairness opinion committee.

In arriving at its opinion, Moelis, among other things:

- reviewed certain publicly available business and financial information relating to Tyme and Syros;
- reviewed certain internal information relating to the business, earnings, cash flow, assets (including estimates of Tyme Net Cash), liabilities and prospects of Tyme furnished to Moelis by Tyme, including financial forecasts and estimates provided to or discussed with Moelis by the management of Tyme under the Tyme Dissolution Case (a dissolution scenario) and the SM-88 Development Case (an alternative operating plan scenario), both of which are further described under "*Certain Prospective Financial Information Considered by Tyme's Board of Directors*");
- reviewed certain internal information relating to the business, earnings, cash flow, assets, liabilities and prospects of Syros furnished to Moelis by Syros and Tyme, including financial forecasts and estimates provided to or discussed with Moelis by Syros, as adjusted by the management of Tyme, which is referred to as Tyme's Adjusted Syros Forecast and is further described under "*Certain Prospective Financial Information Considered by Tyme's Board of Directors*";
- reviewed certain information relating to the capitalization of Tyme and Syros furnished to Moelis by Tyme and Syros;
- reviewed estimates prepared and provided to Moelis by the management of Tyme as to (1) Tyme's projected utilization on a standalone basis of net operating losses to achieve future tax savings and (2) Syros's projected utilization on a standalone basis of net operating losses to achieve future tax savings;
- considered certain potential pro forma impacts of the merger on the combined company resulting from the merger, including estimates prepared and provided to Moelis by the management of Tyme as to the combined company's projected utilization of net operating losses to achieve future tax savings (referred to in this section as the "Combined Company NOL Utilization Estimates");
- conducted discussions with members of senior management and representatives of Tyme and Syros concerning the publicly available and internal information described in the foregoing, as well as the business and prospects of Tyme and Syros, generally;
- reviewed publicly available financial and stock market data of certain other companies in lines of business that Moelis deemed relevant;
- considered the results of efforts by or on behalf of Tyme, including by Moelis at Tyme's direction, to solicit indications of interest from third parties with respect to a possible acquisition of all or a portion of Tyme;
- reviewed an execution version of the Merger Agreement made available to Moelis on July 2, 2022;
- participated in certain discussions and negotiations among representatives of Tyme and Syros and their respective advisors; and
- conducted such other financial studies and analyses and took into account such other information as Moelis deemed appropriate.

In connection with its review, Moelis with the consent of Tyme's board of directors relied on the information supplied to, discussed with or reviewed by Moelis for purposes of this opinion being complete and accurate in all material respects. Moelis did not assume any responsibility for independent verification of, and Moelis did not independently verify, any of such information. With the consent of Tyme's board of directors, Moelis relied upon, without independent verification, the assessment of Tyme and its legal, tax, regulatory and accounting advisors with respect to legal, tax, regulatory and accounting matters. In light of Tyme's management's views regarding the achievability of, and financing needed to successfully pursue, the SM-88 Development Case, Tyme's board of directors directed Moelis to use and rely on the Tyme Dissolution Case for purposes of its analyses and opinion. With respect to the Tyme Dissolution Case and Tyme's Adjusted Syros Forecast, Moelis

assumed, at the direction of Tyme's board of directors, that they had been reasonably prepared on a basis reflecting the best currently available estimates and judgments of the management of Tyme as to the future performance of Tyme and Syros, respectively. With respect to the Combined Company NOL Utilization Estimates referred to above, Moelis assumed, at the direction of Tyme's board of directors, that they had been reasonably prepared on a basis reflecting the best currently available estimates and judgments of the management of Tyme as to the matters covered thereby. At the direction of Tyme's board of directors, Moelis assumed that Tyme Dissolution Case, Tyme's Adjusted Syros Forecast and the Combined Company NOL Utilization Estimates were a reasonable basis upon which to evaluate Tyme, Syros and the merger and at the direction of Tyme's board of directors Moelis relied upon these financial forecasts for purposes of its analyses and opinion. Moelis expressed no views as to the reasonableness of any such financial forecasts or other information or the assumptions on which they were based. Moelis also relied, without independent verification, upon the assessment of the management of Tyme as to (i) the validity and marketability of, and risks associated with, the existing and future technology and products of Tyme and Syros and (ii) the probabilities of success used to develop financial forecasts attributable to existing and future technology and products of Tyme and Syros. In addition, with the consent of Tyme's board of directors, Moelis did not make any independent evaluation or appraisal of any of the assets or liabilities (contingent, derivative, off-balance-sheet, or otherwise) of Tyme or Syros, nor was Moelis furnished with any such evaluation or appraisal. With the consent of Tyme's board of directors, Moelis assumed that any adjustment made to the Exchange Ratio pursuant to the Merger Agreement or otherwise would not be material to its analyses or opinion.

Moelis' opinion did not address Tyme's underlying business decision to effect the merger or the relative merits of the merger as compared to any alternative business strategies or transactions that might be available to Tyme and does not address any legal, regulatory, tax or accounting matters (including any tax implications to Tyme's stockholders). At the direction of Tyme's board of directors, Moelis had not been asked to, nor did it, offer any opinion as to any terms of the Merger Agreement or any aspect or implication of the merger or the PIPE Financing (but Moelis' analyses of the Exchange Ratio reflected consummation of the PIPE Financing), except for the fairness of the Exchange Ratio from a financial point of view to the holders of Tyme common stock. Moelis' opinion did not address any aspect or implication of any voting agreement previously entered into, or any voting, support or lock-up agreement entered into or to be entered into in connection with the merger, by any holder of Tyme Common Stock. Moelis did not express any opinion as to fair value or the solvency of Tyme or Syros following the closing of the merger or at any time. Moelis noted its understanding that the Merger Agreement permits Tyme, with the consent of Syros and subject to the terms thereof, to sell, assign, license or otherwise dispose of some or all of its non-cash assets prior to or concurrent with the closing of the merger, with the proceeds of any such disposition to be distributed to holders of Tyme Common Stock or included in the calculation of Tyme Net Cash. Moelis expressed no views as to the fairness or value of any such disposition or any such proceeds. Moelis did not express any opinion as to what the value of shares of Syros common stock actually would be when issued in the merger or the prices at which shares of Tyme common stock or Syros common stock may trade at any time. Moelis assumed that the shares of Syros common stock to be issued in the merger would be approved for trading on The Nasdaq Stock Market. In rendering its opinion, Moelis assumed, with the consent of Tyme's board of directors, that the final executed form of the Merger Agreement would not differ in any material respect from the version that Moelis had reviewed, that the merger and the PIPE Financing would each be consummated in accordance with its respective terms without any waiver or modification that could be material to its analysis, and that the parties to the Merger Agreement would comply with all the material terms of the Merger Agreement. Moelis assumed, with the consent of Tyme's board of directors, that all governmental, regulatory or other consents or approvals necessary for the completion of the merger would be obtained, except to the extent that could not be material to Moelis' analysis.

Moelis' opinion was necessarily based on economic, monetary, market and other conditions as in effect on, and the information made available to Moelis as of, the date of the opinion and Moelis assumed no responsibility to update its opinion for developments occurring or coming to its attention after the date thereof. Moelis evaluated the Exchange Ratio by comparing the range of values indicated by its discounted cash flow analysis for a share of Syros common stock (after giving effect to (x) the consummation of the merger and the PIPE Financing and

(y) the Exchange Ratio) to the range of values indicated by its discounted cash flow analysis for a share of Tyme common stock on a standalone basis using the Tyme Dissolution Case.

In addition, Moelis did not express any opinion as to the fairness of the amount or nature of any compensation to be received by any officers, directors or employees of any parties to the merger, or any class of such persons, relative to the Exchange Ratio or otherwise. Moelis' opinion did not address the fairness of the merger or any aspect or implication thereof to, or any other consideration of or relating to, the holders of any class of securities, creditors or other constituencies of Tyme, other than the fairness of the Exchange Ratio provided in the merger pursuant to the Merger Agreement from a financial point of view to the holders of Tyme common stock. Except as described in this summary, Tyme and Tyme's board of directors imposed no limitations on Moelis with respect to the investigations made or procedures followed by Moelis in rendering its opinion.

The following is a summary of the material financial analyses presented by Moelis to Tyme's board of directors at its meeting held on July 2, 2022 in connection with its opinion.

Financial Analyses

As noted above, Moelis evaluated the Exchange Ratio by comparing the range of values indicated by its discounted cash flow analysis for a share of Syros common stock (after giving effect to (x) the consummation of the merger and the PIPE Financing and (y) the Exchange Ratio) to the range of values indicated by its discounted cash flow analysis for a share of Tyme common stock on a standalone basis using the Tyme Dissolution Case.

Discounted Cash Flow Analysis—Tyme

Moelis performed a discounted cash flow, or DCF, analysis of Tyme based on the Tyme Dissolution Case provided by Tyme's management to calculate the present value of the estimated cash returned to Tyme's stockholders if Tyme were to liquidate in lieu of consummating a merger. In performing this analysis, Moelis calculated the sum of the undiscounted initial distribution projected by Tyme to be made on September 30, 2022 and a discounted final distribution projected by Tyme to be made on September 30, 2024. To calculate the estimated present value of that final projected distribution as of September 30, 2022, Moelis utilized a range of discount rates of 2.84% to 9.06% (reflecting a risk-free rate, based on yields as of July 1, 2022 of two-year treasury notes, on the low end, and the sum of that risk-free rate plus an equity market risk premium, on the high end). This analysis indicated an implied per share value range for Tyme common stock of $0.28 to $0.29. At Tyme's request, Moelis also calculated a DCF range assuming Tyme were able (x) to achieve incremental value, prior to the date of the final distribution, attributable to a future disposition of its existing non-cash assets of an illustrative $5 million and (y) to require a lower level of costs attributable to the dissolution of Tyme by $1.1 million (the scenarios in clauses (x) and (y), collectively, the "Dissolution Enhancements"), and such analysis yielded a range of $0.31 to $0.32.

Discounted Cash Flow Analysis—Pro Forma Combined Company

Moelis performed a DCF analysis of Syros, after giving effect to (x) the consummation of the merger and the PIPE Financing and (y) the Exchange Ratio, to derive an estimated range of potential per share value holders of Tyme common stock are entitled to receive in the merger. In its DCF analysis, Moelis used discount rates, based on an estimated range of weighted average cost of capital, ranging from 13.75% to 17.75% and perpetuity growth rates, based on guidance from Tyme's management, ranging from negative 70% to negative 30%. Based on Tyme's Adjusted Syros Forecast and the Combined Company NOL Utilization Estimates, Moelis derived an implied present value range for the common stock of Syros (after giving effect to certain limitations, as a result of the merger, on the combined company's ability to utilize Syros's and Tyme's net operating losses), as of September 30, 2022, of $90 million to $198 million. Moelis then added to this range Tyme's estimate of Tyme Net Cash as of September 30, 2022, and the gross proceeds expected to be received in the PIPE Financing and deducted Tyme's estimate of transaction expenses in order to derive an implied present value range for the pro

forma combined company. After application of the Exchange Ratio, this analysis indicated an implied per share value range of Syros common stock to be received per share of Tyme common stock of $0.42 to $0.54, as compared to closing stock price for Tyme common stock on July 1, 2022 of $0.27 per share and the implied per share value ranges for Tyme common stock derived from the standalone DCF analysis for Tyme described above of $0.28 to $0.29 (or $0.31 to $0.32 in the event Tyme were able realize the Dissolution Enhancements).

Other Information

Moelis also noted for Tyme's board of directors certain additional factors that were not considered part of Moelis' financial analysis with respect to its opinion but were referenced for informational purposes only, including, among other things:

- a DCF analysis of Tyme, based on the SM-88 Development Case using the same discount rate range and perpetuity growth rate range used in the DCF of the pro forma combined company described above, indicated a per share value range for Tyme common stock of $0.10 to $0.16;
- a DCF analysis of Syros, based on Tyme's Adjusted Syros Forecast, using the same discount rate range and perpetuity growth rate range used in the DCF of the pro forma combined company described above, indicated an implied aggregate present value range for the common stock of Syros, on a standalone basis, as of September 30, 2022, of $105 million to $217 million;
- the historical closing trading prices for Tyme common stock during the period from January 26, 2022 (the date of Tyme's announcement of discontinuation of SM-88 in a metastatic pancreatic cancer trial) through July 1, 2022, which reflected low and high closing stock prices during such period of approximately $0.23 per share and $0.37 per share, respectively;
- the historical closing trading prices for Tyme common stock during the52-week period ending July 1, 2022, which reflected low and high closing stock prices during such period of approximately $0.23 per share and $1.38 per share, respectively;
- the aggregate equity values for Syros implied by the historical closing trading prices for Syros common stock during the period from January 26, 2022 through July 1, 2022, which reflected low and high equity values for Syros during such period of approximately $48 million and $132 million, respectively;
- the aggregate equity values for Syros implied by the historical closing trading prices for Syros common stock during the52-week period ending July 1, 2022, which reflected low and high equity values for Syros during such period of approximately $45 million and $390 million, respectively;
- the six publicly traded companies that Moelis included for informational purposes only traded, as of July 1, 2022 and based on Wall Street research analyst estimates of future financial performance, with implied total enterprise value to 2027E revenue multiples ranging from 0.9x to 2.0x (with mean and median multiples of 1.4x and 1.4x, respectively); and
- one-year forward stock price targets for Syros common stock in selected recently published, publicly available Wall Street research analysts' reports, which indicated low and high stock price targets of $9.00 per share and $23.00 per share, respectively.

Miscellaneous

This summary of the analyses is not a complete description of Moelis' opinion or the analyses underlying, and factors considered in connection with, Moelis' opinion. The preparation of a fairness opinion is a complex analytical process and is not necessarily susceptible to partial analysis or summary description. Selecting portions of the analyses or summary set forth above, without considering the analyses as a whole, could create an incomplete view of the processes underlying Moelis' opinion. In arriving at its fairness determination, Moelis considered the results of all of its analyses and did not attribute any particular weight to any factor or analysis.

Rather, Moelis made its fairness determination on the basis of its experience and professional judgment after considering the results of all of its analyses.

No other company used in the analyses described above is identical to Tyme or Syros. In addition, such analyses do not purport to be appraisals, nor do they necessarily reflect the prices at which businesses or securities actually may be sold. Analyses based upon forecasts of future results are not necessarily indicative of actual future results, which may be significantly more or less favorable than suggested by such analyses. Because the analyses described above are inherently subject to uncertainty, being based upon numerous factors or events beyond the control of the parties or their respective advisors, neither Tyme nor Moelis or any other person assumes responsibility if future results are materially different from those forecasts.

The Exchange Ratio was determined through arms' length negotiations between Tyme and Syros and was approved by Tyme's board of directors. Moelis did not recommend any specific consideration to Tyme or Tyme's board of directors, or that any specific amount or type of consideration constituted the only appropriate consideration for the merger.

Moelis acted as financial advisor to Tyme in connection with the merger and will receive for its services a fee, contingent upon the closing of a merger, of up to $2,000,000. Tyme also paid Moelis an initial retainer fee of $125,000 upon execution of the engagement letter with Moelis, and Moelis also became entitled to an opinion fee of $1,250,000 in connection with the preparation of its opinion, regardless of the conclusion reached therein, which retainer fee and opinion fee, to the extent paid, are creditable against the Moelis' fee due at closing of the merger. In addition, Tyme has agreed to indemnify Moelis for certain liabilities, including liabilities under the federal securities laws, arising out of its engagement.

Moelis' affiliates, employees, officers and partners may at any time own securities (long or short) of Tyme and Syros. In the future, Moelis may provide investment banking and other services to Tyme and Syros and may receive compensation for such services.

Tyme's board of directors selected Moelis as its financial advisor in connection with the merger because Moelis had substantial experience in similar transactions. Moelis is regularly engaged in the valuation of businesses and their securities in connection with mergers and acquisitions, strategic transactions, corporate restructurings, and valuations for corporate and other purposes.

Certain Prospective Financial Information Considered by Tyme's Board of Directors

Tyme does not, as a matter of course, regularly develop or publicly disclose long-term projections of its clinical, commercial or financial results due to, among other reasons, the uncertainty of the underlying assumptions and estimates. However, in connection with its evaluation of the transaction, Tyme's board of directors considered:

- certain non-public unaudited projections relating to Tyme, prepared by Tyme management reflecting a potential plan to develop and commercialize a certain SM-88 candidate, and adjusted for its estimates of probabilities of success, or theSM-88 Development Case;
- certain non-public unaudited projections prepared by Tyme management of distributions that would be made to Tyme stockholders reflecting a potential suspension of Tyme's operations and dissolution of the corporation, or the Tyme Dissolution Case; and
- certain non-public unaudited projections relating to Syros, provided by Syros' management and adjusted by Tyme's management for among other things its estimates of probabilities of success, orthe Tyme's Adjusted Syros Forecast.

While each of the projections described above, collectively, the Tyme Models, were also provided to Moelis for analysis, Tyme's board of directors determined, in light of the risks and challenges associated with executing on

the plan contemplated by the SM-88 Development Case, to direct Moelis to use and rely specifically on the Tyme Dissolution Case for purposes of its opinion, as more fully described under "*Opinion of Moelis & Company LLC*." None of the Tyme Models were made available to Syros.

As noted above, Tyme's Adjusted Syros Forecasts are based upon forecasts that Syros provided to Tyme, but reflect adjustments by Tyme management. Neither Tyme's Adjusted Syros Forecasts nor any of the adjustments made by Tyme's management were made available to, discussed with or approved by Syros or its representatives. These adjustments resulted in a significant reduction of revenue, gross profit, and earnings before income taxes as compared to the non-risk-adjusted forecast provided by Syros, largely due to the application of an adjustment to take into account probability of success but also due to Tyme management adjusting downward certain of Syros' estimates about peak commercial uptake and launch year pricing.

Certain Limitations on the Tyme Models

The Tyme Models were not prepared with a view to public disclosure, but are included in this proxy statement/prospectus because such information was made available to Tyme's board of directors and Moelis, and used by them in the process leading to the execution of the Merger Agreement. The summary of the Tyme Models is not included in this proxy statement/prospectus in order to induce any Tyme or Syros stockholder to vote in favor of the merger or any other matter, or to influence any person to make any investment decision (with respect to the merger or otherwise). The Tyme Models should be evaluated, if at all, in conjunction with Tyme's and Syros' historical financial statements and other information regarding Tyme and Syros contained in or incorporated by reference into this proxy/prospectus and the following factors.

The Tyme Models were not prepared with a view to compliance with GAAP, the published guidelines of the SEC regarding projections, forward-looking statements or pro forma financial information or the guidelines established by the American Institute of Certified Public Accountants for preparation and presentation of prospective or pro forma financial information.

No independent accounting firm has audited, reviewed, examined, compiled or applied agreed-upon procedures with respect to the Tyme Models and, accordingly, no independent accounting firm expresses an opinion or any other form of assurance with respect thereto. The reports of Tyme's and Syros' auditors included or incorporated by reference in this proxy statement/prospectus relate only to those of Tyme's and Syros' previously issued financial statements specified therein. Those reports do not extend to the Tyme Models and should not be read to do so. The Tyme Models include non-GAAP financial measures, including earnings before income taxes, or EBIT, and unlevered free cash flow. Non-GAAP financial measures should not be considered in isolation from, or as a substitute for, financial information presented in compliance with GAAP, and non-GAAP financial measures as used by Tyme in the Tyme Models may not be comparable to similarly titled amounts used by other companies or in other contexts. These non-GAAP measures are included in this proxy statement/prospectus because such information was made available to Tyme's board of directors and Moelis and used by them in the process leading to the execution of the Merger Agreement, as described elsewhere in this proxy statement/prospectus.

Although a summary of the Tyme Models is presented with numerical specificity, this information is not factual and should not be relied upon as being necessarily predictive of actual future results. This summary is also not a complete statement of the Tyme Models or their underlying assumptions. The Tyme Models are forward-looking statements and based on numerous assumptions and estimates. Many of such assumptions and estimates relate to highly uncertain and unknowable factors and so are, by necessity, highly speculative. The SM-88 Development Case and the Tyme's Adjusted Syros Forecast include extended timelines, which not only increases the uncertainty but also could result in inaccurate or assumptions being compounded and magnified. Important factors that may affect actual results and cause the Tyme Models not to be achieved include any error or inaccuracy of the assumptions and estimates underlying the Tyme Models (including, among others, those

described below under "*—Certain Underlying Assumptions*"), clinical and regulatory developments, general economic conditions, changes in actual or projected cash flows, commercial considerations, competitive pressures, and the other factors, including those described under "*Cautionary Statement Concerning Forward-Looking Statements*" beginning on page 138 of this proxy statement/prospectus. As a result, there can be no assurance that any of the Tyme Models will be realized, and actual results may be materially better or worse than those contained in the Tyme Models. **The inclusion of this information should not be regarded as an indication that Tyme, Moelis, their respective representatives or any other person considered, or now considers, the Tyme Models to be material information of Tyme or Syros or necessarily predictive of actual future results nor should it be construed as financial, clinical, regulatory or other guidance, and it should not be relied upon as such.**

None of the Tyme Models give effect to the Merger or reflect any synergies from the Merger or value that Syros might generate from Tyme assets after the Merger.

The Tyme Models do not take into account any circumstances or events occurring after the date that they were prepared.**Except to the extent required by applicable U.S. federal securities laws, neither Tyme nor Syros intends, and each expressly disclaims any responsibility, to update or otherwise revise the Tyme Models to reflect circumstances existing after the respective dates on which they were prepared or to reflect the occurrence of future events or changes in general economic or industry conditions, even if any of the assumptions underlying the Tyme Models are shown to be in error.** Neither Tyme nor Syros can give any assurance that, had the Tyme Models been prepared either as of the date of the Merger Agreement or as of the date of this proxy statement/prospectus, similar estimates and assumptions would be used.

This summary includes information presented in tabular format, which tables must be read together with the description of the corresponding Tyme Model, its limitations and the key assumptions.

None of Tyme or Syros nor any of their respective affiliates, directors, officers, advisors or other representatives has made or makes any representation to any Tyme stockholder or other person regarding the ultimate performance of Tyme or Syros compared to the information contained in the Tyme Models or that the Tyme Models could or will actually be achieved.

In light of the foregoing factors and the uncertainties inherent in the Tyme Models and considering that the Tyme Special Meeting will be held several months after the Tyme Models were prepared, Tyme stockholders are urge and cautioned not to rely on the Tyme Models included in this proxy statement/prospectus.

Certain Underlying Assumptions

The Tyme Models reflect numerous assumptions and estimates as to future events made using information available at the time.

The SM-88 Development Case reflects the following assumptions, among others:

- SM-88 would prove to be clinically successful and commercially viable for a metastatic breast cancer indication, notwithstanding Tyme's recent clinical setbacks in the development of SM-88 for pancreatic cancer, with market entry in 2030.
- Estimates of cumulative probabilities of success attributable to the commercialization of SM-88 in breast cancer of 5.6%, based on academic literature clinical trial benchmarks.
- Tyme would focus its resources solely on the development of an injectable form of SM-88 and primarily for the breast cancer indication.

- SM-88 would achieve peak market penetration of 20% of the target population of approximately 30,000 patients per year in second or third-line post-CDK4/6 setting. Within this population would see patient compliance of 70% with an estimated treatment duration of 11 months.
- Tyme would retain exclusivity for SM-88 until 2041, at which time estimated revenues would peak.
- Tyme would be able to meet the critical financing needs to support successful development and launch of SM-88.
- Research and development costs and SG&A costs required to reach approval would be $37 million and $36 million, respectively.

The Tyme Dissolution Case reflects the following assumptions, among others:

- Tyme's stockholders would approve a dissolution of Tyme by September 30, 2022 and Tyme would cease operations (other than those in furtherance of the dissolution) on or about such date.
- Tyme would promptly distribute $30 million (representing approximately 60% of the anticipated net cash that would be ultimately available for distribution) on September 30, 2022, but would retain the remainder of its cash until a final distribution projected for September 30, 2024, with the amount and timing of such distributions intended to balance Tyme's desire to promptly return capital against its obligation to ensure adequate resources are retained to satisfy any and all liabilities.
- Tyme would be able to delist from Nasdaq and suspend its public reporting obligations by early 2023, allowing for a significant reduction in expenditures thereafter.
- As the base case, Tyme would not be able to realize material cash value from its non-cash assets. However, Tyme's board of directors also considered an alternative where $5 million in cash could be generated from the liquidation of such non-cash assets.
- As the base case, approximately $1.1 million (representing 5% of the cash anticipated to remain after the initial dividend and satisfaction of known liabilities) would be consumed by unexpected liabilities. However, Tyme's board of directors also considered an alternative where this "buffer" would not be consumed and would be returned to stockholders.

Tyme's Adjusted Syros Forecast reflects the following assumptions, among others:

- Tamilbarotene and SY-2101 would prove to be clinically successful and commercially viable, with market entry in 2025 and 2027, respectively.
- Estimates of probabilities of success attributable to the commercialization of 45% for tamilbarotene and 62% for SY-2102 based on academic literature clinical trial benchmarks.
- Committed costs through year-end 2024, including operating expenses (R&D, SG&A) aligned to product-specific probability of success adjustments to revenue; for unallocated operating expenses and other cash flow items, the probability-adjusted expenses were aligned to the Tamibarotene probability of success adjustment of 45%, which aligns success of the broader company pipeline to success of the lead asset.
- Tamibarotene pricing during its launch year and peak commercial uptake for first-line treatment of MDS would be consistent with Tyme management's estimates.
- Syros would focus its resources solely on the development of tamilbarotene, SY-2101 and SY-5609.
- Syros would be able to meet the critical financing needs to support successful development and launch of tamilbarotene and SY-2101.

The Tyme Models

SM-88 Development Case

The following tables presents certain key components of the SM-88 Development Case for the periods of 2022-2032 and 2033-2042, respectively:

($ in millions; risk-adjusted)	**2022E(1)**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**	**2032E**
Total revenue	—	—	—	—	—	—	—	—	$4	$9	$19
Earnings before interest and income taxes (EBIT)(2)(3)	($6)	($24)	($27)	($19)	($22)	($7)	($9)	($5)	($3)	$0	$9
Unlevered free cash flow(2)(4)	($6)	($24)	($27)	($19)	($22)	($7)	($9)	($5)	($3)	($0)	$8

($ in millions; risk-adjusted)	**2033E**	**2034E**	**2035E**	**2036E**	**2037E**	**2038E**	**2039E**	**2040E**	**2041E**	**2042E**
Total revenue	$ 29	$ 40	$ 47	$ 54	$ 56	$ 58	$ 60	$ 62	$ 64	$ 32
Earnings before income taxes (EBIT)(2)(3)	$ 18	$ 25	$ 30	$ 34	$ 36	$ 37	$ 38	$ 39	$ 41	$ 20
Unlevered free cash flow(2)(4)	$ 16	$ 23	$ 21	$ 25	$ 26	$ 27	$ 28	$ 29	$ 30	$ 18

(1) 2022E figures include on the period from September 30, 2022 to December 31, 2022.
(2) Non-GAAP Metric.
(3) Earnings before interest and income taxes is defined as revenue, less cost of sales, less operating expenses before interest expense, income taxes, gain (loss) on sale of assets, (income) loss from closed locations, and other non-cash or special items including asset impairments, facility closure costs, acquisition costs, severance, conversion, transaction and integration costs, and stock compensation expense.
(4) Unlevered free cash flow is defined as earnings before interest and income taxes less cash taxes, less capital expenditures, less increases in net working capital, plus decreases in net working capital.

Tyme Dissolution Case

The following table presents certain key components of the Tyme Dissolution Case:

	(amounts in millions)
Balance of cash and cash equivalents upon commencement of dissolution	$ 74.1
Costs to wind down clinical, manufacturing, and pre-clinical operations and contracts; employee severance and retention payments; transaction fees for completion of dissolution and strategic review process	$ (11.9)
Mandatory warrant repurchase obligation	$ (0.2)
Ongoing costs until final dissolution (including insurance premiums; potential litigation expenses; personnel costs, rent and other operating expenses)	$ (10.1)
Net cash remaining after satisfaction of anticipated liabilities	$ 51.9
5% buffer for unanticipated costs or liabilities	$ (1.1)
Total amount to be distributed to Tyme Stockholders	**$ 50.9**
Initial liquidating dividend—September 30, 2022	$ 30.0
Final liquidating dividend—September 30, 2024	$ 20.9

Tyme's Adjusted Syros Forecast

The following tables presents certain key components of Tyme's Adjusted Syros Forecast for the periods of 2022-2029 and 2030-2037, respectively.

($ in millions)	**2022E(1)**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**
Total revenue	$4	$3	—	$6	$36	$103	$160	$183
Earnings before interest and income taxes(2)(3)	($25)	($78)	($88)	($54)	($18)	$62	$120	$141
Unlevered free cash flow(2)(4)(5)	($24)	($80)	($83)	($53)	($20)	$43	$90	$111

($ in millions)	**2030E**	**2031E**	**2032E**	**2033E**	**2034E**	**2035E**	**2036E**	**2037E**
Total revenue	$ 194	$ 202	$ 208	$ 218	$ 192	$ 173	$ 180	$ 188
Earnings before interest and income taxes(2)(3)	$ 152	$ 158	$ 165	$ 173	$ 148	$ 130	$ 137	$ 144
Unlevered free cash flow(2)(4)(5)	$ 120	$ 126	$ 131	$ 138	$ 121	$ 106	$ 109	$ 115

(1) 2022E figures include on the period from September 30, 2022 to December 31, 2022.
(2) Non-GAAP metric.
(3) Earnings before interest and income taxes is defined as revenue, less cost of sales, less operating expenses before interest expense, income taxes, gain (loss) on sale of assets, (income) loss from closed locations, and other non-cash or special items including asset impairments, facility closure costs, acquisition costs, severance, conversion, transaction and integration costs, and stock compensation expense.
(4) Unlevered free cash flow is defined as earnings before interest and income taxes less cash taxes, less capital expenditures, less increases in net working capital, plus decreases in net working capital, plus other non-cash outflows such as bonus accruals and other non-cash expense items included in earnings before interest and income taxes.
(5) Unlevered free cash flow presented in Tyme's Adjusted Syros Forecast does not reflect the use of any U.S. federal income tax net operating losses, or NOLs, to reduce cash taxes. Tyme's management prepared a separate non-public unaudited projection of the combined company's projected utilization of NOLs after the merger, taking into account limitations on the use of NOLs that may be imposed under Section 382 of the Internal Revenue Code as a result of the merger and the PIPE Financing (the "Combined Company NOL Utilization Estimates"). The Combined Company NOL Utilization Estimates showed an aggregate of approximately $27 million of estimated cash tax savings from the use of NOLs over the period covered by Tyme's Adjusted Syros Forecast (2022 to 2037). The Combined Company NOL Utilization Estimates reflect numerous assumptions, including an assumption that there would be no material change in applicable tax rates or laws governing the use of NOLs.

Interests of Syros Directors and Executive Officers in the Merger

In considering the recommendation of the Syros board of directors with respect to issuing shares of Syros common stock in the merger and the PIPE Financing, and the other matters to be acted upon by the Syros stockholders at the Syros special meeting, the Syros stockholders should be aware that Syros' directors and executive officers have interests in the merger that are different from, or in addition to, the interests of Syros' stockholders generally. These interests may present them with actual or potential conflicts of interest, and these interests, to the extent material, are described below.

The Syros board of directors was aware of these potential conflicts of interest and considered them, among other matters, in reaching its decision to approve the Merger Agreement, the merger, the Securities Purchase Agreement and the PIPE Financing, and to recommend that the Syros stockholders approve the proposals to be presented to the Syros stockholders for consideration at the Syros special meeting as contemplated by this joint proxy statement/prospectus.

PIPE Financing

Srinivas Akkaraju, M.D., Ph.D., a member of the Syros board of directors, is one of the managers of Samsara BioCapital GP, LLC, which is the general partner of Samsara BioCapital, L.P., a venture capital firm that agreed

to purchase 6,914,893 shares of Syros common stock and warrants to purchase 6,914,893 shares of Syros common stock in the PIPE Financing at an aggregate purchase price of $6,499,999.42.

Douglas Cole, M.D., a general partner of Flagship Pioneering, or Flagship, is the spouse of Nancy Simonian, M.D., President, Chief Executive Officer and member of the Syros board of directors. Flagship has agreed to purchase 7,000,000 shares of Syros common stock, pre-funded warrants to purchase 14,200,000 shares of common stock and warrants to purchase 21,200,000 shares of Syros common stock in the PIPE Financing at an aggregate purchase price of $19,926,580.00. In connection with the PIPE Financing, Flagship will have the right to designate a member of the board of directors of the combined company.

Ownership Interests

As of June 30, 2022, (i) Syros' current non-employee directors and executive officers owned, in the aggregate, less than 8% of the outstanding shares of Syros common stock, and (ii) to the knowledge of Syros, Syros' former executive officers who served as executive officers of Syros since the beginning of Syros' last fiscal year beneficially owned, in the aggregate, less than 1% of the outstanding shares of Syros common stock, which for purposes of this subsection excludes any Syros shares issuable upon exercise of Syros stock options held by such individuals. The affirmative vote of the holders of a majority of the shares present in attendance or represented by proxy at the Syros special meeting and entitled to vote on the matter, assuming a quorum is present, is required for approval of Proposal Nos. 1, 4 and 5. The affirmative vote of the holders of a majority of the outstanding shares of Syros common stock entitled to vote at the Syros special meeting is required for approval of Proposal Nos. 2 and 3. Each of Syros' non-employee directors have also entered into a support agreement in connection with the merger. For a more detailed discussion of the support agreements, please see the section titled "*Agreements Related to the Merger—Support Agreements*" beginning on page 222 of this joint proxy statement/prospectus.

Director Positions Following the Merger

Each of the current directors of Syros is expected to continue as a director of the combined company after the effective time of the merger.

Indemnification and Insurance

For a discussion of the indemnification and insurance provisions related to the Syros directors and officers under the Merger Agreement, please see the section titled "*The Merger Agreement—Indemnification and Insurance for Officers and Directors*" beginning on page 213 of this joint proxy statement/prospectus.

Director Compensation

Syros compensates its non-employee directors for their service on the Syros board of directors pursuant to its director compensation program. The chair of each committee and the chair of the board of directors receive higher retainers for such service. These fees are payable in arrears in four equal quarterly installments on the last day of each quarter, subject to proration for any portion of such quarter that the director is not serving on the Syros board of directors, on such committee or in such position. Pursuant to the director compensation program, non-employee directors are also eligible to receive initial and annual grants of stock options. Syros does not pay any compensation to Dr. Simonian, its president and chief executive officer, in connection with her service on the Syros board of directors.

In addition to the current members of the Syros board of directors who are expected to continue to serve on the Syros board of directors, following the closing of the merger, Tyme will have the right to designate one member of the Syros board of directors and investors in the PIPE Financing will have the right to designate up to two members of the Syros board of directors, who will each be eligible to be compensated as a non-employee director of Syros pursuant to the Syros director compensation program.

Executive Employment Arrangements

Syros has entered into written offer letters with Dr. Simonian, Mr. Haas, Dr. Roth, Dr. Olson, Mr. Chee and Ms. Stephens, pursuant to which each are eligible to receive certain severance payments and benefits under certain circumstances.

The offer letter with Dr. Simonian provides that if her employment is terminated by Syros without cause, or by her with good reason, as such terms are defined in her offer letter, she will receive monthly severance payments equal to her then-current monthly salary rate for 12 months and payment of an incentive bonus pro-rated for the portion of the then-current calendar year during which she was employed by Syros, subject to certain conditions, including the execution of a release of all claims against Syros. In addition, in the event of a change in control of Syros, as defined in the offer letter, all unvested stock options then held by Dr. Simonian will vest in full 12 months after the change in control, or earlier if her employment is terminated by Syros without cause or by her for good reason in contemplation of, pursuant to or following a change in control, referred to as the CIC Equity Vesting.

The offer letter with each of Mr. Haas, Dr. Roth, Mr. Chee and Ms. Stephens provides that if his or her employment is terminated by Syros without cause, or by him or her with good reason, as such terms are defined in the executive's offer letter, the executive will receive monthly severance payments equal to his or her then-current monthly rate of salary for nine months, subject to certain conditions, including the execution of a release of all claims against Syros. In addition, if within the three months prior to a change in control or in the twelve months following a change in control, the employment of any of Mr. Haas, Dr. Roth, Mr. Chee or Ms. Stephens is terminated by Syros without cause or by such executive with good reason, subject to certain conditions, Syros will (i) extend the severance benefits of such executive for an additional three months, such that the total severance benefit period shall be one year, (ii) pay to such executive a lump sum amount equal to his or her target bonus in effect for the fiscal year in which his or her separation from employment occurs and (iii) accelerate the vesting of all unvested stock options held by such executive as of the date his or her employment is terminated such that 100% of such options shall become fully vested and exercisable effective as of such date.

The offer letter with Dr. Olson provides that if his employment is terminated by Syros without cause, or by him with good reason, as such terms are defined in his offer letter, he will receive monthly severance payments equal to his then-current monthly rate of salary for six months, subject to certain conditions, including the execution of a release of all claims against Syros. Dr. Olson is also eligible for the CIC Equity Vesting.

The closing of the merger, the PIPE Financing and the related transactions do not constitute a change in control for purposes of the executive employment arrangements described this subsection. Each of Dr. Simonian, Mr. Haas, Dr. Roth, Dr. Olson, Mr. Chee and Ms. Stephens is expected to continue as an officer of the combined company after the effective time of the merger. In addition, Gerald S. Quirk, a former executive officer of Syros, is party to a consulting agreement with Syros, which consulting agreement is expected to remain in effect after the effective time of the merger.

Interests of Tyme Directors and Executive Officers in the Merger

In considering the recommendation of Tyme's board of directors to adopt the Merger Agreement, Tyme stockholders should be aware that Tyme's directors and executive officers have interests in the merger that may be different from, or in addition to, the interests of Tyme stockholders generally. Tyme's board of directors was aware of these interests and considered them, among other matters, in evaluating and negotiating the Merger Agreement, in reaching its decision to approve the Merger Agreement, and in recommending to Tyme stockholders that the Merger Agreement be adopted and to approve the proposals to be presented to the Tyme stockholders for consideration at the Tyme special meeting as contemplated by this joint proxy statement/prospectus.

Ownership Interests

As of July 1, 2022, Tyme's directors and executive officers beneficially owned, in the aggregate, 11.8% of the outstanding shares of common stock of Tyme (non-employee director, Steve Hoffman, owned approximately 11.6% of the outstanding shares of Tyme common stock), which excludes any Tyme shares issuable upon the exercise of options to purchase shares of Tyme common stock. The affirmative vote of the holders of a majority of the shares of Tyme common stock having voting power present or represented by proxy at the Tyme special meeting is required for approval of Tyme Proposal Nos. 2 and 4. The affirmative vote of the holders of a majority of shares of Tyme common stock having voting power outstanding on the record date for the Tyme meeting is required for approval of Proposal Nos. 1 and 3. Mr. Hoffman has entered into a voting agreement with Tyme, and certain of Tyme's officers and directors have also entered into support agreements in connection with the merger. For a more detailed discussion of the support agreements see the section entitled "*Agreements Related to the Merger—Support Agreements*" beginning on page 22 of this joint proxy statement/prospectus.

Treatment of Tyme Options

Under the terms of the Merger Agreement, each option to purchase shares of Tyme common stock that is granted to an individual who continues as a service provider to Tyme at the effective time and is outstanding and unexercised immediately prior to the effective time of the merger, whether or not vested, will be converted into a number of options to purchase shares of Syros common stock to be determined by the exchange ratio. Each outstanding and unexercised option to purchase shares of Tyme common stock that is not assumed by Syros pursuant to the merger agreement will be terminated and no consideration will be delivered for such options. Accordingly, from and after the effective time of the merger: (i) each outstanding Tyme stock option assumed by Syros may be exercised solely for shares of Syros common stock; (ii) the number of shares of Syros common stock subject to each outstanding Tyme stock option assumed by Syros will be determined by multiplying (A) the number of shares of Tyme common stock that were subject to such Tyme stock option, as in effect immediately prior to the effective time of the merger, by (B) the exchange ratio, and rounding the resulting number down to the nearest whole number of shares of Syros common stock; (iii) the per share exercise price of Syros common stock issuable upon exercise of each Tyme stock option assumed by Syros will be determined by dividing (A) the per share exercise price of Tyme common stock subject to such Tyme stock option, as in effect immediately prior to the effective time of the merger, by (B) the exchange ratio and rounding the resulting exercise price up to the nearest whole cent; and (iv) any restriction on the exercise, and any provision providing for the acceleration of vesting and/or exercisability, of any Tyme stock option assumed by Syros will continue in full force and effect and the term, exercisability, vesting schedule, acceleration rights and other provisions of such Tyme stock option will otherwise remain unchanged.

It is anticipated that Tyme's executive officers will enter into cooperation agreements with Tyme that will, among other things, extend the exercise period for each assumed Tyme option with an exercise price of less than $2.00 per share of Tyme common stock that such executive officer holds as of immediately following closing of the merger to the second anniversary of such executive officer's termination date, or, if earlier, until the earliest of (i) the second anniversary of the effective time, (ii) the original expiration date of such option, and (iii) any earlier termination or cashing out of options at Syros generally applicable to its option holders. See the subsection titled "*—Interests of Tyme Directors and Executive Officers in the Merger—Cooperation Agreements*" in this joint proxy statement/prospectus for further details related to the cooperation agreements.

The table below sets forth information regarding the number of Tyme Options held by each Tyme executive officer and director as of July 1, 2022.

Name	Number of Vested Tyme Options Held	Weighted Average Exercise Price of Vested Tyme Options ($)	Number of Unvested Tyme Options Held	Weighted Average Exercise Price of Unvested Tyme Options ($)
Tyme Executive Officers and Directors				
Christine Baker	33,111	0.35	179,777	0.35
James Biehl	1,158,200	2.01	1,037,200	0.91
David Carberry	331,000	1.87	22,000	1.10
Richard Cunningham	875,000	1.09	2,951,000	0.77
Donald W. DeGolyer	331,000	1.87	22,000	1.10
Jonathan Eckard	1,428,448	2.78	955,452	0.86
Barbara C. Galaini	612,196	1.80	580,804	0.93
Steve Hoffman	0	0.00	0	0.00
Douglas A. Michels	326,833	1.85	22,000	1.10
Frank L. Porfido	181,248	1.43	940,552	0.96
Dr. Gerald Sokol	331,000	2.31	22,000	1.10
Timothy C. Tyson	381,958	2.55	22,000	1.10

Employment Agreements with Executive Officers

Richie Cunningham, Tyme's Chief Executive Officer and Frank Porfido, Tyme's Chief Financial Officer and Barbara Galaini, Tyme's Corporate Controller, are each party to an employment agreement with Tyme that provides for enhanced severance benefits in the event of a qualifying termination within twelve months following a change in control. The merger will constitute a change in control for purposes of these employment agreements.

The employment agreements provide that, upon a qualifying termination, Mrs. Cunningham, Mr. Porfido and Ms. Galaini would be entitled to:

- cash severance equal to 1.5x 12 months of base salary, 1.0x 12 months of base salary and .75x 12 months of base salary, respectively, payable in installments in the form of continuation of base salary payments ;
- cash severance equal to 1.5x his cash target incentive award,1.0x his cash target incentive award and 0.75x her cash target incentive award, respectively, in each case, either the cash target incentive for the year in which the termination occurs or if it has not yet been established, the cash target incentive in the immediately preceding year, payable in the same manner and at the same time as would otherwise have been paid pursuant to Tyme's equity plans ;
- payment of the cost of health care coverage in effect at the time of termination of employment for a period of 18 months, 12 months and 9 months, respectively, of the executive officer's premiums under the Consolidated Omnibus Budget Reconciliation Act of 1985, or COBRA, to continue such coverage; and
- accelerated vesting of any then-unvested time-based equity awards held at the time of termination.

In addition, each of James Biehl, Tyme's Chief Legal Officer and Jonathan Eckard, Tyme's Chief Business Officer, are party to employment agreements with Tyme that provide for severance benefits in the event of a

termination without cause (as defined in each agreement). Upon such a termination, Messrs. Biehl and Eckard would be entitled to:

- an aggregate amount equal to the sum of base salary he would have received from the termination date through the agreement expiration date in the case of Mr. Biehl and an aggregate amount equal to 1.0x 12 months of base salary in the case of Mr. Eckard, which, in each case, will be payable in the same amounts and at the same intervals as if the employment period had not ended;
- immediate and full vesting of all equity held at the time of termination; and
- payment of the cost of health care coverage in effect at the time of termination of employment for a period of 18 months of the executive officer's premiums under COBRA to continue such coverage.

Payments and benefits under each of the employment agreements are subject to the applicable executive officer's execution and non-revocation of a general release of claims in favor of Tyme.

The estimated aggregate amount that would be payable to Mr. Cunningham, Mr. Porfido, Mr. Biehl, Mr. Eckard and Ms. Galaini under each executive officer's employment agreement if the merger was to be completed and such executive officers were to experience a qualifying termination on July 11, 2022 is $1,317,420, $563,310, $1,181,854, $471,751 and $312,576, respectively, which includes severance payments and in the case of certain executive officers, medical premium payments. Although the executives' employment agreements provides that certain severance payments will be made in installments over time following the termination of their employment, the Merger Agreement contemplates and Tyme currently expects that such severance will, to the maximum extent permitted by Section 409A of the Code, be paid in lump sum as soon as practicable following the date of such officer's separation from service, subject to certain conditions.

Retention Agreements

Tyme is party to retention agreements with each of its executive officers, including Richard Cunningham, Frank Porfido, Jonathan Eckard, James Biehl and Barbara Galaini. The retention agreements provide for a retention cash bonus in an amount equal to the executive officer's respective target bonus for the fiscal year ending March 31, 2023, to be payable within 20 days following the effective time, provided that such executive officer is employed at the effective time or upon a qualifying termination prior to the effective time; provided that the effective time occurs on or before March 31, 2023.

The estimated retention bonus payments that the executive officers would be entitled to receive are reflected in the table below.

Name	Retention Bonus
Richie Cunningham	$ 292,760
Frank Porfido	$ 152,704
Jonathan Eckard	$ 171,392
James Biehl	$ 197,627
Barbara Galaini	$ 85,160

Cooperation Agreements

In connection with the execution of the Merger Agreement, the Tyme Compensation Committee approved the entrance into cooperation agreements with all Tyme employees in good standing, including Tyme's executive officers, pursuant to the exercise period for any Tyme stock option held by a Tyme executive officer immediately following the effective time with an exercise price of less than $2.00 per share of Tyme common stock will be extended until the second anniversary of such individual's termination or, if earlier, until the earliest of (i) the second anniversary of the effective time, (ii) the original expiration date of such option, and (iii) any earlier termination or cashing out of options at Syros generally applicable to its option holders (as might occur in a change in control of Syros).

The estimated aggregate change in fair value associated with the option extension for Mr. Cunningham, Mr. Porfido, Mr. Biehl, Mr. Eckard and Ms. Galaini is $170,000, $43,500, $64,260, $62,395 and $39,285, respectively.

Director Positions Following the Merger

Pursuant to the Merger Agreement, Tyme will be entitled to appoint a director to serve on the Syros' board of directors as of the closing of the merger. Such director will receive compensation following the merger in accordance with Syros' non-employee director compensation policy.

Indemnification and Insurance

Tyme's directors and executive officers are entitled to certain indemnification and liability insurance coverage, along with continued indemnification pursuant to the terms of the Merger Agreement. For a discussion of the indemnification and insurance provisions related to Tyme's directors and executive officers under the Merger Agreement, please see the section titled "*The Merger Agreement—Indemnification and Insurance for Officers and Directors*" beginning on page 213 of this joint proxy statement/prospectus.

Tyme has entered into indemnification agreements with each of its directors and officers. These indemnification agreements may require Tyme, among other things, to indemnify its directors and officers for some expenses, including attorneys' fees, judgments, fines and settlement amounts incurred by a director or officer in any action or proceeding arising out of his or her service as one of Tyme's directors or officers, or any of Tyme's subsidiaries or any other company or enterprise to which the person provides services at Tyme's request.

Tyme Golden Parachute Compensation

This section sets forth the information required by Item 402(t) of RegulationS-K regarding the compensation of each of Tyme's Named Executive Officers that is based on or otherwise relates to the merger. The consummation of the merger will constitute a change in control of Tyme under the terms of the employment agreements between Tyme and its Named Executive Officers, and each of Tyme's Named Executive Officers is eligible to receive certain severance payments and benefits upon a qualifying termination of their employment following the merger as described above in the subsections entitled *"—Interests of Tyme Directors and Executive Officers in the Merger—Employment Agreements with Executive Officers*" *"—Interests of Tyme Directors and Executive Officers in the Merger—Retention Agreements*," and *"—Interests of Tyme Directors and Executive Officers in the Merger—Cooperation Agreements.*"

Tyme Golden Parachute Compensation Table

The table below describes the estimated potential payments to each of Tyme's Named Executive Officers under the terms of the employment agreements, retention agreements, cooperation agreements and their respective outstanding equity awards. Mr. Hoffman was a Named Executive Officer for the year ended March 31, 2022, but his employment with Tyme ended on March 21, 2022 and, accordingly, he is not entitled to any golden parachute compensation and is not included on the table below. Please note the amounts shown in the table are estimates only and are based on assumptions regarding events that may or may not actually occur, including assumptions described in this joint proxy statement/prospectus and in the notes to the table below, which may or may not actually occur or may occur at times different than the time assumed.

The amounts set forth below represent an estimate of each Tyme Named Executive Officer's golden parachute compensation, assuming the following:

- that consummation of the merger constitutes a change of control for purposes of the applicable compensation plan, arrangement or agreement;
- that the merger was consummated on July 11, 2022;

- each Tyme Named Executive Officer's employment is terminated by Tyme without "cause" or by such Tyme Named Executive Officer for "good reason" immediately following the merger;
- the value of the vesting acceleration of the Tyme Named Executive Officer's equity awards is calculated assuming a price per share of Tyme common stock of $.2780, which represents the average closing market price of Tyme's common stock over the first five business days following the first public announcement of the merger;
- each Tyme Named Executive Officer's base salary and target annual bonus is that in place as of July 11, 2022;
- no Tyme Named Executive Officer receives any additional equity grants prior to or at the time of the closing of the merger; and
- no Tyme Named Executive Officer enters into new agreements or is otherwise legally entitled to, prior to the closing of the merger, additional compensation or benefits; provided that the below assumes each Tyme Named Executive Officer has entered into a cooperation agreement.

	Golden Parachute Compensation			
	Cash(2)	Equity(3)	COBRA Benefits(4)	Total
Richie Cunningham	$1,610,180	$170,000	$ 0	$1,780,180
Frank Porfido	687,166(1)	43,500	28,847	759,513
James Biehl	1,350,451(1)	64,260	29,030	1,443,741

(1) The cash severance payments to Mr. Biehl of $1,350,451, pursuant to the terms his employment agreement, was calculated using a qualifying termination date of July 11, 2022, however, due to the auto-renewal provisions in his employment agreement, if such qualifying terminations was to occur at a later date, it is possible that Mr. Biehl could receive a cash severance payments of up to $1,432,796.
(2) Represents (i) severance payments under employment agreements and (ii) retention bonus payments pursuant to retention agreements.
(3) Represents the change in fair value of existing stock option awards as a result of the extension of the exercise period of certain stock options pursuant to cooperation agreements as determined in accordance with ASC 718 and using assumptions set forth in Note 12 to Tyme's consolidated financial statements for the year ended March 31, 2022. No value is attributed to the acceleration of any equity awards because the exercise price of all such equity awards are out-of-the-money as compared to the assumed price per share of $0.2780. referenced above.
(4) Represents medical premium payments under employment agreements.

Limitations of Liability and Indemnification

In addition to the indemnification obligations required by the restated certificate of incorporation and amended and restatedby-laws of Syros and Tyme, each of Syros and Tyme has entered into indemnification agreements with each of its respective directors and executive officers. These agreements provide for the indemnification of the applicable company's directors and executive officers to the fullest extent permitted by law for claims arising in his or her capacity as a director or executive officer, as applicable, provided that he or she acted in good faith and in a manner that he or she reasonably believed to be in, or not opposed to, the company's best interests and, with respect to any criminal proceeding, had no reasonable cause to believe that his or her conduct was unlawful. Each of these indemnification agreements provides that in the event that the applicable company does not assume the defense of a claim against a director or executive officer, as applicable, the company is required to advance his or her expenses in connection with his or her defense, provided that he or she undertakes to repay all amounts advanced if it is ultimately determined that he or she is not entitled to be indemnified by such company.

Each of Syros and Tyme believes that these provisions and agreements are necessary to attract and retain qualified persons as directors and executive officers. Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers or persons controlling the applicable company pursuant to the foregoing provisions, each of Syros and Tyme understands that in the opinion of the SEC such indemnification is against public policy as expressed in the Securities Act and is therefore unenforceable.

In addition, each of Syros and Tyme maintains standard policies of insurance under which coverage is provided to its directors and officers against losses arising from claims made by reason of breach of duty or other wrongful act, and to the applicable company with respect to payments which may be made by it to such directors and officers pursuant to the above indemnification provisions or otherwise as a matter of law.

Form of the Merger

The Merger Agreement provides that at the effective time, Merger Sub will be merged with and into Tyme and Tyme will continue as the surviving corporation and will be a wholly owned subsidiary of Syros.

Merger Consideration and Adjustment

At the effective time:

- each share of Tyme common stock outstanding immediately prior to the effective time will be converted into the right to receive a number of shares of Syros common stock based on the agreed upon Exchange Ratio;
- each option to purchase shares of Tyme common stock, or Tyme Option, that is outstanding and unexercised immediately prior to the effective time granted under Tyme equity-related plans, or each, a Tyme Plan, to an individual who continues as a service provider to Tyme at the effective time, whether or not vested, will be, along with the Tyme Plan, assumed by Syros, and will become an option to purchase solely that number of shares of Syros common stock equal to the product obtained by multiplying (a) the number of shares of Tyme common stock that were subject to such Tyme Option immediately prior to the effective time by (b) the Exchange Ratio, and rounding the resulting number down to the nearest whole number of shares of Syros common stock;
- the per share exercise price for Syros common stock issuable upon exercise of each Tyme Option assumed by Syros shall be determined by dividing (a) the per share exercise price of Tyme common stock subject to such Tyme Option, as in effect immediately prior to the effective time, by (b) the Exchange Ratio, and rounding the resulting exercise price up to the nearest whole cent;
- any restriction on the exercise of any Tyme Option assumed by Syros will continue in full force and effect and the term, exercisability, vesting schedule and other provisions of such Tyme Option shall otherwise remain unchanged;
- any Tyme Option that is not assumed in accordance with the foregoing as of the effective time shall cease to exist and no consideration shall be delivered in exchange therefor; provided, such holders will be given notice of a 30 day period prior to the effective time of the merger in which such holders will be able to exercise their options;
- the warrant to purchase Tyme common stock issued by Tyme on May 20, 2020, or the 2020 Tyme Warrant, shall be purchased by Tyme from the holder thereof on the terms set forth in such warrant agreement immediately prior to the effective time;
- each other warrant (other than the 2020 Tyme Warrant) to purchase shares of Tyme common stock that is outstanding and unexercised immediately prior to the effective time (such outstanding warrants, the Tyme Warrants) will be converted into and become a warrant to purchase (and Syros shall assume each such Tyme Warrant in accordance with its terms) solely that number of shares of Syros common stock equal to the product obtained by multiplying (a) the number of shares of Tyme common stock that were subject to such Tyme Warrant immediately prior to the effective time by (b) the Exchange Ratio, and rounding the resulting number down to the nearest whole number of shares of Syros common stock;
- the per share exercise price for Syros common stock issuable upon exercise of each Tyme Warrant assumed by Syros shall be determined by dividing (a) the per share exercise price of Tyme common stock subject to such Syros Warrant, as in effect immediately prior to the effective time, by (b) the Exchange Ratio, and rounding the resulting exercise price up to the nearest whole cent; and

- any restriction on the exercise of any Tyme Warrant assumed by Syros will continue in full force and effect and the term, exercisability, vesting schedule and other provisions of such Tyme Warrant shall otherwise remain unchanged.

The Exchange Ratio is calculated as the quotient (rounded down to four decimal places) obtained by dividing the Tyme per share value by $0.94. The Tyme per share value means the quotient of dividing the Tyme valuation, which is $7.5 million plus Tyme net cash, by the number of shares of Tyme common stock actually issued and outstanding immediately prior to the effective time.

The Exchange Ratio was initially estimated to be 0.4312 shares of Syros common stock for each share of Tyme common stock, but the actual Exchange Ratio will depend on Tyme's net cash and the number of shares of Tyme common stock outstanding at the closing of the merger. The Exchange Ratio also does not give effect to the proposed reverse stock split of Syros common stock because the proposed reverse stock split is a range and is not final. Based upon the initially estimated exchange ratio, following the merger and giving effect to the PIPE Financing, (i) Syros securityholders immediately before the merger together with the investors in the PIPE Financing are expected to own approximately 63% of the aggregate number of outstanding shares of Syros common stock following the merger and (ii) Tyme securityholders immediately before the merger are expected to own approximately 37% of the aggregate number of outstanding shares of Syros common stock following the merger, subject to certain assumptions (including as to the amount of Tyme net cash at closing, which could be materially different). Assuming the exercise of all Syros pre-funded warrants, including the Pre-Funded PIPE Warrants and the Pre-Funded 2020 Warrants, without giving effect to any beneficial ownership limitations applicable thereto, then (i) Syros securityholders immediately before the merger together with the investors in the PIPE Financing would own approximately 73% of the aggregate number of outstanding shares of Syros common stock following the merger and (ii) Tyme securityholders immediately before the merger would own approximately 27% of the aggregate number of outstanding shares of Syros common stock following the merger, subject to certain assumptions (including as to the amount of Tyme net cash at closing, which could be materially different). The foregoing percentages do not give effect to the exercise or conversion of outstanding stock options or warrants other than as set forth above.

Examples

For illustrative purposes only, the examples presented below calculate the Exchange Ratio under various Tyme net cash scenarios. These examples have assumed: (i) the effective time occurs on July 1, 2022 and (ii) Tyme has 172,206,894 shares of common stock outstanding immediately prior to the effective time, and (iii) Syros has 126,860,798 shares of common stock outstanding immediately prior to the effective time, after giving effect to the PIPE Financing and assuming the exercise of all Syros pre-funded warrants, including the Pre-Funded PIPE Warrants and the Pre-Funded 2020 Warrants, without giving effect to any beneficial ownership limitations applicable thereto, but before the issuance of shares in the merger, and without giving effect to the exercise or conversion of outstanding stock options or warrants other than as set forth above.

Tyme Net Cash	Exchange Ratio	Post-Merger Ownership by Tyme Securityholders	Post-Merger Ownership by Syros Securityholders (including PIPE Financing Investors)
$50,000,000	0.3552	23.23%	76.77%
$55,000,000	0.3861	24.75%	75.25%
$60,000,000	0.4170	26.21%	73.79%
$62,300,000	0.4312	26.87%	73.13%
$65,000,000	0.4479	27.62%	72.38%
$70,000,000	0.4788	28.97%	71.03%

For each $1.0 million increase (decrease) in Tyme net cash, the exchange ratio will increase (decrease) by approximately 0.0062.

No fractional shares of Syros common stock will be issuable pursuant to the Merger Agreement to Tyme stockholders. Instead, each Tyme stockholder who would otherwise be entitled to receive a fraction of a share of Syros common stock (after aggregating all fractional shares of Syros common stock issuable to such holder), will be entitled to receive cash (without interest and subject to applicable tax withholding) in an amount equal to such fractional part of a share of Syros common stock multiplied by the last reported sale price of Syros common stock at the 4:00 p.m., Eastern time, end of regular trading hours on The Nasdaq Global Select Market on the last trading day prior to the effective time.

The Merger Agreement includes conditions to each party's obligation to close the merger that requires Tyme's net cash to have been finally determined in accordance with the Merger Agreement and for such net cash to be at least $50.0 million. The closing could be delayed if Syros and Tyme are not able to agree upon the amount of Tyme's net cash as of Tyme's cash determination time.

Pursuant to the terms of the Merger Agreement, Tyme's "net cash" means, as of the cash determination time, the*sum* of (without duplication) the following:

- Tyme's unrestricted free cash, cash equivalents and marketable securities

  minus

- the *sum* (without duplication) of:
  - all accounts payable, accrued expenses (including accrued tax liabilities) and Tyme's other short- and long-term liabilities payable in cash (except to the extent such liabilities are with respect to employees that Syros intends to retain and realize the benefit of after closing (disregarding any cooperation provided pursuant to certain provisions of the Merger Agreement));
  - any transaction expenses of Tyme or for which Tyme is liable; and
  - any indebtedness of Tyme.

  minus

- any projected liabilities payable in cash associated with the shut-down of anyon-going clinical trials of Tyme that will not be continued after the closing

  plus

- certain prepaid Tyme expenses that may be refunded in cash or used toward satisfying liabilities of Syros or the surviving corporation payable in cash

  plus

- the aggregate amount of any costs or expenses, including attorneys' fees or settlement costs, or litigation losses, incurred and paid by Tyme prior to the closing in successfully defending or enforcing its rights with respect to any potential or actual transaction litigation.

Each component of Tyme net cash shall be determined in accordance with GAAP applied on a basis consistent with the application of GAAP in the preparation of Tyme's most recent audited financial statements.

Procedures for Exchanging Tyme Stock Certificates

As soon as reasonably practicable after the effective time, the exchange agent will mail to each holder of record of Tyme common stock that was converted into the right to receive merger consideration a letter of transmittal in a customary form and instructions for use in effecting the surrender of the record holder's stock certificates in

exchange for certificates or book entry records representing shares of Syros common stock (plus cash in lieu of fractional shares, if any, of Syros common stock and any dividends or distributions). Upon surrender of a Tyme certificate for cancellation together with a properly completed and duly executed letter of transmittal and such other documents as may be reasonably required by Syros and the exchange agent, the holder of such Tyme stock certificate will be entitled to receive a stock certificate or book entry record representing the number of whole shares of Syros common stock issuable to such holder pursuant to the Merger Agreement and cash in lieu of any fractional share of Syros common stock issuable to such holder and any dividends or distributions then payable to such holder pursuant to the Merger Agreement. The surrendered certificates representing Tyme common stock will be cancelled.

In the event of a transfer of ownership of Tyme common stock that is not registered in the transfer records of Tyme, a certificate representing the proper number of whole shares of Syros common stock plus cash in lieu of fractional shares and any dividends or distributions then payable may be issued or paid to a person other than the person in whose name the surrendered Tyme stock certificate is registered, only if such certificate is presented to the exchange agent, accompanied by all documents required to evidence and effect such transfer and by evidence that any applicable stock transfer taxes have been paid. From and after the effective time, each certificate representing shares of Tyme common stock that has not been surrendered will represent only the right to receive shares of Syros common stock issuable pursuant to the Merger Agreement and cash in lieu of any fractional share of Syros common stock issuable to such holder and any dividends or distributions then payable to such holder pursuant to the Merger Agreement.

Any holder or former holder of Tyme common stock may be subject to withholding under the Code, or under another provision of state, local or foreign tax law. To the extent such amounts are withheld they will be treated as having been paid to the person to whom such amounts would otherwise have been paid.

HOLDERS OF TYME COMMON STOCK SHOULD NOT SEND IN THEIR TYME STOCK CERTIFICATES UNTIL THEY RECEIVE A LETTER OF TRANSMITTAL FROM THE EXCHANGE AGENT WITH INSTRUCTIONS FOR THE SURRENDER OF TYME STOCK CERTIFICATES.

Effective Time of the Merger

The Merger Agreement requires the parties to consummate the merger as promptly as practicable (and in any event within two business days unless any conditions remain unsatisfied or unwaived) after all of the conditions to the consummation of the merger contained in the Merger Agreement are satisfied or waived, including the adoption of the Merger Agreement by the Tyme stockholders and the approval by the Syros stockholders of the issuance of Syros common stock in connection with the merger, and the other transactions proposed under the Merger Agreement, other than those conditions that by their nature are to be satisfied at the closing of the merger. The merger will become effective upon the filing of a certificate of merger with the Secretary of State of the State of Delaware or at such later time as is agreed by Syros and Tyme and specified in the certificate of merger. Neither Syros nor Tyme can predict the exact timing of the consummation of the merger.

Regulatory Approvals

In the United States, Syros must comply with applicable federal and state securities laws and the rules and regulations of Nasdaq in connection with the issuance of shares of Syros common stock to Tyme's stockholders in connection with the transactions contemplated by the Merger Agreement and the PIPE Financing, and the filing of this joint proxy statement/prospectus with the SEC. Syros is not required to, and does not intend to, seek any regulatory approval from antitrust authorities to consummate the transactions.

Tax Treatment of the Merger

Syros and Tyme intend that, for U.S. federal income Tax purposes: (i) if Section 368 of the Code applies, (a) the Merger Agreement shall constitute a "plan of reorganization" within the meaning of Section 368 and the

Treasury Regulations promulgated thereunder and (b) the Merger shall constitute a "reorganization" within the meaning of Section 368(a) of the Code; and (ii) if Section 351 of the Code applies, the Merger and PIPE Financing, taken together as an integrated transaction, shall constitute a transfer which qualifies under Section 351 of the Code.

Material U.S. Federal Income Tax Consequences of the Merger

The following is a discussion of the material U.S. federal income tax consequences of the merger to U.S. Holders (as defined below) who exchange their Tyme common stock for Syros common stock in the merger. The discussion does not purport to be a complete analysis of all potential tax consequences to such a U.S. Holder. The effects of other U.S. federal tax laws, such as estate and gift tax laws, and any applicable state, local or non-U.S. tax laws are not addressed in this discussion. This discussion is based on the Code, Treasury Regulations promulgated thereunder, judicial decisions, and published rulings and administrative pronouncements of the IRS, in each case in effect as of the date hereof. These authorities may change or be subject to differing interpretations. Any such change or differing interpretation may be applied retroactively impacting the U.S. federal income tax consequences of the merger in a manner that could adversely affect a U.S. Holder. Neither Syros nor Tyme has sought or intends to seek any rulings from the IRS regarding the matters discussed below. There can be no assurance the IRS or a court will not take a position regarding the U.S. federal income tax consequences of the merger contrary to that discussed below. This discussion assumes that the merger will be consummated in accordance with the Merger Agreement and as described in this joint proxy statement/prospectus.

This discussion is limited to U.S. Holders that hold Tyme common stock as a "capital asset" within the meaning of Section 1221 of the Code (generally, property held for investment). Furthermore, this discussion does not address all U.S. federal income tax consequences relevant to a U.S. Holder's particular circumstances, including the impact of the alternative minimum tax or the Medicare contribution tax on net investment income. In addition, it does not address consequences relevant to U.S. Holders subject to special rules, including, without limitation:

- U.S. expatriates and former citizens or long-term residents of the United States;
- U.S. Holders whose functional currency is not the U.S. dollar;
- persons holding Tyme common stock as part of a hedge, straddle or other risk reduction strategy or as part of a conversion transaction or other integrated investment;
- banks, insurance companies, and other financial institutions;
- real estate investment trusts or regulated investment companies;
- brokers, dealers or traders in securities;
- "controlled foreign corporations," "passive foreign investment companies," and corporations that accumulate earnings to avoid U.S. federal income tax;
- S corporations, partnerships or other entities or arrangements treated as partnerships for U.S. federal income tax purposes (and investors therein);
- persons for whom Tyme common stock constitutes "qualified small business stock" within the meaning of Section 1202 of the Code or as "Section 1244 stock" for purposes of Section 1244 of the Code;
- tax-exempt organizations or governmental organizations;
- persons subject to special tax accounting rules as a result of any item of gross income with respect to Tyme common stock being taken into account in an "applicable financial statement" (as defined in the Code);
- persons deemed to sell Tyme common stock under the constructive sale provisions of the Code;

- persons who hold or received Tyme common stock pursuant to the exercise of any employee stock option or otherwise as compensation;
- tax-qualified retirement plans; and
- U.S. Holders of warrants, options, or other stock rights or persons who acquired their shares upon the exercise or conversion thereof.

If an entity treated as a partnership for U.S. federal income tax purposes holds Tyme common stock, the tax treatment of a partner in the partnership will depend on the status of the partner, the activities of the partnership and certain determinations made at the partner level. Accordingly, partnerships holding Tyme common stock and the partners in such partnerships should consult their tax advisors regarding the U.S. federal income tax consequences of the merger to them.

THIS DISCUSSION IS FOR INFORMATION PURPOSES ONLY AND DOES NOT CONSTITUTE TAX ADVICE. HOLDERS SHOULD CONSULT THEIR TAX ADVISORS WITH RESPECT TO THE APPLICATION OF THE U.S. FEDERAL INCOME TAX LAWS TO THEIR PARTICULAR SITUATIONS AS WELL AS ANY TAX CONSEQUENCES OF THE MERGER ARISING UNDER THE U.S. FEDERAL ESTATE OR GIFT TAX LAWS OR UNDER THE LAWS OF ANY STATE, LOCAL OR NON-U.S. TAXING JURISDICTION OR UNDER ANY APPLICABLE INCOME TAX TREATY.

For purposes of this discussion, a U.S. Holder is a beneficial owner of Tyme common stock that, for U.S. federal income tax purposes, is:

- an individual who is a citizen or resident of the United States;
- a corporation, or entity treated as a corporation, created or organized under the laws of the United States, any state thereof, or the District of Columbia;
- an estate, the income of which is subject to U.S. federal income tax regardless of its source; or
- a trust (i) over which a court within the United States is able to exercise primary supervision, and of which one or more United States persons (within the meaning of Section 7701(a)(30) of the Code) is authorized or has the authority to control all substantial decisions, or (ii) that has a valid election in effect to be treated as a United States person for U.S. federal income tax purposes.

U.S. Federal Income Tax Consequences of the Merger to U.S. Holders

Tax Characterization of the Merger

The merger is intended to qualify as either a tax-free contribution pursuant to Section 351 of the Code, taken together with the PIPE Financing, or a "reorganization" within the meaning of Section 368(a) of the Code. However, neither Syros nor Tyme intends to obtain a ruling from the IRS with respect to the tax consequences of the merger. In addition, no opinion of counsel has been obtained or will be obtained regarding the treatment of the merger as a tax-free contribution or a tax-free reorganization.

If the merger qualifies as neither a tax-free contribution pursuant to Section 351 of the Code nor a "reorganization" within the meaning of Section 368(a) of the Code, the U.S. federal income tax consequences of the merger to U.S. Holders would generally be as described below under the section titled "— *Tax Consequences if the Merger Fails to Qualify for the Intended Tax Treatment*."

It is expected that the Tyme stockholders, taken together with the investors in the PIPE Financing, will be in "control" (within the meaning of Section 368(c) of the Code) of Syros immediately after the merger such that the merger should qualify as a transfer of property to a "controlled corporation" under Section 351(a) of the Code for U.S. federal income tax purposes, although the number of shares of Syros common stock to be issued to Tyme

stockholders in the merger will not be known until immediately prior to the effective time of the merger and is dependent on certain facts. "Control" for purposes of Section 351 of the Code is defined as the ownership of stock possessing at least 80 percent of the total combined voting power of all classes of stock entitled to vote and at least 80 percent of the total number of shares of each other class of stock of the corporation. For this purpose, Syros and Tyme have assumed that the Pre-Funded PIPE Warrants to acquire Syros common stock issued in the PIPE Financing are treated as exercised given that the exercise price of the Pre-Funded PIPE Warrants is $0.0001 and such warrants are exercisable at any time. If the Pre-Funded PIPE Warrants are not treated as exercised for this purpose, but rather are treated as a class of non-voting stock, then the control requirement would not be satisfied and the merger would not satisfy the requirements of Section 351 of the Code. In addition, if the Tyme stockholders or investors in the PIPE Financing take actions as part of a plan with the merger or PIPE Financing that would cause such stockholders to lose "control" of Syros immediately after the merger within the meaning of Section 368(c) of the Code as interpreted by applicable case law and IRS guidance, such as a previously negotiated sale to a third party under certain circumstances, the merger would not satisfy the requirements of Section 351 of the Code.

If the requirements of Section 351 of the Code are not satisfied, it is expected that the merger will still qualify as a "reorganization" under Section 368(a) of the Code. However, whether the merger qualifies as such a reorganization will depend on the actual facts and circumstances at and after the effective time of the merger.

If the merger qualifies as a tax-free contribution under Section 351(a) of the Code or a "reorganization" under Section 368(a) of the Code, the U.S. federal income tax consequences to the U.S. Holders generally should be the same.

Unless otherwise indicated, the remainder of this discussion assumes the merger qualifies as either a tax-free contribution pursuant to Section 351 of the Code, taken together with the PIPE Financing, or a "reorganization" within the meaning of Section 368(a) of the Code.

Tax Consequences if the Merger Qualifies for the Intended Tax Treatment

Assuming the merger qualifies for the intended tax treatment described above, a U.S. Holder:

- will not recognize any gain or loss upon the exchange of shares of Tyme common stock for shares of Syros common stock in the merger, except with respect to cash received in lieu of fractional shares (as discussed below);
- will have an aggregate tax basis in the shares of Syros common stock received in the merger (including fractional shares deemed received and redeemed as described below) equal to the aggregate adjusted tax basis of the shares of Tyme common stock surrendered in exchange therefor; and
- will have a holding period for the shares of Syros common stock received in the merger (including fractional shares deemed received) that includes the holding period of the shares of Tyme common stock surrendered in exchange therefor.

Treasury Regulations provide detailed rules for allocating the tax basis and holding period of the shares of Tyme common stock surrendered to the shares of Syros common stock received. U.S. Holders of shares of Tyme capital stock acquired on different dates and at different prices should consult their tax advisors regarding the allocation of the tax basis and holding period of such shares.

Cash in Lieu of Fractional Shares

A U.S. Holder that receives cash in lieu of a fractional share of Tyme common stock in the merger generally will be treated as having received such fractional share and then as having received such cash in redemption of the fractional share. Gain or loss generally will be recognized based on the difference between the amount of cash

received in lieu of the fractional share of Tyme common stock and the portion of the U.S. Holder's aggregate adjusted tax basis in the shares of Tyme common stock surrendered that is allocable to the fractional share of Tyme common stock deemed received. Such gain or loss generally will be long-term capital gain or loss if the U.S. Holder's holding period for its shares of Tyme common stock exceeds one year at the effective time of the merger.

Tax Consequences if the Merger Fails to Qualify for the Intended Tax Treatment

If the merger qualifies as neither a tax-free contribution pursuant to Section 351 of the Code nor a "reorganization" within the meaning of Section 368(a) of the Code, a U.S. Holder generally would recognize gain or loss for U.S. federal income tax purposes with respect to the Tyme common stock surrendered in the merger in an amount equal to the difference between the fair market value, at the time of the merger, of the Syros common stock received in the merger (plus any cash received in lieu of a fractional share) and such U.S. Holder's aggregate adjusted tax basis in the Tyme common stock surrendered therefor in the merger. Gain or loss must be calculated separately for each block of Tyme common stock exchanged by such U.S. Holder if such blocks were acquired at different times or for different prices. Any gain or loss recognized generally would be capital gain or loss, and generally would be long-term capital gain or loss if the U.S. Holder's holding period in a particular block of Tyme common stock exceeds one year at the effective time of the merger. Long-term capital gain of non-corporate U.S. Holders (including individuals) generally is taxed at reduced U.S. federal income tax rates. The deductibility of capital losses is subject to limitations. A U.S. Holder's tax basis in shares of Syros common stock received in the merger would be equal to the fair market value thereof as of the effective time of the merger, and such U.S. Holder's holding period in such shares would begin on the day following the merger.

Reporting Requirements under Sections 351 and 368

If the merger qualifies a tax-free contribution pursuant to Section 351 of the Code, current Treasury Regulations require certain U.S. Holders who are "significant transferors" of Tyme common stock to comply with certain reporting requirements, including filing a statement with the IRS. Under Treasury Regulation Section 1.351-3, a significant transferor includes a person that transfers property to a corporation and receives stock of the transferee corporation in an exchange described in Section 351 of the Code if, immediately after the exchange, such person owns at least five percent (by vote or value) of the total outstanding stock of the transferee corporation and the stock owned by such person is publicly traded. If the merger qualifies as a "reorganization" under Section 368(a) of the Code, current Treasury Regulations require certain U.S. Holders who are "significant holders" of Tyme common stock to comply with certain reporting requirements, including filing a statement with the IRS. Under Treasury Regulation Section 1.368-3, a significant holder includes a person who transfers stock of a target corporation and receives stock of an acquirer in a reorganization transaction if, immediately before the exchange, such person owned at least five percent (by vote or value) of the total outstanding stock of the target corporation and the stock owned by such person is publicly traded. In either case, the statement must include, among other things, the significant transferor's or significant holder's, as applicable, tax basis in the Tyme stock surrendered, the fair market value of such stock, the date of the merger, and the name and employer identification number of each party to the merger. U.S. Holders should consult their tax advisors to determine whether they are required to provide either of the foregoing statements.

Information Reporting and Backup Withholding

A U.S. Holder may be subject to information reporting and backup withholding when such holder receives cash in lieu of fractional shares of Syros common stock in the merger. Certain U.S. Holders are exempt from backup withholding, including corporations and certain tax-exempt organizations. A U.S. Holder will be subject to backup withholding unless such holder properly establishes an exemption or the holders certifies under penalties of perjury that the holder has furnished a correct taxpayer identification number and that the IRS has not notified the holder that the holder is subject to backup withholding.

Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules may be allowed as a refund or a credit against a U.S. Holder's U.S. federal income tax liability, provided the required information is timely furnished to the IRS. U.S. Holders should consult their tax advisors regarding their qualification for an exemption from backup withholding and the procedures for obtaining such an exemption.

The foregoing summary is of a general nature only and is not intended to be, and should not be construed to be, legal, business or tax advice to any particular Tyme stockholder. The U.S. federal income tax consequences of the merger to a U.S. Holder are complex and will depend on such U.S. Holder's personal tax situation. Accordingly, each U.S. Holder is strongly urged to consult such holder's own tax advisor with respect to the specific tax consequences of the merger, taking into account the holder's personal circumstances.

Anticipated Accounting Treatment

The merger is being accounted for as an in-substance recapitalization of Syros, as the transaction is, in essence, an exchange of Syros common shares for cash and cash equivalents and highly liquid assets presented by marketable securities. Apart from cash and cash equivalents and other highly liquid assets, the other assets and liabilities being acquired are nominal. Tyme's cash and cash equivalents, marketable securities and nominal assets and liabilities will be measured and recognized at their fair values as of the closing date of the merger, and will be consolidated with the assets, liabilities and results of operations of Syros after the consummation of the merger. Syros and Tyme both prepare their consolidated financial statements in accordance with GAAP. Syros' fiscal year end is December 31 while Tyme's fiscal year end is March 31. Accordingly, adjustments for the conversion from a fiscal year end of March 31 to December 31 are reflected in the unaudited pro forma condensed combined financial statements included elsewhere in this prospectus.

Syros Nasdaq Listing; Delisting of Tyme Stock

Shares of Syros common stock are currently listed on The Nasdaq Global Select Market under the symbol "SYRS." Syros has agreed to use commercially reasonable efforts to cause the shares of Syros common stock being issued in the merger to be approved for listing (subject to notice of issuance) on The Nasdaq Global Select Market at or prior to the effective time.

In addition, under the Merger Agreement, each of Syros' and Tyme's obligation to complete the merger is subject to the satisfaction or waiver by each of the parties, at or prior to the merger, of various conditions, including that the shares of Syros common stock to be issued in the merger have been approved for listing (subject to official notice of issuance) on Nasdaq as of the closing of the merger.

Syros anticipates that the common stock of the combined company will be listed on The Nasdaq Global Select Market following the closing of the merger under the trading symbol "SYRS." Following the effective time, Tyme will undertake to delist the Tyme common stock from The Nasdaq Capital Market.

Appraisal Rights and Dissenters' Rights

In accordance with Section 262(b)(1) of the DGCL, no statutory appraisal rights shall be available for to the holders of Tyme common stock in connection with the adoption of the Merger Agreement or the merger. Under the DGCL, Syros stockholders are not entitled to appraisal rights in connection with the merger.

The following is a summary of the material terms of the Merger Agreement. A copy of the Merger Agreement is attached to this joint proxy statement/prospectus as Annex A and is incorporated by reference into this joint proxy statement/prospectus. The Merger Agreement has been attached to this joint proxy statement/prospectus to provide you with information regarding its terms. It is not intended to provide any other factual information about Syros, Tyme or Merger Sub. The following description does not purport to be complete and is qualified in its entirety by reference to the Merger Agreement. You should refer to the full text of the Merger Agreement for details of the merger and the terms and conditions of the Merger Agreement.

The Merger Agreement contains representations and warranties that Syros and Merger Sub, on the one hand, and Tyme, on the other hand, have made to one another as of specific dates. These representations and warranties have been made for the benefit of the other parties to the Merger Agreement and may be intended not as statements of fact but rather as a way of allocating the risk to one of the parties if those statements prove to be incorrect. In addition, the assertions embodied in the representations and warranties are qualified by information in confidential disclosure schedules exchanged by the parties in connection with signing the Merger Agreement. While Syros and Tyme do not believe that these disclosure schedules contain information required to be publicly disclosed under the applicable securities laws, other than information that has already been so disclosed, the disclosure schedules do contain information that modifies, qualifies and creates exceptions to the representations and warranties set forth in the attached Merger Agreement. Accordingly, you should not rely on the representations and warranties as current characterizations of factual information about Syros or Tyme, because they were made as of specific dates, may be intended merely as a risk allocation mechanism between Syros, Merger Sub and Tyme and are modified by the disclosure schedules.

Structure

Subject to the terms and conditions of the Merger Agreement, and in accordance with Delaware law, at the completion of the merger, Merger Sub, a wholly owned subsidiary of Syros formed by Syros in connection with the merger, will merge with and into Tyme, with Tyme surviving as a wholly owned subsidiary of Syros.

Completion and Effectiveness of the Merger

The merger will be completed as promptly as practicable after all of the conditions to completion of the merger are satisfied or waived, including the receipt of the required approvals by the stockholders of Syros and Tyme. Syros and Tyme are working to complete the merger as quickly as practicable and expect that the merger will be completed in the second half of 2022, soon after the Syros special meeting of stockholders and the Tyme special meeting of stockholders, each of which is scheduled to be held on September 15, 2022. However, Syros and Tyme cannot predict the completion of the merger or the exact timing of the completion of the merger because it is subject to various conditions.

Merger Consideration

At the effective time, upon the terms and subject to the conditions set forth in the Merger Agreement, each share of Tyme common stock outstanding immediately prior to the effective time will be converted into the right to receive a number of shares of Syros common stock based on agreed upon ratio by the parties, or the Exchange Ratio. The Exchange Ratio was initially estimated to be 0.4312 shares of Syros common stock for each share of Tyme common stock, but the actual Exchange Ratio will depend on Tyme's net cash and the number of shares of Tyme common stock outstanding at the closing of the merger. The Exchange Ratio also does not give effect to the proposed reverse stock split of Syros common stock because the proposed reverse stock split is a range and is not final. Based upon the initially estimated exchange ratio, following the merger and giving effect to the PIPE Financing, (i) Syros securityholders immediately before the merger together with the investors in the PIPE Financing are expected to own approximately 63% of the aggregate number of outstanding shares of Syros

common stock following the merger and (ii) Tyme securityholders immediately before the merger are expected to own approximately 37% of the aggregate number of outstanding shares of Syros common stock following the merger, subject to certain assumptions (including as to the amount of Tyme net cash at closing, which could be materially different). Assuming the exercise of all Syros pre-funded warrants, including the Pre-Funded PIPE Warrants and the Pre-Funded 2020 Warrants, without giving effect to any beneficial ownership limitations applicable thereto, then (i) Syros securityholders immediately before the merger together with the investors in the PIPE Financing would own approximately 73% of the aggregate number of outstanding shares of Syros common stock following the merger and (ii) Tyme securityholders immediately before the merger would own approximately 27% of the aggregate number of outstanding shares of Syros common stock following the merger, subject to certain assumptions (including as to the amount of Tyme net cash at closing, which could be materially different). The foregoing percentages do not give effect to the exercise or conversion of outstanding stock options or warrants other than as set forth above.

Treatment of Syros Common Stock and Equity Awards

Each share of Syros common stock issued and outstanding at the time of the merger will remain issued and outstanding. In addition, each option to purchase shares of Syros common stock and each other equity award that covers Syros common stock that is outstanding immediately prior to the effective time of the merger, whether vested or unvested, will survive the closing and remain outstanding in accordance with its terms. The number of shares of Syros common stock underlying such options and the exercise prices for such stock options, and each other equity award that covers Syros common stock, will be appropriately adjusted to reflect the proposed reverse stock split, if the Syros reverse stock split proposal is approved and the Syros board of directors determines to effect the reverse stock split.

Treatment of Tyme Equity Awards and Warrants

As of the effective time, each option to purchase shares of Tyme common stock, each, a Tyme Option, that is outstanding and unexercised immediately prior to the effective time granted under Tyme equity-related plans, each, a Tyme Plan, to an individual who continues as a service provider to Tyme at the effective time, whether or not vested, will be, along with the Tyme Plan, assumed by Syros and will become an option to purchase solely that number of shares of Syros common stock equal to the product obtained by multiplying (i) the number of shares of Tyme common stock that were subject to such Tyme Option immediately prior to the effective time by the Exchange Ratio, and rounding the resulting number down to the nearest whole number of shares of Syros common stock. The per share exercise price for Syros common stock issuable upon exercise of each Tyme Option assumed by Syros shall be determined by dividing (a) the per share exercise price of Tyme common stock subject to such Tyme Option, as in effect immediately prior to the effective time, by (b) the Exchange Ratio, and rounding the resulting exercise price up to the nearest whole cent. Any restriction on the exercise of any Tyme Option assumed by Syros will continue in full force and effect and the term, exercisability, vesting schedule and other provisions of such Tyme Option shall otherwise remain unchanged. Any Tyme Option that is not assumed in accordance with the foregoing as of the effective time shall cease to exist and no consideration shall be delivered in exchange therefor; provided, such holders will be given notice of a 30 day period prior to the effective time of the merger in which such holders will be able to exercise their options.

It is anticipated that Tyme's executive officers will enter into cooperation agreements with Tyme that will, among other things, extend the exercise period for each assumed Tyme option with an exercise price of less than $2.00 per share of Tyme common stock that such executive officer holds as of immediately following closing of the merger to the second anniversary of such executive officer's termination date, or, if earlier, until the earliest of (i) the second anniversary of the effective time, (ii) the original expiration date of such option, and (iii) any earlier termination or cashing out of options at Syros generally applicable to its option holders. See the subsection titled "*The Merger—Interests of Tyme Directors and Executive Officers in the Merger—Cooperation Agreements*" in this joint proxy statement/prospectus for further details related to the cooperation agreements.

Furthermore, the warrant to purchase Tyme common stock issued by Tyme on May 20, 2020, or the 2020 Tyme Warrant, shall be purchased by Tyme from the holder thereof on the terms set forth in such warrant agreement

immediately prior to the effective time. At the effective time, each other warrant (other than the 2020 Tyme Warrant) to purchase shares of Tyme common stock that is outstanding and unexercised immediately prior to the effective time (such outstanding warrants being referred to herein as the Tyme Warrants) will be converted into and become a warrant to purchase (and Syros shall assume each such Tyme Warrant in accordance with its terms) solely that number of shares of Syros common stock equal to the product obtained by multiplying (i) the number of shares of Tyme common stock that were subject to such Tyme Warrant immediately prior to the effective time by (ii) the Exchange Ratio, and rounding the resulting number down to the nearest whole number of shares of Syros common stock. The per share exercise price for Syros common stock issuable upon exercise of each Tyme Warrant assumed by Syros shall be determined by dividing (a) the per share exercise price of Tyme common stock subject to such Syros Warrant, as in effect immediately prior to the effective time, by (b) the Exchange Ratio, and rounding the resulting exercise price up to the nearest whole cent. Any restriction on the exercise of any Tyme Warrant assumed by Syros will continue in full force and effect and the term, exercisability, vesting schedule and other provisions of such Tyme Warrant shall otherwise remain unchanged.

Fractional Shares

The Merger Agreement provides that no fractional shares of Syros common stock will be issued in connection with the merger, and no certificates or scrip for any such fractional shares will be issued and such fractional share interests shall not entitle the owner thereof to vote or to any other rights of a stockholder of Syros. Any fractional shares of Syros common stock resulting from the conversion of Tyme common stock into the right to receive a number of shares of Syros common stock equal to the exchange ratio (after aggregating all fractional shares of Syros common stock issuable to such holder) will be rounded down to the nearest whole share of Syros common stock, with cash being paid in lieu of such fractional shares of Syros common stock eliminated by such rounding.

Representations and Warranties

The Merger Agreement contains customary representations and warranties of Syros and Tyme for a transaction of this type relating to, among other things:

- due organization and subsidiaries;
- organizational documents;
- authority to enter into the Merger Agreement and the related agreements and the binding nature of the Merger Agreement;
- the vote required by Tyme stockholders to adopt the Merger Agreement and approve the contemplated transactions;
- the absence of certain conflicts and the consents required in connection with the Merger Agreement or the consummation of the transactions contemplated thereby;
- capitalization;
- financial statements, documents filed with the SEC and the accuracy of information contained in those documents;
- material changes or events;
- liabilities;
- title to assets;
- real property and leaseholds;
- IP;
- contracts;

- compliance with laws, permits and regulatory matters;
- litigation;
- tax matters;
- employee and labor matters; employee benefit plans;
- environmental matters;
- insurance;
- certain transactions or relationships with affiliates;
- financial advisors;
- privacy and data security;
- with respect to Syros, the valid issuance in the merger of Syros common stock; and
- with respect to Syros, representations relating to the PIPE Financing.

The representations and warranties are, in many respects, qualified by materiality and knowledge, and will not survive the merger, but their accuracy forms the basis of one of the conditions to the obligations of Syros and Tyme to complete the merger.

Covenants; Conduct of Business Pending the Merger

Syros has agreed that, except as permitted by the Merger Agreement or unless Tyme has provided written consent, during the period commencing on the date of the Merger Agreement and continuing until the earlier to occur of the effective time and the termination of the Merger Agreement, Syros and its subsidiaries will use commercially reasonable efforts to conduct their business and operations in the ordinary course of business consistent in all material respects with past practice taking into account any acts or omissions that have been taken to comply with any quarantine, "shelter in place", "stay at home", workforce reduction, social distancing, shutdown, closure, sequester or any other law, order, guideline or recommendation by any governmental authority in connection with or in response to the COVID-19 pandemic, and in compliance with all applicable laws, regulations and certain contracts, and to maintain and preserve its and each of its subsidiaries' business organization, assets and properties, keep available the services of its present officers and certain key employees, and preserve its advantageous business relationships with customers, strategic partners, suppliers, distributors and others. Syros has also agreed that, subject to certain limited exceptions, without the consent of Tyme, it will not, and will not cause or permit any of its subsidiaries to, during the period commencing on the date of the Merger Agreement and continuing until the earlier to occur of the effective time and the termination of the Merger Agreement:

- (i) subject to certain exceptions, declare, set aside or pay any dividends on, or make any other distributions in respect of, any of its capital stock; (ii) except as contemplated by the increase of authorized shares contemplated by the Merger Agreement, split, combine or reclassify any of its capital stock or issue or authorize the issuance of any other securities in respect of, in lieu of or in substitution for shares of its capital stock or any of its other securities; or (iii) subject to certain exceptions, purchase, redeem or otherwise acquire any shares of its capital stock or any other of its securities or any rights, warrants or options to acquire any such shares or other securities;
- subject to certain exceptions (including in connection with the PIPE Financing), issue, deliver, sell, grant, pledge or otherwise dispose of or encumber any shares of its capital stock, any other voting securities or any securities convertible into or exchangeable for, or any rights, warrants or options to acquire, any such shares, voting securities or convertible or exchangeable securities;
- except as contemplated by the increase of authorized shares contemplated by the Merger Agreement, amend its certificate of incorporation, bylaws or other comparable charter or organizational documents

or effect or be a party to any merger, consolidation, share exchange, business combination, recapitalization, reclassification of shares, stock split or reverse stock split or form any new subsidiary or acquire any equity interest or other interest in any other person;

- subject to certain exceptions, acquire (i) by merging or consolidating with, or by purchasing all or a substantial portion of the assets or any stock of, or by any other manner, any business or any corporation, partnership, joint venture, limited liability company, association or other business organization or division thereof or (ii) any assets, except for purchases of inventory and raw materials in the ordinary course of business, that are material, in the aggregate, to Syros and its subsidiaries, taken as a whole;
- except in the ordinary course of business and in certain other circumstances, sell, lease, license, pledge, or otherwise dispose of or encumber any properties or assets of Syros or any of its subsidiaries;
- subject to certain exceptions, sell, dispose of or otherwise transfer any assets material to Syros and its subsidiaries, taken as a whole;
- (i) incur or suffer to exist any indebtedness for borrowed money or guarantee any such indebtedness of another person, (ii) issue, sell or amend any debt securities or warrants or other rights to acquire any debt securities of Syros or any of its subsidiaries, guarantee any debt securities of another person, enter into any "keep well" or other agreement to maintain any financial statement condition of another person or enter into any arrangement having the economic effect of any of the foregoing, (iii) make any loans, advances (other than routine advances to employees of Syros in the ordinary course of business pursuant to Syros employee benefit plans) or capital contributions to, or investment in, any other person, other than Syros or any of its direct or indirect wholly owned subsidiaries or (iv) enter into any hedging agreement or other financial agreement or arrangement designed to protect Syros or its subsidiaries against fluctuations in commodities prices or exchange rates;
- subject to certain exceptions, make any capital expenditures or other expenditures with respect to property, plant or equipment for Syros and its subsidiaries in excess of $500,000 in the aggregate for Syros and its subsidiaries, taken as a whole;
- make any changes in accounting methods, principles or practices, except insofar as may have been required by the SEC or a change in GAAP or, except as so required, change any assumption underlying, or method of calculating, any bad debt, contingency or other reserve;
- subject to certain exceptions, (i) modify or amend in any material respect, or terminate, any material contract or agreement to which Syros or any of its subsidiaries is party, or (ii) knowingly waive, release or assign any material rights or claims;
- terminate the PIPE Financing securities purchase agreement or make certain amendments thereto;
- subject to certain exceptions, (i) enter into any material contract or agreement relating to the rendering of services or the distribution, sale or marketing by third parties of the products, of, or products licensed by, Syros or any of its subsidiaries or (ii) license any material IP rights to or from any third party;
- subject to certain exceptions, (i) take any action with respect to, adopt, enter into, terminate or amend any employment, severance or similar agreement or benefit plan for the benefit or welfare of any current or former director, officer, employee or consultant or any collective bargaining agreement, (ii) increase in any material respect the compensation or fringe benefits of, or pay any material bonus to, any director, officer, employee or consultant, (iii) amend or accelerate the payment, right to payment or vesting of any compensation or benefits, including any outstanding equity or equity-based incentive awards, (iv) pay any material benefit not provided for as of the date of the Merger Agreement under any Syros employee plan, (v) grant any awards under any Syros employee plan (or under any benefit or compensation plan, program, policy, agreement or arrangement subject to certain limitations), or (vi) take any action to fund or in any other way secure the payment of compensation or

benefits under any Syros employee plan (or under any other employee benefit or compensation plan, program, policy, agreement or arrangement subject to certain limitations);

- make or change any material tax election, change an annual accounting period, enter into any closing agreement, waive or extend any statute of limitations with respect to taxes, settle or compromise any material tax liability, claim or assessment, surrender any right to claim a refund of material taxes, or amend any income or other material tax return;
- commence any offering of shares of Syros common stock pursuant to any employee stock purchase plan;
- initiate, compromise or settle any material litigation or arbitration proceeding;
- open or close any facility or office;
- fail to use commercially reasonable efforts to maintain insurance at levels substantially comparable to levels existing as of the date of the Merger Agreement;
- suspend any clinical trials sponsored by Syros or involving any products marketed or in development by Syros;
- fail to pay accounts payable and other obligations in the ordinary course of business; or
- authorize any of, or commit or agree, in writing or otherwise, to take any of, the foregoing actions or any action that would make any representation or warranty of Syros in the Merger Agreement untrue or incorrect in any material respect, or would materially impair, delay or prevent the satisfaction of any conditions to obligations of the parties to effect the Merger.

Tyme has agreed that, except as permitted by the Merger Agreement (including as described below under "*—Pre-Closing Tyme Asset Transactions*"), as required by law, or unless Syros shall have provided written consent, during the period commencing on the date of the Merger Agreement and continuing until the earlier to occur of the effective time and the termination of the Merger Agreement, Tyme will, and shall cause each of its subsidiaries to, use commercially reasonable efforts to conduct its business and operations in the ordinary course of business and in compliance with all applicable laws, regulations and certain contracts, and to maintain and preserve its and each of its subsidiaries' business organization, assets and properties, keep available the services of its present officers and certain key employees, and preserve its advantageous business relationships with customers, strategic partners, suppliers, distributors and others. Tyme has also agreed that, subject to certain limited exceptions, without the consent of Syros, it will not, during the period commencing on the date of the Merger Agreement and continuing until the earlier to occur of the effective time and the termination of the Merger Agreement:

- (i) subject to certain exceptions, declare, set aside or pay any dividends on, or make any other distributions in respect of, any of its capital stock; (ii) split, combine or reclassify any of its capital stock or issue or authorize the issuance of any other securities in respect of, in lieu of or in substitution for shares of its capital stock or any of its other securities; or (iii) subject to certain exceptions, purchase, redeem or otherwise acquire any shares of its capital stock or any other of its securities or any rights, warrants or options to acquire any such shares or other securities;
- subject to certain exceptions, issue, deliver, sell, grant, pledge or otherwise dispose of or encumber any shares of its capital stock, any other voting securities or any securities convertible into or exchangeable for, or any rights, warrants or options to acquire, any such shares, voting securities or convertible or exchangeable securities;
- amend its certificate of incorporation, bylaws or other comparable charter or organizational documents or effect or be a party to any merger, consolidation, share exchange, business combination, recapitalization, reclassification of shares, stock split or reverse stock split or form any new subsidiary or acquire any equity interest or other interest in any other person;

- acquire (i) by merging or consolidating with, or by purchasing all or a substantial portion of the assets or any stock of, or by any other manner, any business or any corporation, partnership, joint venture, limited liability company, association or other business organization or division thereof or (ii) any assets that are material, in the aggregate, to Tyme and its subsidiaries, taken as a whole;
- whether or not in the ordinary course of business, sell, lease, license, pledge, or otherwise dispose of or encumber any material properties or assets of Tyme or any of its subsidiaries;
- subject to certain exceptions, sell, dispose of or otherwise transfer any assets material to Tyme and its subsidiaries, taken as a whole;
- (i) subject to certain exceptions, incur or suffer to exist any indebtedness for borrowed money or guarantee any such indebtedness of another person, (ii) issue, sell or amend any debt securities or warrants or other rights to acquire any debt securities of Tyme or any of its subsidiaries, guarantee any debt securities of another person, enter into any "keep well" or other agreement to maintain any financial statement condition of another person or enter into any arrangement having the economic effect of any of the foregoing, (iii) make any loans, advances (other than routine advances to employees of Tyme in the ordinary course of business pursuant to Tyme employee plans) or capital contributions to, or investment in, any other person, other than Tyme or any of its direct or indirect wholly owned subsidiaries or (iv) enter into any hedging agreement or other financial agreement or arrangement designed to protect Tyme or its subsidiaries against fluctuations in commodities prices or exchange rates;
- subject to certain exceptions, make any capital expenditures or other expenditures with respect to property, plant or equipment for Tyme and its subsidiaries, taken as a whole;
- make any changes in accounting methods, principles or practices, except insofar as may have been required by any change in GAAP or, except as so required, change any assumption underlying, or method of calculating, any bad debt, contingency or other reserve;
- subject to certain exceptions, (i) modify or amend in any material respect, or terminate, any material contract or agreement to which Tyme or any of its subsidiaries is party, or (ii) knowingly waive, release or assign any material rights or claims;
- except in the ordinary course of business, (i) enter into any material contract or agreement relating to the rendering of services or the distribution, sale or marketing by third parties of the products, of, or products licensed by, Tyme or any of its subsidiaries or (ii) license any material IP rights to or from any third party;
- except as required to comply with applicable law and subject to certain exceptions, (i) other than in the ordinary course of business, adopt, enter into, terminate or amend any Tyme employee plan (or any other employee benefit or compensation plan, program, policy, agreement or arrangement, subject to certain limitations) or any collective bargaining agreement, (ii) increase in any material respect the compensation or fringe benefits of, or pay any material bonus to, any director, officer, employee or consultant, (iii) amend or accelerate the payment, right to payment or vesting of any compensation or benefits, including any outstanding equity or equity-based incentive awards, (iv) pay any material benefit not provided for as of the date of the Merger Agreement under any Tyme employee plan, (v) grant any awards under any Tyme employee plan (or under any other employee benefit or compensation plan, program, policy, agreement or arrangement, subject to certain limitations), or (vi) take any action other than in the ordinary course of business to fund or in any other way secure the payment of compensation or benefits under any Tyme employee plan (or under any other employee benefit or compensation plan, program, policy, agreement or arrangement, subject to certain limitations);
- make or change any material tax election, change an annual accounting period, enter into any closing agreement, waive or extend any statute of limitations with respect to taxes, settle or compromise any

material tax liability, claim or assessment, surrender any right to claim a refund of material taxes, or amend any income or other material tax return;

- commence any offering of shares of Tyme common stock pursuant to any employee stock purchase plan;
- initiate, compromise or settle any material litigation or arbitration proceeding;
- open any facility or office, or close any facility or office without prior consultation with Syros;
- fail to use commercially reasonable efforts to maintain insurance at levels substantially comparable to levels existing as of the date of the Merger Agreement;
- fail to pay accounts payable and other obligations in the ordinary course of business;
- suspend any clinical trials sponsored by Tyme or involving any products marketed or in development by Tyme; or
- authorize any of, or commit or agree, in writing or otherwise, to take any of, the foregoing actions or any action that would make any representation or warranty of Tyme in the Agreement untrue or incorrect in any material respect, or would materially impair, delay or prevent the satisfaction of any conditions to obligations of the parties to effect the Merger.

Pre-Closing Tyme Asset Transactions

The Merger Agreement permits Tyme, with the prior written consent by Syros (which consent shall not be unreasonably withheld, conditioned or delayed) and subject to any required Tyme stockholder approval, to sell, assign, license, or otherwise dispose of, in one or more transactions, some or all of Tyme's clinical pipeline candidates, including but not limited to, SM-88 in all formulations, TYME-18 and TYME-19. Any proceeds of such disposition may be distributed as a dividend to Tyme's stockholders as of a record date prior to the closing of the merger or retained, with up to (but no more than) $5 million of such retained proceeds being included in the calculation of Tyme's net cash.

Non-Solicitation

Each of Syros and Tyme have agreed that, except as described below, Syros and Tyme and any of their respective subsidiaries will not, and each party and its subsidiaries will use reasonable best efforts to cause their respective directors, officers, members, employees, agents, attorneys, consultants, contractors, accountants, financial advisors or other representatives retained by it or any of its subsidiaries to not, directly or indirectly:

- solicit, seek or initiate or knowingly take any action to facilitate or encourage any offers, inquiries or the making of any proposal or offer that constitutes, or could reasonably be expected to lead to any Acquisition Proposal (as defined below);
- enter into, continue or otherwise participate or engage in any discussions or negotiations regarding any Acquisition Proposal, or furnish to any person any non-public information or afford any person other than Syros or Tyme, as applicable, access to such party's property, books or records (except pursuant to a request by a governmental entity) in connection with any offers, inquiries or the making of any proposal or offer that constitutes, or could reasonably be expected to lead to, any Acquisition Proposal;
- take any action to make the provisions of any takeover statute inapplicable to any transactions contemplated by an Acquisition Proposal; or
- publicly propose to do any of the foregoing.

An "Acquisition Proposal" means, with respect to Syros or Tyme, (a) any inquiry, proposal or offer for a merger, consolidation, conversion, dissolution, sale of substantial assets, recapitalization, share exchange, tender offer or

other business combination involving such party and its subsidiaries, other than mergers, consolidations, conversions, recapitalizations, share exchanges or other business combinations involving solely such party and/or one or more subsidiaries of such party, (b) any proposal for the issuance by such party of 15% or more of its equity securities, or (c) any proposal or offer to acquire in any manner, directly or indirectly, 15% or more of the equity securities or consolidated total assets of such party and its subsidiaries, in each case other than the transactions contemplated by the Merger Agreement, other than, with respect to Syros, the PIPE Financing.

Notwithstanding the foregoing, before the earlier of the effective time of the merger and either party obtaining the applicable approvals of the Syros stockholders or Tyme stockholders required pursuant to the Merger Agreement, each party may furnish non-public information regarding such party and its subsidiaries to, and may engage in discussions or negotiations with, any third party making an unsolicited Acquisition Proposal, which such party's board of directors determines in good faith, after consultation with such party's outside financial advisors and outside legal counsel, constitutes or is reasonably expected to lead to a Superior Proposal (as defined below) and which Acquisition Proposal has not resulted from a material breach by such party of its obligations under Sections 6.1(a) or 6.1(e) of the Merger Agreement, if:

- neither such party nor any representative of such party has materially breached the non-solicitation provisions of the Merger Agreement described above;
- such party's board of directors has determined, after consultation with outside financial advisors and outside legal counsel, that the failure to take such actions would reasonably be expected to be inconsistent with the fiduciary duties of such board of directors under applicable legal requirements; and
- such party receives from the third party an executed confidentiality agreement containing provisions at least as favorable to such party as those contained in the confidentiality agreement between Syros and Tyme.

A "Superior Proposal" means, with respect to Syros or Tyme, any bona fide, unsolicited written proposal made by a third party to acquire 50% or more of the equity securities or consolidated total assets of such party and its subsidiaries, pursuant to a tender or exchange offer, a merger, a consolidation, conversion, business combination or recapitalization or a sale or exclusive license of its assets, (a) on terms which the board of directors of such party determines in its good faith judgment to be more favorable to the holders of such party's capital stock than the transactions contemplated by the Merger Agreement, after consultation with its financial and legal advisors, taking into account all the terms and conditions of such proposal and the Merger Agreement (including any termination or break-up fees and conditions to consummation, as well as any written, binding offer by the other party hereto to amend the terms of the Merger Agreement, which offer is not revocable for at least four business days) that the board of directors of such party determines to be relevant, and (b) which board of directors of such party has determined to be reasonably capable of being completed on the terms proposed, taking into account all financial, regulatory, legal and other aspects of such proposal that the board of directors of such party determines to be relevant (including the likelihood and timing of consummation as compared to the transactions contemplated by the Merger Agreement); provided, however, an upsized or modified PIPE Financing or any private placement or offering of securities for cash or similar cash-raising transaction by Syros shall not be considered a Superior Proposal.

The Merger Agreement also provides that each party will promptly advise the other of the status and terms of, and keep the other party reasonably informed with respect to, any Acquisition Proposal or any material change or proposed material change to that Acquisition Proposal. In addition to the foregoing, each party must provide the other party with written notice of any determination by its board of directors to consider any Acquisition Proposal, to enter into discussions or negotiations concerning any Acquisition Proposal, to provide non-public information with respect to such to any person, or that such Acquisition Proposal constitutes a Superior Proposal.

Board Recommendation Change

Subject to specified exceptions described in the Merger Agreement and summarized below, Syros agreed that its board of directors may not take any of the following actions, each of which are referred to in this joint proxy statement/prospectus as a Syros board recommendation change:

- withhold, withdraw or modify, or publicly propose to withhold, withdraw or modify, the approval or recommendation of the Syros board of directors with respect to the Share Issuance or Syros Authorized Stock Increase (as such terms are defined in the Merger Agreement);
- fail to recommend against acceptance of a tender offer within ten business days after commencement; or
- publicly propose to adopt, approve or recommend any Acquisition Proposal.

Subject to specified exceptions described in the Merger Agreement and summarized below, Tyme agreed that its board of directors may not take any of the following actions, each of which are referred to in this proxy statement/prospectus as a Tyme board recommendation change:

- withhold, withdraw or modify, or publicly propose to withhold, withdraw or modify, the approval or recommendation of Tyme's board of directors with respect to the merger;
- fail to recommend against acceptance of a tender offer within ten business days after commencement; or
- publicly propose to adopt, approve or recommend any Acquisition Proposal.

Tyme's board of directors may nevertheless effect a Tyme board recommendation change and Syros' board of directors may nevertheless effect a Syros board recommendation change in response to either (1) a Superior Proposal (as described above) or (2) an Intervening Event, subject to satisfaction of the following conditions:

1. such board of directors shall have determined (after consultation with its outside financial advisors and outside legal counsel) that the failure to effect such board recommendation would be inconsistent with its fiduciary obligations under applicable law;
2. such party has provided at least four business days prior written notice to the other party that it intends to effect a board recommendation change;
3. such party has complied in all material respects with the requirements of the merger agreement limiting solicitation of Acquisition Proposals or a board recommendation change; and
4. such party's board of directors shall have determined (after consultation with its outside financial advisors and outside legal counsel), after considering the terms of any counteroffer by the other party, that the failure to effect a board recommendation change would be inconsistent with its fiduciary duties under applicable Law.

The merger agreement defines an "Intervening Event" as an effect, change, event, circumstance or development not resulting from a material breach of this Agreement or the Securities Purchase Agreement by the party seeking to claim an Intervening Event and that (a) was not known to or reasonably foreseeable by Syros' board of directors (with respect to a Syros board recommendation change) or Tyme's board of directors (with respect to a Tyme board recommendation change) (or, to the extent known or reasonably foreseeable, the consequences of which were not known or reasonably foreseeable) and (b) does not relate to an Acquisition Proposal.

Disclosure Documents

As promptly as practical after the execution of the Merger Agreement, Syros and Tyme have agreed to jointly prepare and cause to be filed this joint proxy statement/prospectus with the SEC. Each of Tyme, Merger Sub and

Syros have agreed to provide to the other parties as promptly as practical all information, including financial statements and descriptions of its business and financial condition, as such other parties may reasonably request for preparation of this joint proxy statement/prospectus and to cause the timely cooperation of its independent public accountants in connection with the preparation and filing of this joint proxy statement/prospectus. Each of Tyme, Merger Sub and Syros has agreed to respond to any comments of the SEC and to use its reasonable best efforts to have this joint proxy statement/prospectus declared effective under the Securities Act as promptly as practicable after filing, and it has agreed to cause this joint proxy statement/prospectus to be mailed to its stockholders at the earliest practicable time after it is declared effective under the Securities Act. Each of Tyme and Syros has also agreed to (i) inform the other promptly upon the receipt of any comments from the SEC or its staff and of any request by the SEC or its staff for amendments or supplements to this joint proxy statement/prospectus, (ii) supply the other with copies of all correspondence between such party or any of its representatives, on the one hand, and the SEC, or its staff, on the other hand, with respect to this Registration Statement, this joint proxy statement/prospectus, the merger or any similar filing pursuant to the Merger Agreement and (iii) use its reasonable best efforts to respond as promptly as practicable to any comments from the SEC with respect to this Registration Statement, this joint proxy statement/prospectus, the merger or any similar such filing pursuant to the Merger Agreement. Each of Tyme and Syros has agreed to use commercially reasonable efforts to cause all documents that it is responsible for filing with the SEC under the Merger Agreement to comply in all material respects with all applicable requirements of law and the rules and regulations promulgated thereunder. Each of Syros and Tyme has agreed to promptly inform the other party of such party becoming aware of any event or information that pursuant to certain laws, rules and statutes should be disclosed in an amendment or supplement to the Registration Statement or joint proxy statement/prospectus, as the case may be, and cooperate with the other party in filing such amendment or supplement with the SEC, and, if appropriate, in mailing such amendment or supplement to the Syros and/or Tyme stockholders.

Meetings of Syros' Stockholders and Tyme's Stockholders

Each of Syros and Tyme is obligated under the Merger Agreement to take all action necessary under applicable law, its certificate of incorporation and bylaws, and Nasdaq rules to duly call, give notice of, convene and hold a meeting of the holders of its common stock for the purpose of considering and voting to approve the proposals. Each of the Syros special meeting and the Tyme special meeting will be held as promptly as practicable after the registration statement on Form S-4 is declared effective under the Securities Act, and in any event no later than 45 days after the effective date of the registration statement on Form S-4.

Indemnification and Insurance for Directors and Officers

Under the Merger Agreement, from the effective time of the merger through the sixth anniversary of the date on which effective time occurs, Syros and the surviving corporation in the merger agreed to indemnify and hold harmless each person who was at the time of the execution of the Merger Agreement, or has been at any time prior to the date of the Merger Agreement, or who becomes prior to the effective time of the merger, a director or officer of Syros or Tyme or any of their respective subsidiaries, against all claims, losses, liabilities, damages, judgments, fines and reasonable fees, costs and expenses, including attorneys' fees and disbursements, incurred in connection with any claim, action, suit, proceeding or investigation, whether civil, criminal, administrative or investigative, arising out of or pertaining to the fact that the indemnified officer or director is or was a director or officer of Syros or of Tyme or any of their respective subsidiaries, whether asserted or claimed prior to, at or after the effective time, to the fullest extent permitted by applicable law. From and after the effective time of the merger, Syros and the surviving corporation in the merger will also fulfill Syros' and Tyme's indemnity obligations, respectively, to each person who is, has been, or who becomes prior to the effective time of the merger, a director or officer of Syros or Tyme.

The Merger Agreement also provides that the provisions of the amended and restated certificate of incorporation and amended and restated bylaws of Tyme with respect to indemnification, advancement of expenses and exculpation of present and former directors and officers of Syros and Tyme that are presently set forth therein

will not be amended, modified or repealed for a period of six years from the effective time of the merger in a manner that would adversely affect the rights thereunder of individuals who, at or prior to the effective time of the merger, were officers or directors of Syros, unless such modification is required by applicable law. The amended and restated certificate of incorporation and amended and restated bylaws of the surviving corporation will contain, and Syros will cause the amended and restated certificate of incorporation and amended and restated bylaws of the surviving corporation to so contain, provisions no less favorable with respect to indemnification, advancement of expenses and elimination of liability for monetary damages as those presently set forth in the certificates of incorporation and bylaws of Tyme and Syros immediately prior to the effective time.

Syros will secure and purchase a six year "tail policy" on Syros' and Tyme's respective existing directors' and officers' liability insurance policies with an effective date as of the date of the closing.

Additional Agreements

Each of Syros and Tyme has agreed to use its commercially reasonable efforts to cause to be taken all actions necessary to consummate the merger and the other transactions contemplated by the Merger Agreement. In connection therewith, each party has agreed to use reasonable best efforts to:

- take, or cause to be taken, all actions, and do, or cause to be done, and to assist and cooperate with the other parties in doing, all things necessary, proper or advisable to consummate and make effective the transactions contemplated by the Merger Agreement and the PIPE Financing as promptly as practicable;
- as promptly as practicable, obtain from any governmental entity or any other third party any consents, licenses, permits, waivers, approvals, authorizations, or orders required to be obtained or made by Syros or Tyme or any of their subsidiaries in connection with the authorization, execution and delivery of the Merger Agreement and the consummation of the transactions contemplated by the Merger Agreement and the PIPE Financing;
- as promptly as practicable, make all necessary filings, and thereafter make any other required submissions, with respect to the Merger Agreement and the merger required under applicable law; and
- execute or deliver any additional instruments necessary to consummate the transactions contemplated by, and to fully carry out the purposes of, the Merger Agreement.

Pursuant to the Merger Agreement, Syros and Tyme have further agreed that:

- Each of Syros and Tyme will use its commercially reasonable efforts to continue the listing of Syros common stock and Tyme common stock, respectively, on Nasdaq during the term of the Merger Agreement and to cause the shares of Syros common stock being issued in the merger to be approved for listing (subject to notice of issuance) on Nasdaq at or prior to the effective time.
- Tyme will cooperate with Syros with respect to the listing application for the Syros common stock and promptly furnish to Syros all information concerning Tyme and its stockholders that may be required or reasonably requested in connection with the Nasdaq listing.

Syros Nasdaq Listing; Delisting of Tyme Common Stock

Shares of Syros common stock are currently listed on The Nasdaq Global Select Market under the symbol "SYRS." Syros has agreed to use commercially reasonable efforts to cause the shares of Syros common stock being issued in the merger to be approved for listing (subject to notice of issuance) on The Nasdaq Global Select Market at or prior to the effective time.

In addition, under the Merger Agreement, each of Syros' and Tyme's obligation to complete the merger is subject to the satisfaction or waiver by each of the parties, at or prior to the merger, of various conditions, including that the shares of Syros common stock to be issued in the merger have been approved for listing (subject to official notice of issuance) on Nasdaq as of the closing of the merger.

Syros anticipates that the common stock of the combined company will be listed on The Nasdaq Global Select Market following the closing of the merger under the trading symbol "SYRS."

Following the effective time, Tyme will undertake to delist the Tyme common stock from The Nasdaq Capital Market.

Directors and Officers of Syros Following the Merger

Each of the current directors and executive officers of Syros is expected to continue as a director of the combined company after the effective time. In addition, effective upon the closing of the merger, Tyme will have the right to designate one member of the Syros board of directors and investors in the PIPE Financing will have the right to designate up to two members of the Syros board of directors, who will each be eligible to be compensated as a non-employee director of Syros pursuant to the Syros director compensation program.

SM-88 Following the Merger

Syros has agreed to explore and consider in good faith the viability of continuing to develop theSM-88 assets (to the extent they are not sold or out-licensed prior to the closing, as contemplated under "*Pre-Closing Tyme Asset Transactions*" above) in parallel with Syros' other drug candidates or the sale or out-license of SM-88, in each case with a view toward maximizing stockholder value.

Conditions to the Completion of the Merger

Each party's obligation to complete the merger is subject to the satisfaction or waiver by each of the parties, at or prior to the closing, of various conditions, which include the following:

- the adoption of the Merger Agreement shall have been approved at a meeting of Tyme's stockholders, at which a quorum is present, by the requisite vote of the stockholders of Tyme under applicable law and Tyme's Certificate of Incorporation. The share issuance in connection with the merger shall have been approved at a meeting of Syros' stockholders, at which a quorum is present, by the requisite vote of the stockholders of Syros under applicable law and stock market regulations;
- other than the filing of the certificate of merger, all authorizations, consents, orders or approvals of, or declarations or filings with, or expirations of waiting periods imposed by, any governmental entity in connection with the merger, the PIPE Financing and the consummation of the other transactions contemplated by the Merger Agreement, the failure of which to file, obtain or occur is reasonably likely to have a material adverse effect on Syros or Tyme, shall have been filed, been obtained or occurred on terms and conditions that would not reasonably be likely to have a material adverse effect on Syros or Tyme;
- the registration statement on Form S-4, of which this joint proxy statement/prospectus is a part shall have become effective under the Securities Act and no stop order suspending the effectiveness of the registration statement shall have been issued and no proceeding for that purpose, and no similar proceeding with respect to this joint proxy statement/prospectus, shall have been initiated or threatened in writing by the SEC or its staff;
- no governmental authority of competent jurisdiction shall have enacted, issued, promulgated, enforced or entered any order, executive order, stay, decree, judgment or injunction (preliminary or permanent) or statute, rule or regulation which is in effect and which has the effect of making the merger illegal or otherwise prohibiting consummation of the merger;
- the approval of the listing of the additional shares of Syros common stock on Nasdaq will have been obtained and the shares of Syros common stock to be issued in the merger pursuant to the Merger Agreement will have been approved for listing (subject to official notice of issuance) on Nasdaq; and

- Tyme's net cash shall have been finally determined in accordance with the Merger Agreement, and such Tyme net cash shall exceed $50.0 million as of the closing date of the merger (excluding the amount by which such Tyme net cash was increased or any litigation losses).

In addition, the obligation of Syros and Merger Sub to complete the merger is further subject to the satisfaction or waiver of the following conditions:

- the representations and warranties regarding certain matters related to due organization and subsidiaries, organizational documents, authority to enter into the Merger Agreement and the related agreements and the binding nature of the Merger Agreement, the vote required by Tyme stockholders to adopt the Merger Agreement and approve the contemplated transactions, the absence of certain conflicts and the consents required in connection with the Merger Agreement or the consummation of the transactions contemplated thereby, certain capitalization matters and material changes or events must be true and correct on the date of the Merger Agreement and on the closing date of the merger with the same force and effect as if made on the date on which the merger is to be completed or, if such representations and warranties address matters as of a particular date, then as of that particular date;
- the representations and warranties regarding certain capitalization matters of Tyme in the Merger Agreement must be true and correct on the date of the Merger Agreement and on the closing date of the merger with the same force and effect as if made on the date on which the merger is to be completed or, if such representations and warranties address matters as of a particular date, then as of that particular date, except for such inaccuracies which are de minimis, in the aggregate;
- the remaining representations and warranties of the other party in the Merger Agreement must be true and correct on the date of the Merger Agreement and on the closing date of the merger with the same force and effect as if made on the date on which the merger is to be completed or, if such representations and warranties address matters as of a particular date, then as of that particular date, except in each case, or in the aggregate, where the failure to be so true and correct would not reasonably be expected to have a material adverse effect on Tyme (without giving effect to any references therein to materiality qualifications);
- Tyme must have performed in all material respects all obligations required to be performed by it under the Merger Agreement on or prior to the closing date;
- no material adverse effect on Tyme shall have occurred since the date of the Merger Agreement; and
- Syros must have received an officers' certificate duly executed by Tyme's chief executive officer and chief financial officer to the effect that certain closing conditions have been satisfied.

In addition, the obligation of Tyme to complete the merger is further subject to the satisfaction or waiver of the following conditions:

- the representations and warranties regarding certain matters related to due organization and subsidiaries, organizational documents, authority to enter into the Merger Agreement and the related agreements and the binding nature of the Merger Agreement, the vote required by Tyme stockholders to adopt the Merger Agreement and approve the contemplated transactions, the absence of certain conflicts and the consents required in connection with the Merger Agreement or the consummation of the transactions contemplated thereby, certain capitalization matters and material changes or events must be true and correct on the date of the Merger Agreement and on the closing date of the merger with the same force and effect as if made on the date on which the merger is to be completed or, if such representations and warranties address matters as of a particular date, then as of that particular date;
- the representations and warranties regarding certain capitalization matters of Syros in the Merger Agreement must be true and correct on the date of the Merger Agreement and on the closing date of the merger with the same force and effect as if made on the date on which the merger is to be completed or, if such representations and warranties address matters as of a particular date, then as of that particular date, except for such inaccuracies which are de minimis, in the aggregate;

- the remaining representations and warranties of the other party in the Merger Agreement must be true and correct on the date of the Merger Agreement and on the closing date of the merger with the same force and effect as if made on the date on which the merger is to be completed or, if such representations and warranties address matters as of a particular date, then as of that particular date, except in each case, or in the aggregate, where the failure to be so true and correct would not reasonably be expected to have a material adverse effect on Syros (without giving effect to any references therein to materiality or material adverse effect qualifications);
- Syros must have performed in all material respects all obligations required to be performed by it under the Merger Agreement on or prior to the closing date;
- no material adverse effect on Syros shall have occurred since the date of the Merger Agreement;
- the securities purchase agreement related to the PIPE Financing must be in full force and effect and all conditions precedent to the PIPE Financing shall have been completed in accordance with the terms thereof or waived, and the PIPE Financing shall be completed substantially concurrently with the Merger with gross proceeds to Syros of at least $100 million;
- Tyme's director nominee shall have been appointed to Syros' board of directors, subject to Tyme's compliance with certain requirements under the Merger agreement; and
- Tyme must have received an officers' certificate duly executed by Syros' chief executive officer and chief financial officer to the effect that certain closing conditions have been satisfied.

With respect to Tyme, a "material adverse effect" for purposes of the Merger Agreement means any effect, change, event, circumstance or development, or an Effect, that, individually or in the aggregate with all other Effects that have occurred through the date of determination, has had, or is reasonably likely to have, a material adverse effect on the assets, liabilities or financial condition of Tyme and its subsidiaries, taken as a whole; provided, however, that no Effect, to the extent resulting from or arising out of any of the following, shall be deemed to be a material adverse effect or be taken into account for purposes of determining whether a material adverse effect has occurred or is reasonably likely to occur:

- adverse developments in Tyme's clinical pipeline that have been disclosed in Tyme's SEC reports as of the date of the Merger Agreement;
- changes after the date of the Merger Agreement in prevailing economic or market conditions in the United States or any other jurisdiction in which such entity has substantial business operations (except
- to the extent those changes have a disproportionate effect on Tyme and its subsidiaries relative to the other participants in their industries);
- changes or events after the date of the Merger Agreement affecting the industry or industries in which Tyme and its subsidiaries operate generally (except to the extent those changes or events have a disproportionate effect on Tyme and its subsidiaries relative to the other participants in their industries);
- changes after the date of the Merger Agreement in GAAP or requirements (except to the extent those changes have a disproportionate effect on Tyme and its subsidiaries relative to the other participants in their industries);
- changes after the date of the Merger Agreement in laws, rules or regulations of general applicability or interpretations thereof by any governmental entity (except to the extent those changes have a disproportionate effect on Tyme and its subsidiaries relative to the other participants in their industries);
- any natural disaster, epidemic, pandemic or other disease outbreak (including the COVID-19 pandemic) or any outbreak of major hostilities in which the United States is involved or any act of terrorism within the United States or directed against its facilities or citizens wherever located (except

to the extent those changes or events have a disproportionate effect on Tyme and its subsidiaries relative to the other participants in their industries);

- a change in the public trading price of Tyme common stock or the implications hereof;
- a change in the trading volume of Tyme common stock due to the announcement of the Merger Agreement or the pendency of the transactions contemplated by the Merger Agreement (including the PIPE Financing);
- any failure by Tyme to meet any public estimates or expectations of Tyme's revenue, earnings or other financial performance or results of operations for any period, or
- any failure by Tyme to meet any internal guidance, budgets, plans or forecasts of its revenues, earnings or other financial performance or results of operations (but not the underlying cause of such changes or failures, unless such changes or failures would otherwise be excepted from the definition of material adverse effect).

With respect to Syros, a "material adverse effect" for purposes of the Merger Agreement means any Effect that, individually or in the aggregate with all other Effects that have occurred through the date of determination, has had, or is reasonably likely to have, a material adverse effect on the business, assets, liabilities, capitalization, financial condition or results of operations of Syros and its subsidiaries, taken as a whole; provided, however, that no Effect, to the extent resulting from or arising out of any of the following, shall be deemed to be a material adverse effect or be taken into account for purposes of determining whether a material adverse effect has occurred or is reasonably likely to occur:

- adverse developments in Syros' clinical pipeline that have been disclosed in Syros' SEC reports as of the date of the Merger Agreement;
- changes after the date of the Merger Agreement in prevailing economic or market conditions in the United States or any other jurisdiction in which such entity has substantial business operations (except to the extent those changes have a disproportionate effect on Syros and its subsidiaries relative to the other participants in their industries);
- changes or events after the date of the Merger Agreement affecting the industry or industries in Syros and its subsidiaries operate generally (except to the extent those changes or events have a disproportionate effect on Syros and its subsidiaries relative to the other participants in their industries);
- changes after the date of the Merger Agreement in GAAP or requirements (except to the extent those changes have a disproportionate effect on Syros and its subsidiaries relative to the other participants in their industries);
- changes after the date of the Merger Agreement in laws, rules or regulations of general applicability or interpretations thereof by any governmental entity (except to the extent those changes have a disproportionate effect on Syros and its subsidiaries relative to the other participants in their industries);
- any natural disaster, epidemic, pandemic or other disease outbreak (including the COVID-19 pandemic) or any outbreak of major hostilities in which the United States is involved or any act of terrorism within the United States or directed against its facilities or citizens wherever located (except to the extent those changes or events have a disproportionate effect on Syros and its subsidiaries relative to the other participants in the industry or industries in which Syros and its subsidiaries operate);
- a change in the public trading price of Syros common stock or the implications hereof;
- a change in the trading volume of Syros common stock due to the announcement of the Merger Agreement or the pendency of the transactions contemplated by the Merger Agreement (including the PIPE Financing);

- any failure by Syros to meet any public estimates or expectations of Syros' revenue, earnings or other financial performance or results of operations for any period; or
- any failure by Syros to meet any internal guidance, budgets, plans or forecasts of its revenues, earnings or other financial performance or results of operations (but not the underlying cause of such failure, unless such changes or failures would otherwise be excepted from the definition of material adverse effect).

Termination

Termination of the Merger Agreement

The Merger Agreement may be terminated at any time before the effective time of the merger, whether before or (subject to the terms of the Merger Agreement) after the required stockholder approvals to complete the merger have been obtained, as set forth below:

(a) by mutual written consent of Syros and Tyme;

(b) by either Syros or Tyme, if the merger has not been consummated by December 31, 2022; *provided*, *however*, that this right to terminate the Merger Agreement will not be available to any party whose action or failure to act has been a principal cause of or resulted in the failure of the merger to occur on or before December 31, 2022;

(c) by either Syros or Tyme, if a court of competent jurisdiction or governmental entity has issued a final andnon-appealable order, decree or ruling or taken any other action that permanently restrains, enjoins or otherwise prohibits the merger; *provided*, *however*, that this right to terminate the Merger Agreement will not be available to any party if the issuance of any such order, decree, ruling or other action is attributable to the failure of such party, or any affiliate of such party, to perform in any material respect any covenant in the Merger Agreement required to be performed by such party, or any affiliate of such party, at or prior to the effective time of the merger;

(d) by either Syros or Tyme, if at the Syros special meeting (including any adjournment or postponement) at which and Syros stockholders have taken a vote on the share issuance in connection with the Merger, and such proposal has not been approved by the Syros stockholders;

(e) by Syros, at any time prior to the approval by Tyme stockholders of the adoption of the Merger Agreement, if any of the following circumstances shall occur:

- Tyme's board of directors has failed to include its recommendation to the approval of the adoption of the Merger Agreement or has withdrawn or modified its recommendation in a manner adverse to Syros;
- after the receipt by Tyme of an Acquisition Proposal, Syros requests in writing that Tyme reconfirm its recommendation of the approval of the adoption of the Merger Agreement and Tyme's board of directors fails to do so within ten business days after receipt of the request;
- Tyme's board of directors has approved or recommended to the stockholders of Tyme an Acquisition Proposal and has not withdrawn such approval or recommendation;
- a tender offer or exchange offer for outstanding shares of Tyme common stock is commenced, other than by Syros or an affiliate of Syros, and Tyme's board of directors recommends that the stockholders of Tyme tender their shares in such tender or exchange offer or, within ten business days of the commencement of such tender offer or exchange offer, Tyme's board of directors fails to recommend against acceptance of such officer; or
- Tyme has materially and willfully breached certain of itsnon-solicitation obligations under the Merger Agreement and such breach, if curable, has not been cured as of the effectiveness of such termination and at least five business days following delivery of written notice from Syros to Tyme of such breach;

(f) by Tyme, at any time prior to the approval by Syros stockholders of the share issuance in connection with the Merger Agreement, if any of the following circumstances shall occur:

- Syros' board of directors has failed to give its recommendation to the approval of the share issuance in connection with the merger and the PIPE Financing or has withdrawn or modified its recommendation in a manner adverse to Tyme;
- if after the receipt by Syros of an Acquisition Proposal, Tyme requests in writing that Syros reconfirm its recommendation of the share issuance in connection with the merger and the PIPE Financing and Syros' board of directors fails to do so within ten business days after receipt of the request;
- Syros' board of directors has approved or recommended to the stockholders of Syros an Acquisition Proposal and has not withdrawn such approval or recommendation;
- a tender offer or exchange offer for outstanding shares of Syros common stock is commenced, other than by Tyme or an affiliate of Tyme, and Syros' board of directors recommends that the stockholders of Syros tender their shares in such tender or exchange offer or, within five business days of the commencement of such tender offer or exchange offer, Syros' board of directors fails to recommend against acceptance of such officer; or
- Syros has materially and willfully breached certain of its non-solicitation obligations under the Merger Agreement and such breach, if curable, has not been cured as of the effectiveness of such termination and at least five business days following delivery of written notice from Syros to Tyme of such breach;

(g) by Syros, if Tyme has breached or failed to perform any of its representations, warranties, covenants or agreements contained in the Merger Agreement (other than those referred to in Section 8.1 (Termination) of the Merger Agreement) such that the conditions to the closing would not be satisfied; provided that Syros is not then in material breach of any representation, warranty, or covenant under the Merger Agreement; provided, further, if such breach or inaccuracy is curable, then the Merger Agreement will not terminate pursuant to this paragraph as a result of a particular breach or inaccuracy until the earlier of the expiration of a 30-day period after delivery of written notice of such breach or inaccuracy from Syros to Tyme (it being understood that the Merger Agreement will not terminate pursuant to this paragraph as a result of such particular breach or inaccuracy if such breach by Tyme is cured prior to such termination becoming effective);

(h) by Tyme, if Syros has breached or failed to perform any of its representations, warranties, covenants or agreements contained in the Merger Agreement (other than those referred to in Section 8.1 (Termination) of the Merger Agreement) such that the conditions to the closing would not be satisfied; provided that Tyme is not then in material breach of any representation, warranty, or covenant under the Merger Agreement; provided, further, if such breach or inaccuracy is curable, then the Merger Agreement will not terminate pursuant to this paragraph as a result of a particular breach or inaccuracy until the earlier of the expiration of a 30-day period after delivery of written notice of such breach or inaccuracy from Tyme to Syros (it being understood that the Merger Agreement will not terminate pursuant to this paragraph as a result of such particular breach or inaccuracy if such breach by Syros is cured prior to such termination becoming effective); or

(i) by either Syros or Tyme if at the Tyme special meeting of stockholders (including any adjournment or postponement), at which a vote to adopt the Merger Agreement is taken, and the requisite vote of the stockholders of Tyme in favor of the proposal to adopt the Merger Agreement is not obtained.

The party desiring to terminate the Merger Agreement will give the other party written notice of such termination, specifying the provisions hereof pursuant to which such termination is made and the basis for termination described in reasonable detail.

Termination Fees

Termination Fees Payable by Syros

Syros must pay Tyme a termination fee of $2.068 million if the Merger Agreement is terminated by (i) Syros or Tyme pursuant to clause (b) or (h) under the heading *"—Termination*" beginning on page 219 of this joint proxy statement/prospectus so long as (A) prior to the termination of the Merger Agreement, any person makes an Acquisition Proposal, and has not withdrawn such Acquisition Proposal, or amends an Acquisition Proposal made prior to the date of the Merger Agreement with respect to Syros; and (B) within 12 months after such termination Syros enters into a definitive agreement to consummate, or consummates, any Acquisition Proposal, regardless of whether made before or after the termination of this Agreement or (ii) Tyme pursuant to clause (f) under the heading *"—Termination*" beginning on page 219 of this joint proxy statement/prospectus.

Termination Fees Payable by Tyme

Tyme must pay Syros a termination fee of $2.443 million if the Merger Agreement is terminated by (i) Syros or Tyme pursuant to clause (b) or (g) above so long as (A) prior to the termination of the Merger Agreement, any person makes an Acquisition Proposal, and has not withdrawn such Acquisition Proposal, or amends an Acquisition Proposal made prior to the date of the Merger Agreement with respect to Tyme; and (B) within 12 months after such termination Tyme enters into a definitive agreement to consummate, or consummates, any Acquisition Proposal, regardless of whether made before or after the termination of this Agreement, or (ii) Syros pursuant to clause (e) above.

Amendment

The Merger Agreement may not be amended except by an instrument in writing signed on behalf of each of Tyme, Merger Sub and Syros. Such amendment requires the approval of the respective boards of directors of Tyme, Merger Sub and Syros at any time, except that after the Merger Agreement has been adopted and approved by the Tyme stockholders or Syros stockholders, no amendment which by law requires further approval by the Tyme stockholders or Syros stockholders, as the case may be, may be made without such further approval.

Expenses

The Merger Agreement provides all fees and expenses incurred in connection with the Merger Agreement and the transactions contemplated thereby shall be paid by the party incurring such expenses, except as described above in the section titled "*—Termination Fees*" beginning on page 221 of this joint proxy statement/prospectus, and except that Tyme and Syros will share equally in any fees and expenses of the exchange agent and in any fees and expenses, other than attorneys' and accountants' fees and expenses, incurred in relation to the printing, filing and mailing of this joint proxy statement/prospectus and the registration statement of which this joint proxy statement/prospectus is part, and any amendments or supplements thereto.

Support Agreements

In order to induce Syros to enter into the Merger Agreement, certain Tyme stockholders are parties to support agreements with Syros and Tyme pursuant to which, among other things, each such Tyme stockholder has agreed, solely in his, her or its capacity as a Tyme stockholder, to vote all of his, her or its shares of Tyme common stock in favor of the adoption of the Merger Agreement. These Tyme stockholders also agreed to vote against any competing Acquisition Proposal with respect to Tyme.

As of June 30, 2022, the Tyme stockholders that are party to a voting agreement with Tyme or a support agreement with Syros and Tyme owned an aggregate of 53,428,292 shares of Tyme common stock, representing approximately 31% of the outstanding shares of Tyme common stock. These stockholders include executive officers and directors of Tyme, as well as certain other stockholders owning a significant portion of the outstanding shares of Tyme common stock.

Under the support agreements with Syros and Tyme, subject to certain exceptions, such Tyme stockholders have also agreed not to sell or transfer their shares of Tyme common stock held by them, or any voting rights with respect thereto, until the earliest of the termination of the Merger Agreement, the completion of the merger, or the date on which the Tyme voting proposals have been approved by the requisite holders of Tyme common stock, subject to certain exceptions. To the extent that any such sale or transfer is permitted pursuant to the exceptions included in the support agreement, each person to which any shares of Tyme common stock are so sold or transferred must agree in writing to be bound by the terms and provisions of the support agreement. Certain Tyme stockholders are not party to such agreements but have previously executed voting agreements pursuant to which they are required to vote on proposals presented to Tyme stockholders in accordance with the recommendations of Tyme's board of directors.

In addition, in order to induce Tyme to enter into the Merger Agreement, certain Syros stockholders have entered into support agreements with Tyme and Syros pursuant to which, among other things, each such Syros stockholder has agreed, solely in his, her or its capacity as a Syros stockholder, to vote all of his, her or its shares of Syros common stock in favor of the Syros share issuance proposal, the increase in the number of authorized shares of Syros common stock to be effectuated prior to the effective time, and such other matters as may require approval of the Syros' stockholders pursuant to the DGCL with respect to the PIPE Financing, subject to the terms of the support agreements. These Syros stockholders also agreed to vote against any competing Acquisition Proposal with respect to Syros.

As of June 30, 2022, the Syros stockholders that are party to a support agreement owned an aggregate of 17,460,552 shares of Syros common stock representing approximately 28% of the outstanding shares of Syros common stock. These stockholders include executive officers and directors of Syros and certain other Syros stockholders holding a significant portion of the outstanding shares of Syros common stock.

Under these support agreements, subject to certain exceptions, such stockholders have also agreed not to sell or transfer their shares of Syros common stock held by them until the earliest of the termination of the Merger Agreement, the completion of the merger, or the date on which the Syros voting proposals have been approved by the requisite holders of Syros common stock, subject to certain exceptions. To the extent that any such sale or transfer is permitted pursuant to the exceptions included in the support agreements, each person to which any shares of Syros common stock are so sold or transferred must agree in writing to be bound by the terms and provisions of the support agreement.

The foregoing description of the support agreements does not purport to be complete and is qualified in its entirety by the full text of the forms of support agreements, which are attached hereto as *Annex D* and *Annex E.*

Lock-Up Agreements

Certain of Syros' and Tyme's executive officers, directors and stockholders have entered into lock-up agreements, pursuant to which such parties have agreed not to, except in limited circumstances, offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, or otherwise transfer or dispose of, any shares of Syros common stock until 90 days after the closing of the merger.

The Syros stockholders who have executed lock-up agreements as of June 30, 2022, are expected to own, in the aggregate, approximately 6% of the shares of the combined company on a pro forma basis, and the Tyme stockholders who have executed lock-up agreements as of June 30, 2022, owned in the aggregate, less than 1% of the shares of the combined company on a pro forma basis. In addition, each of Syros and Tyme is obligated under the merger agreement to use commercially reasonable efforts prior to the closing of the merger to obtain a lock-up agreement from any person who will serve as a director or officer of the combined company following completion of the merger.

The foregoing description of the lock-up agreement does not purport to be complete and is qualified in its entirety by the full text of the form of lock-up agreement, which is attached hereto as *Annex G.*

Securities Purchase Agreement and Registration Rights Agreements

Securities Purchase Agreement

Immediately prior to the execution and delivery of the Merger Agreement, Syros entered into the Securities Purchase Agreement with certain investors, pursuant to which Syros agreed to issue and sell to the investors the PIPE Financing an aggregate of 63,871,778 shares of Syros common stock and, in lieu of shares of Syros common stock to certain investors, Pre-Funded PIPE Warrants to purchase an aggregate of 74,267,400 shares of Syros common stock, and, in each case, accompanying PIPE Warrants to purchase an aggregate of up to 138,139,178 additional shares of Syros common stock (or Pre-Funded PIPE Warrants to purchase common stock in lieu thereof) at a price of $0.94 per share and accompanying PIPE Warrant (or $0.9399 per Pre-Funded PIPE Warrant and accompanying PIPE Warrant). The price per Pre-Funded PIPE Warrant and accompanying PIPE Warrant represents the price of $0.94 per share and accompanying PIPE Warrant to be sold in the PIPE Financing, minus the $0.0001 per share exercise price of each such Pre-Funded PIPE Warrant. The exercise price of the PIPE Warrants is $1.034 per share, or if exercised for a Pre-Funded PIPE Warrant in lieu thereof, $1.0339 per Pre-Funded PIPE Warrant (representing the PIPE Warrant exercise price of $1.034 per share minus the $0.0001 per share exercise price of each such Pre-Funded PIPE Warrant). The PIPE Warrants are exercisable beginning six months after the closing date of the PIPE Financing and prior to five years after the closing date of the PIPE Financing. The Pre-Funded PIPE Warrants are exercisable at any time after their original issuance and will not expire.

The PIPE Warrants and Pre-Funded PIPE Warrants to be issued in the PIPE Financing will provide that a holder of PIPE Warrants or Pre-Funded PIPE Warrants will not have the right to exercise any portion of its PIPE Warrants or Pre-Funded PIPE Warrants for shares of Syros common stock if such holder, together with its affiliates, would beneficially own in excess of either 4.99%, 9.99% or 19.99%, as selected by the holder of such PIPE Warrants or Pre-Funded PIPE Warrants, of the number of shares of Syros common stock outstanding immediately after giving effect to such exercise; provided, however, that each holder may increase or decrease its beneficial ownership limitation by giving notice to Syros, but not to any percentage in excess of 19.99%.

The closing of the PIPE Financing is conditioned upon the satisfaction or waiver of the conditions to the closing of the merger as well as certain other conditions.

The Securities Purchase Agreement contains customary representations and warranties of Syros. The Securities Purchase Agreement also contains customary representations and warranties of the investors party thereto.

Each investor's obligation to purchase the shares of Syros common stock,Pre-Funded PIPE Warrants and PIPE Warrants from Syros pursuant to the Securities Purchase Agreement is subject to the satisfaction or waiver of certain conditions, including:

- the satisfaction or waiver of each of the conditions to the consummation of the merger set forth in the Merger Agreement, including, without limitation, the approval of Syros stockholders of the Syros stockholder proposals and the approval of the Tyme stockholders of the Tyme stockholder proposals, other than those conditions which, by their nature, are to be satisfied at the closing of the merger pursuant to the Merger Agreement;
- the terms of the Merger Agreement shall not have been amended, modified or waived in a manner that would reasonably be expected to materially and adversely affect the economic benefits that the investor (in its capacity as such) would reasonably expect to receive under the Securities Purchase Agreement unless the investor has consented in writing to such amendment, modification or waiver;
- all representations and warranties of Syros contained in the Securities Purchase Agreement (as qualified therein) shall be true and correct in all material respects (other than representations and warranties that are qualified as to materiality, which representations and warranties shall be true and correct in all respects) as of the date of the closing of the PIPE Financing (except to the extent any such representation or warranty expressly speaks as of an earlier date, in which case such representation or warranty shall be true and correct in all material respects as of such earlier date);
- no judgment, writ, order, injunction, award or decree of or by any court, or judge, justice or magistrate, including any bankruptcy court or judge, or any order of or by any governmental authority, shall have been issued, and no action or proceeding shall have been instituted by any governmental authority, enjoining or preventing the consummation of the PIPE Financing;
- Syros shall have performed in all material respects all obligations and covenants required by the Securities Purchase Agreement to be performed by Syros on or prior to the closing of the PIPE Financing; and
- Syros shall have obtained all consents, permits, approvals, registrations and waivers necessary for the consummation of the PIPE Financing.

Syros' obligation to sell the shares of Syros common stock,Pre-Funded PIPE Warrants and PIPE Warrants to each investor pursuant to the Securities Purchase Agreement is subject to the satisfaction or waiver of certain conditions, including:

- all representations and warranties of the investor contained in the Securities Purchase Agreement shall be true and correct in all material respects (other than representations and warranties that are qualified as to materiality, which representations and warranties shall be true and correct in all respects) as of the date of the closing of the PIPE Financing (except to the extent any such representation or warranty expressly speaks as of an earlier date, in which case such representation or warranty shall be true and correct in all material respects as of such earlier date); and
- the investor shall have performed in all material respects all obligations and covenants required by the Securities Purchase Agreement to be performed by the investor on or prior to the closing of the PIPE Financing.

The Securities Purchase Agreement terminates (i) upon the mutual written consent of Syros and the investors that agreed to purchase a majority of the shares of Syros common stock to be issued and sold pursuant to the Securities Purchase Agreement, or (ii) by either Syros or any investor (with respect to itself only) if the closing of the PIPE Financing has not occurred on or prior to the date that is six (6) months after the date of execution of the Securities Purchase Agreement if the closing of the merger has not occurred on or before such date.

The foregoing description of the Securities Purchase Agreement does not purport to be complete and is qualified in its entirety by the full text of the Securities Purchase Agreement, which is attached hereto as *Annex F*.

Registration Rights Agreement

Concurrently with the execution of the Securities Purchase Agreement, Syros entered into the Registration Rights Agreement with the investors in the PIPE Financing, pursuant to which Syros agreed to register for resale the shares of Syros common stock and the issuance of the shares of Syros common stock underlying the PIPE Warrants and Pre-Funded PIPE Warrants held by the investors pursuant to a registration statement to be filed within 30 days of the closing of the PIPE Financing. Syros has agreed to use commercially reasonable efforts to cause such registration statement to become effective as soon as practicable and to keep such registration statement effective until the date the shares of Syros common stock and the shares of common stock underlying the PIPE Warrants and Pre-Funded PIPE Warrants covered by such registration statement have been sold or may be resold pursuant to Rule 144 without restriction. Syros has agreed to be responsible for all fees and expenses incurred in connection with the registration of the securities pursuant to the terms of the Registration Rights Agreement.

In the event (i) the registration statement has not been filed within 30 days following the closing date of the PIPE Financing, or the Registration Statement Filing Deadline, (ii) the registration statement has not been declared effective prior to the earlier of (A) five business days after the date which Syros is notified by the SEC that the registration statement will not be reviewed by the SEC staff or is not subject to further comment by the SEC staff, or (B) 60 days following the Registration Statement Filing Deadline (or, in the event the SEC reviews and has written comments to the registration statement, 120 days following the Registration Statement Filing Deadline) or (iii) after the registration statement has been declared effective by the SEC, sales cannot be made pursuant to the registration statement for any reason including by reason of a stop order or Syros' failure to update such registration statement, subject to certain limited exceptions, then Syros has agreed to make pro rata payments to each investor in the PIPE Financing as liquidated damages in an amount equal to 1% of the aggregate amount invested by each such investor in the securities to be registered pursuant to the Registration Rights Agreement per 30-day period or pro rata for any portion thereof for each such month during which such event continues, subject to certain caps set forth in the Registration Rights Agreement.

Syros has granted the investors customary indemnification rights in connection with the registration statement. The investors have also granted Syros customary indemnification rights in connection with the registration statement.

Affiliate Registration Rights Agreement

Concurrently with the execution of the Securities Purchase Agreement and the Registration Rights Agreement, Syros also entered into the Affiliate Registration Rights Agreement with the Baker Funds, pursuant to which the Baker Funds are entitled to certain resale registration rights with respect to the shares of Syros common stock held by the Baker Funds. Under the Affiliate Registration Rights Agreement, following a request by the Baker Funds, Syros is obligated to file a resale registration statement on Form S-3, or other appropriate form, covering the shares of Syros common stock held by the Baker Funds. Syros has agreed to file such resale registration statement as promptly as reasonably practicable following such request, and in any event within sixty (60) days of such request. Syros' obligations to file such registration statement are subject to specified exceptions, and suspension and deferral rights as are set forth in the Affiliate Registration Rights Agreement. Under specified circumstances, Syros may also include securities of Syros in any such registration statement. Under the Affiliate Registration Rights Agreement, the Baker Funds also have the right to one underwritten offering per calendar year, but no more than three underwritten offerings in total and not more than two underwritten offerings or "block trades" (as defined in the Affiliate Registration Rights Agreement) in any twelve month period, to effect the sale or distribution of the shares of Syros common stock held by the Baker Funds, subject to specified exceptions, conditions and limitations.

Oxford Finance Loan Agreement Amendment

Also on July 3, 2022, Syros entered into the Loan Amendment to the Loan Agreement. In its capacity as lender, Oxford is referred to herein as the Lender, and in its capacity as collateral agent, Oxford is referred to herein as the Agent. Pursuant to the Loan Amendment, the Lender and Agent have agreed to modify the Loan Agreement in order to, among other things, (i) consent to the entry into the Merger Agreement, and subject to certain conditions, the consummation of the merger, (ii) upon the consummation of the merger and the PIPE Financing and the receipt of proceeds therefrom, and subject to the payment of certain fees, extend the interest only period from March 1, 2023 to March 1, 2024 and extend the maturity date from February 1, 2025 to February 1, 2026, and (iii) upon the achievement of certain milestones and subject to the payment of certain fees, further extend the interest only period to September 1, 2024 and maturity date to August 1, 2026.

MATTERS BEING SUBMITTED TO A VOTE OF SYROS STOCKHOLDERS

SYROS PROPOSAL NO. 1:

APPROVAL, FOR PURPOSES OF NASDAQ LISTING RULES 5635(A) AND (D), OF THE ISSUANCE OF SHARES OF SYROS COMMON STOCK PURSUANT TO THE TERMS OF THE MERGER AGREEMENT AND THE SECURITIES PURCHASE AGREEMENT

General

At the Syros special meeting, Syros stockholders will be asked to approve, in accordance with applicable rules of the Nasdaq Stock Market, the issuance of shares of Syros common stock pursuant to the terms of the Merger Agreement and the Securities Purchase Agreement.

Pursuant to the terms of the Merger Agreement, at the effective time of the merger, outstanding shares of Tyme common stock will be converted into shares of Syros common stock. Syros expects to issue approximately 74,300,000 shares of its common stock to Tyme stockholders in connection with the merger. The actual number of shares of Syros common stock to be issued in the merger and the exchange ratio will be determined based on the amount of Tyme's net cash at closing and the number of Tyme shares outstanding at closing.

Pursuant to the terms of the Securities Purchase Agreement, immediately prior to the effective time of the merger, Syros will issue to certain investors in the PIPE Financing (i) an aggregate of 63,871,778 shares of Syros common stock and, in lieu of shares of Syros common stock to certain investors, pre-funded warrants to purchase an aggregate of 74,267,400 shares of Syros common stock and (ii) in each case, accompanying warrants to purchase an aggregate of up to 138,139,178 additional shares of Syros common stock (or pre-funded warrants in lieu thereof), at a price per unit of $0.94 (or $0.9399 per unit comprising a pre-funded warrant and accompanying warrant).

As of June 30, 2022, Syros had 62,989,020 shares of common stock outstanding. Based upon the initially estimated exchange ratio, following the merger and giving effect to the PIPE Financing, (i) Syros securityholders immediately before the merger together with the investors in the PIPE Financing are expected to own approximately 63% of the aggregate number of outstanding shares of Syros common stock following the merger and (ii) Tyme securityholders immediately before the merger are expected to own approximately 37% of the aggregate number of outstanding shares of Syros common stock following the merger, subject to certain assumptions (including as to the amount of Tyme net cash at closing, which could be materially different). Assuming the exercise of all Syros pre-funded warrants, including the Pre-Funded PIPE Warrants and the Pre-Funded 2020 Warrants, without giving effect to any beneficial ownership limitations applicable thereto, then (i) Syros securityholders immediately before the merger together with the investors in the PIPE Financing would own approximately 73% of the aggregate number of outstanding shares of Syros common stock following the merger and (ii) Tyme securityholders immediately before the merger would own approximately 27% of the aggregate number of outstanding shares of Syros common stock following the merger, subject to certain assumptions (including as to the amount of Tyme net cash at closing, which could be materially different). The foregoing percentages do not give effect to the exercise or conversion of outstanding stock options or warrants other than as set forth above.

The PIPE Warrants and Pre-Funded PIPE Warrants to be issued in the PIPE Financing will provide that a holder of PIPE Warrants orPre-Funded PIPE Warrants will not have the right to exercise any portion of its PIPE Warrants or Pre-Funded PIPE Warrants for shares of Syros common stock if such holder, together with its affiliates, would beneficially own in excess of either 4.99%, 9.99% or 19.99%, as selected by the holder of such PIPE Warrants or Pre-Funded PIPE Warrants, of the number of shares of Syros common stock outstanding immediately after giving effect to such exercise; provided, however, that each holder may increase or decrease its beneficial ownership limitation by giving notice to Syros, but not to any percentage in excess of 19.99%.

The terms of, reasons for and other aspects of the merger, the Merger Agreement, the PIPE Financing and the Securities Purchase Agreement are described in detail in the other sections in this joint proxy statement/

prospectus. A copy of the Merger Agreement is attached as *Annex A* to this proxy statement/prospectus, and a copy of the Securities Purchase Agreement is attached as *Annex F* to this proxy statement/prospectus.

Stockholder Approval Requirement for Purposes of Nasdaq Listing Rule 5635

Pursuant to Nasdaq Listing Rule 5635(a), stockholder approval is required prior to the issuance of common stock or other securities convertible into or exercisable for common stock, in connection with the acquisition of the stock or assets of another company, if such securities are not issued in a public offering and (i) the common stock has, or will have upon issuance, voting power equal to or in excess of 20% of the voting power outstanding before the issuance of such securities, or (ii) the number of shares of common stock to be issued is or will be equal to or in excess of 20% of the number of shares of common stock outstanding before the issuance of such securities.

Additionally, pursuant to Nasdaq Listing Rule 5635(d), stockholder approval is required for a transaction other than a public offering involving the sale, issuance or potential issuance by an issuer of common stock (or securities convertible into or exercisable for common stock) at a price that is less than the lower of (i) the closing price immediately preceding the signing of the binding agreement or (ii) the average closing price of the common stock for the five trading days immediately preceding the signing of the binding agreement, if the number of shares of common stock (or securities convertible into or exercisable for common stock) to be issued equals to 20% or more of the common stock, or 20% or more of the voting power, outstanding before the issuance.

In connection with the consummation of the merger and the closing of the PIPE Financing, Syros expects to issue (i) approximately 74,300,000 shares of Syros common stock to the stockholders of Tyme in accordance with the terms and subject to the conditions of the Merger Agreement, and (ii) an aggregate of 63,871,778 shares of its common stock and, in lieu of shares of Syros common stock to certain investors, pre-funded warrants to purchase an aggregate of 74,267,400 shares of Syros common stock, and in each case, accompanying warrants to purchase an aggregate of up to 138,139,178 additional shares of Syros common stock (or pre-funded warrants in lieu thereof) to certain investors in the PIPE Financing in accordance with the terms and subject to the conditions of the Securities Purchase Agreement. Accordingly, because the aggregate number of shares of Syros common stock that Syros will issue in connection with the merger and the PIPE Financing will exceed 20% of both the voting power and the number of shares of Syros common stock outstanding before such issuance, Syros is seeking the approval of its stockholders for the issuance of shares of Syros common stock pursuant to the Merger Agreement and the PIPE Financing pursuant to Nasdaq Listing Rules 5635(a) and (d).

Reasons for the Transactions

After consideration and consultation with its senior management and its financial and legal advisors, the Syros board of directors determined that the Merger Agreement, the merger, the Securities Purchase Agreement and the PIPE Financing are advisable and in the best interests of Syros and its stockholders. The Syros board of directors considered various reasons to reach its determination, as discussed elsewhere in this joint proxy statement/prospectus, including, but not limited to, "*The Merger—Syros Reasons for the Merger*" beginning on page 159 of this joint proxy statement/prospectus.

Syros needs substantial additional funding to execute its operating plan and continue to operate as a going concern, and, if Syros is unable to raise capital, Syros could be forced to delay, reduce or eliminate its product development programs or commercialization efforts. As previously disclosed in its Quarterly Report on Form 10-Q for the quarter ended March 31, 2022, Syros believes that its cash, cash equivalents and marketable securities as of March 31, 2022 will enable it to fund its planned operating expense and capital expenditure requirements into the second quarter of 2023. These funds may not be sufficient to fund operations for at least the next twelve months from the date of issuance of Syros' consolidated financial statements which raises substantial doubt about Syros' ability to continue as a going concern. Syros' future viability beyond one year from the date of issuance of its consolidated financial statements is dependent on its ability to raise additional capital to finance its operations.

The net proceeds from the merger and the PIPE Financing are expected to be used to advance Syros' clinical development pipeline, business development activities, working capital and other general corporate purposes. Following the closing of the merger, PIPE Financing and Loan Amendment, the total cash balance of the combined company is expected to be approximately $240 million (after transaction expenses), which Syros believes will be sufficient to fund its planned operating expenses and capital expenditure requirements into 2025, allowing it to advance its late-stage clinical programs toward commercialization, including tamibarotene, currently being studied in the SELECT-MDS-1 trial and the randomized portion of the SELECT-AML-1 trial, and SY-2101, which it plans to advance into a Phase 3 trial for the treatment of APL in the second half of 2023. Because Syros has limited financial resources, it has focused and intends to focus on developing product candidates for specific indications that it identifies as most likely to succeed, in terms of both their potential for marketing approval and commercialization. As a result, Syros has needed to, and may in the future need to, forego or delay pursuit of opportunities with other product candidates or for other indications that may prove to have greater commercial potential. In this regard, Syros previously announced that it does not plan to pursue Phase 3 development of SY-2101 unless and until it secures additional capital, and has more recently announced that it expects to initiate a Phase 3 clinical trial of SY-2101 in the second half of 2023 upon consummation of the merger, the PIPE Financing and the Loan Amendment. In the event that this proposal is not approved by Syros stockholders, the merger and the PIPE Financing cannot be consummated.

The PIPE Financing is expected to close substantially concurrently with the merger. The closing of the merger is subject to certain closing conditions that must be satisfied or waived, including the closing of the PIPE Financing. The closing of the PIPE Financing is conditioned upon the satisfaction or waiver of the conditions to the closing of the merger as well as certain other conditions.

Required Vote

The affirmative vote of a majority of the total votes cast by the holders of Syros common stock entitled to vote on the matter at the Syros special meeting is required for approval, for purposes of Nasdaq Listing Rules 5635(a) and (d), of the issuance of shares of Syros common stock pursuant to the terms of the Merger Agreement and the Securities Purchase Agreement.

Pursuant to support agreements, each of Syros' directors and officers and certain other stockholders have agreed to vote in favor of the Syros share issuance proposal. As of the date of this joint proxy statement/prospectus, such stockholders own approximately 28% of the outstanding shares of Syros common stock.

SYROS' BOARD OF DIRECTORS UNANIMOUSLY RECOMMENDS A VOTE "FOR" THIS PROPOSAL NO. 1 TO APPROVE, FOR PURPOSES OF NASDAQ LISTING RULES 5635(A) AND (D), THE ISSUANCE OF SHARES OF SYROS COMMON STOCK PURSUANT TO THE TERMS OF THE MERGER AGREEMENT AND THE SECURITIES PURCHASE AGREEMENT.

Unless otherwise instructed, it is the intention of the persons named in the accompanying proxy card to vote shares represented by properly executed proxy cards "FOR" the approval, for purposes of Nasdaq Listing Rules 5635(a) and (d), of the issuance of Syros common stock pursuant to the terms of the Merger Agreement and the Securities Purchase Agreement.

SYROS PROPOSAL NO. 2

APPROVAL OF AMENDMENT TO SYROS' RESTATED CERTIFICATE OF INCORPORATION TO INCREASE THE NUMBER OF AUTHORIZED SHARES OF SYROS COMMON STOCK

On July 14, 2022, Syros' board of directors approved and declared advisable, subject to stockholder approval, an amendment to Syros' restated certificate of incorporation to (i) increase the number of authorized shares of capital stock from 210,000,000 shares to 710,000,000 shares and (ii) increase the number of authorized shares of Syros common stock from 200,000,000 shares to 700,000,000 shares.

Syros' restated certificate of incorporation currently authorizes 200,000,000 shares of common stock, par value $0.001 per share, and 10,000,000 shares of preferred stock, par value $0.001 per share. As of June 30, 2022, out of the 200,000,000 shares of common stock presently authorized, 114,945,098 shares remained available for future issuance and 85,054,902 shares were issued or reserved for issuance, as follows:

- 62,989,020 shares of Syros common stock are outstanding;
- 711,782 shares of Syros common stock are issuable upon exercise of outstanding stock options pursuant to Syros' 2012 Stock Incentive Plan;
- 5,810,340 shares of Syros common stock are issuable upon exercise of outstanding stock options pursuant to Syros' 2016 Stock Incentive Plan, 4,235,325 shares of Syros common stock are issuable upon vesting of outstanding restricted stock units pursuant to Syros' 2016 Stock Incentive Plan, and 466,410 shares of Syros common stock are reserved for future issuance under Syros' 2016 Stock Incentive Plan;
- 352,400 shares of Syros common stock are issuable upon vesting of outstanding restricted stock units pursuant to Syros' 2022 Inducement Stock Incentive Plan and 647,600 shares of Syros common stock are reserved for future issuance under Syros' 2022 Inducement Stock Incentive Plan;
- 2,724,369 shares of Syros common stock are reserved for future issuance under Syros' 2016 Employee Stock Purchase Plan;
- 1,127,500 shares of Syros common stock are issuable upon exercise of outstanding stock options to certain employees and consultants, outside of the 2012 Stock Incentive Plan, the 2016 Stock Incentive Plan or the 2022 Inducement Stock Incentive Plan; and
- 5,990,156 shares of Syros common stock are issuable upon exercise of outstanding warrants andpre-funded warrants to purchase shares of Syros common stock.

As described in greater detail in Syros Proposal No. 1, or the Syros share issuance proposal, Syros will be required to reserve approximately 350,500,000 shares of common stock in connection with the merger and the PIPE Transaction. This number includes (i) the estimated approximately 74,300,000 shares of common stock issuable to Tyme stockholders pursuant to the terms of the Merger Agreement, (ii) the 138,139,178 shares of common stock and pre-funded warrants issuable to investors in the PIPE Financing pursuant to the terms of the Securities Purchase Agreement and (iii) the 138,139,178 shares of common stock issuable to investors upon the exercise of accompanying warrants or pre-funded warrants issuable to investors in the PIPE Financing pursuant to the terms of the Securities Purchase Agreement. As a result, even if Syros' stockholders approve the Syros share issuance proposal, Syros will not have sufficient authorized shares to close the PIPE Financing, and the merger may not be completed unless this Proposal No. 2 is approved. The approval of this Proposal No. 2 is therefore required for Syros to complete the PIPE Financing and, unless waived by Tyme, the merger.

In addition, if Proposal No. 4, or the Syros equity plan proposal, is approved, Syros will reserve 30,000,000 additional shares of its common stock for future issuance under Syros' 2022 Equity Incentive Plan.

The proposed amendment to Syros' restated certificate of incorporation would not increase or otherwise affect Syros' authorized preferred stock. As of June 30, 2022, there were no shares of Syros preferred stock outstanding.

Syros' common stock is all of a single class, with equal voting, distribution, liquidation and other rights. The additional common stock to be authorized by adoption of the amendment would have rights identical to Syros' currently outstanding common stock. A copy of the amendment to Syros' restated certificate of incorporation is attached as *Annex H* to this joint proxy statement/prospectus. If Syros' stockholders approve the proposal, subject to the discretion of Syros' board of directors, Syros intends to file the amendment to its restated certificate of incorporation with the Secretary of State of the State of Delaware immediately prior to the effective time of the merger.

For a discussion of the Syros reverse stock split proposal, please see Proposal 3 (Approval of Amendment to Syros' Restated Certificate of Incorporation to Effect a Reverse Stock Split of Syros Common Stock by a Ratio of Not Less Than 1-for-5 and Not More Than 1-for-15, and a Proportionate Reduction in the Number of Authorized Shares of Common Stock, Such Ratio and the Implementation and Timing of the Reverse Stock Split to be Determined in the Discretion of Syros' Board Of Directors) beginning on page 232 below. To the extent Proposal 3 is approved and the reverse stock split of Syros common stock is implemented, the authorized shares of Syros will be proportionately reduced in accordance with the split ratio determined by Syros' board of directors.

Purpose

After consideration and consultation with its senior management and its financial and legal advisors, the Syros' board of directors determined that the Merger Agreement, the merger, the Securities Purchase Agreement and the PIPE Financing are advisable and in the best interests of Syros and its stockholders. The Syros' board of directors considered various reasons to reach its determination, as discussed elsewhere in this joint proxy statement/prospectus. The amendment to Syros' restated certificate of incorporation as described in this Proposal No. 2 is necessary for Syros to have sufficient authorized shares to close the PIPE Financing, which is in turn a condition to Tyme's obligation to complete the merger.

In addition, if Proposal No. 4, or the Syros equity plan proposal, is approved, Syros will reserve 30,000,000 additional shares of its common stock for future issuance under Syros' 2022 Equity Incentive Plan.

At this time, Syros does not have any plans, commitments, arrangements, understandings or agreements regarding the issuance of common stock following the increase of its authorized shares, except as described in this Proposal No 2.

Possible Effects of the Amendment

If the amendment to Syros' restated certificate of incorporation is approved and adopted and filed with the Secretary of State of the State of Delaware, the additional authorized shares would be available for issuance at the discretion of Syros' board of directors and without further stockholder approval, except as may be required by law or the rules of The Nasdaq Stock Market on which Syros' common stock is listed. The additional shares of authorized common stock would have the same rights and privileges as the shares of common stock currently issued and outstanding. Holders of Syros common stock have no preemptive rights.

The issuance of additional shares of common stock is likely to, among other things, have a dilutive effect on earnings per share and on stockholders' equity and voting rights. Furthermore, future sales of substantial amounts of Syros common stock, or the perception that these sales might occur, could adversely affect the prevailing market price of Syros common stock or limit Syros' ability to raise additional capital.

SYROS' BOARD OF DIRECTORS RECOMMENDS A VOTE "FOR" THE APPROVAL OF THE AMENDMENT TO SYROS' RESTATED CERTIFICATE OF INCORPORATION TO INCREASE THE NUMBER OF AUTHORIZED SHARES OF SYROS COMMON STOCK.

SYROS PROPOSAL NO. 3

APPROVAL OF AMENDMENT TO SYROS' RESTATED CERTIFICATE OF INCORPORATION TO EFFECT A REVERSE STOCK SPLIT OF SYROS COMMON STOCK BY A RATIO OF NOT LESS THAN 1-FOR-5 AND NOT MORE THAN 1-FOR-15, AND A PROPORTIONATE REDUCTION IN THE NUMBER OF AUTHORIZED SHARES OF COMMON STOCK, SUCH RATIO AND THE IMPLEMENTATION AND TIMING OF THE REVERSE STOCK SPLIT TO BE DETERMINED IN THE DISCRETION OF SYROS' BOARD OF DIRECTORS

Syros is seeking stockholder approval for a proposal to adopt an amendment to its restated certificate of incorporation, as amended, to effect a reverse stock split, or the Syros reverse stock split, of Syros' issued common stock by a ratio of not less than 1-for-5 and not more than 1-for-15, and a proportionate reduction in the number of authorized shares of Syros common stock, such ratio and the implementation and timing of the Syros reverse stock split to be determined in the discretion of Syros' board of directors.

The form of the amendment to Syros' restated certificate of incorporation, as amended, to effect the Syros reverse stock split, and proportionate reduction in the number of authorized shares of common stock, which the Syros' board of directors approved and declared advisable on July 14, 2022, subject to stockholder approval, is attached as *Annex I* to this joint proxy statement/prospectus. Approval of the proposal would permit (but not require) Syros' board of directors to effect the Syros reverse stock split by a ratio of not less than 1-for-5 and not more than 1-for-15, with the exact ratio to be set within this range as determined by Syros' board of directors in its sole discretion, provided that the board of directors must determine to effect the Syros reverse stock split and such amendment must be filed with the Secretary of State of the State of Delaware no later than March 31, 2023. If the certificate of amendment effecting the Syros reverse stock split has not been filed with the Secretary of State of the State of Delaware on or before March 31, 2023, Syros' board of directors will abandon the Syros reverse stock split. The exact ratio of the Syros reverse stock split will be determined by the Syros board of directors prior to the effective time of the Syros reverse stock split and will be publicly announced prior to the effective time of the Syros reverse stock split. Syros believes that enabling its board of directors to set the ratio of the Syros reverse stock split within the stated range will provide it with the flexibility to implement the Syros reverse stock split in a manner designed to maximize the anticipated benefits for its stockholders. In determining a ratio of the Syros reverse stock split, if any, following the receipt of stockholder approval, Syros' board of directors may consider, among other things, factors such as:

- the historical trading prices and trading volume of Syros common stock;
- the number of shares of Syros common stock outstanding;
- the then-prevailing trading price and trading volume of Syros common stock and the anticipated or actual impact of the Syros reverse stock split on the trading price and trading volume for Syros common stock;
- the anticipated impact of a particular ratio on Syros' ability to reduce administrative and transactional costs; and
- prevailing general market and economic conditions.

Although Syros' board of directors may effect the Syros reverse stock split any time on or before March 31, 2023, Syros' board of directors may determine to effect the Syros reverse stock split promptly following receipt of stockholder approval of this Proposal 3, or soon thereafter. In the event that Syros' board of directors determines to effect the authorized share increase that is the subject of Syros Proposal No. 2 and the reverse stock split that is the subject of this Syros Proposal No. 3, assuming that each proposal is approved by Syros' stockholders, the Syros board of directors would effect the authorized share increase before effecting the reverse stock split. In addition, Syros' board of directors reserves the right to elect to abandon the Syros reverse stock split, including at any or all proposed ratios for the Syros reverse stock split, if it determines, in its sole discretion, that the Syros reverse stock split is no longer in the best interests of Syros and its stockholders.

Depending on the ratio for the Syros reverse stock split determined by Syros' board of directors, no fewer than every five and no more than every 15 shares of issued common stock will be reclassified into one share of common stock. The amendment to implement the Syros reverse stock split would also proportionately reduce the number of authorized shares of common stock of Syros, as described in the form of amendment attached as *Annex I.* Such amendment will not change the number of authorized shares of preferred stock of Syros, or the par value of Syros common stock or preferred stock.

Background and Reasons for the Reverse Stock Split; Potential Consequences of the Reverse Stock Split

Syros' common stock is listed on The Nasdaq Global Select Market under the symbol "SYRS." According to applicable Nasdaq Listing Rules, in order for Syros common stock to continue to be listed on Nasdaq, Syros must satisfy certain requirements established by Nasdaq, including with regard to its market price. The listing standards of Nasdaq require Syros to have, among other things, a $1.00 per share minimum bid price. Syros' board of directors expects that the Syros reverse stock split will have the effect of increasing the market price of Syros common stock so that Syros will be better able to maintain compliance with the relevant Nasdaq listing requirements.

In addition, Syros' board of directors believes that a higher stock price may help generate investor interest in Syros and help Syros attract and retain employees. If the reverse stock split successfully increases the per share price of Syros common stock, Syros' board of directors also believes this increase could result in the potential for increased trading volume in Syros common stock and the potential for future financings by Syros.

While reducing the number of outstanding shares of Syros common stock through the Syros reverse stock split is intended, absent other factors, to increase the per share market price of Syros common stock, other factors, such as factors relating to the proposed merger and PIPE Financing described elsewhere in this joint proxy statement/prospectus, Syros' financial results, market conditions and the market perception of Syros' business may adversely affect the market price of Syros common stock. As a result, there can be no assurance that the Syros reverse stock split, if effected, will result in the intended benefits described above, that the market price of Syros common stock will increase following the Syros reverse stock split or that the market price of Syros common stock will not decrease in the future. Additionally, Syros cannot assure you that the market price per share of its common stock after the Syros reverse stock split will increase in proportion to the reduction in the number of shares of Syros common stock outstanding before the Syros reverse stock split. Accordingly, the total market capitalization of Syros common stock after the Syros reverse stock split may be lower than the total market capitalization before the Syros reverse stock split.

The amendment to implement the Syros reverse stock split will also proportionately reduce the number of shares of common stock that Syros' board of directors is authorized to issue under Syros' restated certificate of incorporation as described in the form of amendment attached hereto as *Annex I.*

Procedure for Implementing the Reverse Stock Split

The Syros reverse stock split would become effective upon the filing of the certificate of amendment to Syros' restated certificate of incorporation, as amended, with the Secretary of State of the State of Delaware. The exact timing of the filing of the certificate of amendment that will effect the Syros reverse stock split will be determined by Syros' board of directors, in its sole discretion, provided that in no event shall the filing of the certificate of amendment effecting the Syros reverse stock split occur after March 31, 2023. Syros' board of directors may determine to effect the Syros reverse stock split immediately upon receipt of stockholder approval of this Proposal 3, or soon thereafter. In addition, Syros' board of directors reserves the right, notwithstanding stockholder approval of this Proposal 3 and without further action by the stockholders, to elect not to proceed with the Syros reverse stock split if, at any time prior to filing the certificate of amendment to Syros' restated certificate of incorporation to effect the Syros reverse stock split, or, in the event that the amendment is not effective until a later time, such later time, Syros' board of directors, in its sole discretion, determines that it is no

longer in Syros' best interests and the best interests of its stockholders to proceed with the Syros reverse stock split. If the certificate of amendment effecting the Syros reverse stock split has not been filed with the Secretary of State of the State of Delaware on or before March 31, 2023, Syros' board of directors will abandon the Syros reverse stock split.

Effect of the Reverse Stock Split on Holders of Outstanding Common Stock

Depending on the ratio for the Syros reverse stock split determined by Syros' board of directors, a minimum of every five and a maximum of every 15 shares of issued common stock will be reclassified into one new share of common stock. Based on 62,989,020 shares of common stock issued and outstanding as of June 30, 2022, immediately following the Syros reverse stock split, Syros would have approximately 12,597,804 shares of common stock issued and outstanding if the ratio for the Syros reverse stock split is 1-for-5, and approximately 4,199,268 shares of common stock issued and outstanding if the ratio for the Syros reverse stock split is 1-for-15. Any other ratio selected within such range would result in a number of shares of common stock issued and outstanding of between approximately 4,499,215 and 10,498,170 shares. In addition, giving effect to the merger and the PIPE Financing, and assuming the exercise of the Pre-Funded PIPE Warrants, without giving effect to any beneficial ownership limitations applicable thereto, based on 62,989,020 shares of common stock issued and outstanding as of June 30, 2022 and based upon the initially estimated exchange ratio, Syros would have approximately 55 million shares of common stock issued and outstanding if the ratio for the Syros reverse stock split is 1-for-5, and approximately 18 million shares of common stock issued and outstanding if the ratio for the Syros reverse stock split is 1-for-15.

The actual number of shares issued and outstanding after giving effect to the Syros reverse stock split, if implemented, will depend on the ratio for the Syros reverse stock split that is ultimately determined by Syros' board of directors.

The Syros reverse stock split will affect all holders of Syros' common stock uniformly and will not affect any stockholder's percentage ownership interest in Syros, except that, as described below under *"—Fractional Shares,"* record holders of common stock otherwise entitled to a fractional share as a result of the Syros reverse stock split will receive cash in lieu of such fractional share. In addition, the Syros reverse stock split will not affect any stockholder's proportionate voting power (subject to the treatment of fractional shares).

The Syros reverse stock split may result in some stockholders owning "odd lots" of less than 100 shares of common stock. Odd lot shares may be more difficult to sell, and brokerage commissions and other costs of transactions in odd lots may be higher than the costs of transactions in "round lots" of even multiples of 100 shares.

After the effective time of the Syros reverse stock split, Syros' common stock will have a new Committee on Uniform Securities Identification Procedures (CUSIP) number, which is a number used to identify its equity securities, and stock certificates with the older CUSIP numbers will need to be exchanged for stock certificates with the new CUSIP numbers by following the procedures described below. After the effectiveness of the Syros reverse stock split, Syros will continue to be subject to the periodic reporting and other requirements of the Exchange Act.

Authorized Shares of Common Stock

The amendment to implement the Syros reverse stock split will also proportionately reduce the number of shares of common stock that Syros' board of directors is authorized to issue under Syros' restated certificate of incorporation, as described in the form of amendment attached hereto as *Annex I.* Except for the issuance of shares pursuant to the terms of the Merger Agreement and the Securities Purchase Agreement, which is the subject of Syros Proposal No. 1 and which is described elsewhere in this joint proxy statement/prospectus, and

the issuance of shares pursuant to the Syros' 2022 Equity Incentive Plan, which is the subject of Syros Proposal No. 4, Syros does not currently have any plans, proposals or arrangement to issue any of its authorized but unissued shares of common stock.

Beneficial Holders of Common Stock (i.e. stockholders who hold in street name)

For purposes of implementing the Syros reverse stock split, Syros intends to treat shares held by stockholders through a bank, broker, custodian or other nominee in the same manner as registered stockholders whose shares are registered in their names. Banks, brokers, custodians or other nominees will be instructed to effect the Syros reverse stock split for their beneficial holders holding Syros common stock in street name. However, these banks, brokers, custodians or other nominees may have different procedures than registered stockholders for processing the Syros reverse stock split. Stockholders who hold shares of Syros common stock with a bank, broker, custodian or other nominee and who have any questions in this regard are encouraged to contact their banks, brokers, custodians or other nominees.

Registered "Book-Entry" Holders of Common Stock (i.e. stockholders that are registered on the transfer agent's books and records but do not hold stock certificates)

Certain of Syros' registered holders of common stock may hold some or all of their shares electronically in book-entry form with the transfer agent. These stockholders do not have stock certificates evidencing their ownership of Syros' common stock. They are, however, provided with a periodic statement reflecting the number of shares registered in their accounts.

Stockholders who hold shares electronically in book-entry form with the transfer agent will not need to take action to receive whole shares of post-split common stock, because the exchange will be automatic.

Exchange of Stock Certificates

If the Syros reverse stock split is effected, stockholders holding certificated shares (i.e., shares represented by one or more physical stock certificates) will be requested to exchange their old stock certificate(s), or Old Certificate(s), for shares held in book-entry form through the Depository Trust Company's Direct Registration System representing the appropriate number of whole shares of Syros common stock resulting from the Syros reverse stock split. Stockholders of record upon the effective time of the Syros reverse stock split will be furnished the necessary materials and instructions for the surrender and exchange of their Old Certificate(s) at the appropriate time by Syros' transfer agent, Computershare. Stockholders will not have to pay any transfer fee or other fee in connection with such exchange. As soon as practicable after the effective time of the Syros reverse stock split, Syros' transfer agent will send a transmittal letter to each stockholder advising such holder of the procedure for surrendering Old Certificate(s) in exchange for new shares held in book-entry form.

YOU SHOULD NOT SEND YOUR OLD CERTIFICATES NOW. YOU SHOULD SEND THEM ONLY AFTER YOU RECEIVE THE LETTER OF TRANSMITTAL FROM THE TRANSFER AGENT.

As soon as practicable after the surrender to the transfer agent of any Old Certificate(s), together with a properly completed and duly executed transmittal letter and any other documents the transfer agent may specify, the transfer agent will have its records adjusted to reflect that the number of whole shares of post-split common stock into which the shares represented by such Old Certificate(s) have been reclassified in connection with the Syros reverse stock split are held in book-entry form in the name of such person.

Until surrendered as contemplated herein, a stockholder's Old Certificate(s) shall be deemed at and after the effective time of the Syros reverse stock split to represent the number of whole shares of Syros common stock resulting from the Syros reverse stock split as well as the right to receive cash in lieu of any fractional shares.

Any stockholder whose Old Certificate(s) have been lost, destroyed or stolen will be entitled to new shares in book-entry form only after complying with the requirements that Syros and its transfer agent customarily apply in connection with lost, stolen or destroyed certificates.

No service charges, brokerage commissions or transfer taxes shall be payable by any holder of any Old Certificate(s), except that if any book-entry shares are to be issued in a name other than that in which the Old Certificate(s) are registered, it will be a condition of such issuance that (1) the person requesting such issuance must pay to Syros any applicable transfer taxes or establish to Syros' satisfaction that such taxes have been paid or are not payable, (2) the transfer complies with all applicable federal and state securities laws, and (3) the surrendered Old Certificate(s) are properly endorsed and otherwise in proper form for transfer. In lieu of holding their shares in book-entry form, any stockholder who holds Old Certificate(s) and wants to continue holding certificated shares may receive new certificates by contacting Syros' transfer agent and complying with the customary requirements that apply to the issuance of certificated shares.

Fractional Shares

Fractional shares will not be issued in connection with the Syros reverse stock split. Stockholders of record and stockholders who hold their shares through a bank, broker, custodian or other nominee who would otherwise hold fractional shares of Syros common stock as a result of the Syros reverse stock split will be entitled to receive cash (without interest and subject to applicable withholding taxes) in lieu of such fractional shares. Each such stockholder will be entitled to receive an amount in cash equal to the fraction of one share to which such stockholder would otherwise be entitled multiplied by the fair value of Syros common stock at the effective time of the Syros reverse stock split to be determined by the average (after taking into account the ratio at which the Syros reverse stock split is effected) of the high and low trading prices of Syros' common stock on The Nasdaq Global Select Market during regular trading hours for the five trading days immediately preceding the effective time of the Syros reverse stock split.

Stockholders should be aware that, under the escheat laws of the various jurisdictions where stockholders reside, where Syros is domiciled and where the funds will be deposited, sums due for fractional interests resulting from the Syros reverse stock split that are not timely claimed after the effective time in accordance with applicable law may be required to be paid to the designated agent for each such jurisdiction. Thereafter, stockholders otherwise entitled to receive such funds may have to seek to obtain them directly from the state to which they were paid.

Effect of the Reverse Stock Split on Employee Plans, Options, Restricted Stock Units, Restricted Stock Awards and Warrants

Pursuant to the various instruments governing Syros' then outstanding stock option awards, restricted stock unit awards and warrants to purchase common stock, in connection with any Syros reverse stock split, Syros' board of directors will reduce the number of shares of common stock issuable upon the exercise of the stock options, vesting of the restricted stock units and exercise of the warrants in proportion to the ratio of the Syros reverse stock split and proportionately increase the exercise price of Syros' outstanding stock options and warrants. In connection with such proportionate adjustments, the number of shares of common stock issuable upon exercise, vesting or conversion, as applicable, of outstanding stock options, restricted stock units and warrants, will be rounded down to the nearest whole share and the exercise prices will be rounded up to the nearest cent, and no cash payment will be made in respect of such rounding.

Accounting Matters

The amendment to Syros' restated certificate of incorporation, as amended, will not affect the par value of Syros' common stock per share, which will remain $0.001 par value per share. As a result, as of the effective time of the Syros reverse stock split, the par value attributable to common stock will decrease with the corresponding increase in the additional paid-in capital account on Syros' balance sheet. Reported per share net income or loss will be higher because there will be fewer shares of common stock outstanding.

No Appraisal Rights

Under the DGCL, Syros' stockholders are not entitled to dissenter's rights or appraisal rights with respect to the Syros reverse stock split and Syros will not independently provide its stockholders with any such rights.

Interest of Certain Persons in Matters to be Acted Upon

No officer or director has any substantial interest, direct or indirect, by security holdings or otherwise, in the Syros reverse stock split that is not shared by all of our other stockholders.

Material U.S. Federal Income Tax Consequences of the Syros Reverse Stock Split

The following is a discussion of the material U.S. federal income tax consequences of the proposed Syros reverse stock split that are applicable to U.S. Holders (as defined below) that hold shares of Syros common stock as capital assets for U.S. federal income tax purposes (generally, property held for investment). This discussion does not purport to be a complete analysis of all potential tax effects to such a U.S. Holder. This discussion is based on the Code, existing Treasury Regulations promulgated thereunder, judicial decisions and published rulings and administrative pronouncements of the IRS, in each case in effect as of the date hereof. These authorities may change or be subject to differing interpretations. Any such change or differing interpretation, which may be retroactive, could impact the U.S. federal income tax consequences described herein in a manner that could adversely affect a U.S. Holder.

This discussion does not address all U.S. federal income tax consequences relevant to U.S. Holders. In addition, it does not address consequences relevant to U.S. Holders that are subject to particular U.S. or non-U.S. tax rules, including, without limitation, to holders of Syros common stock that are:

- U.S. expatriates and former citizens or long-term residents of the United States;
- U.S. Holders whose functional currency is not the U.S. dollar;
- persons holding Syros common stock as part of a hedge, straddle or other risk reduction strategy or as part of a conversion transaction or other integrated investment;
- banks, insurance companies, and other financial institutions;
- real estate investment trusts or regulated investment companies;
- brokers, dealers or traders in securities;
- "controlled foreign corporations," "passive foreign investment companies," and corporations that accumulate earnings to avoid U.S. federal income tax;
- S corporations, partnerships or other entities or arrangements treated as partnerships for U.S. federal income tax purposes (and investors therein);
- persons for whom Syros common stock constitutes "qualified small business stock" within the meaning of Section 1202 of the Code or as "Section 1244 stock" for purposes of Section 1244 of the Code;
- tax-exempt organizations or governmental organizations;
- persons subject to special tax accounting rules as a result of any item of gross income with respect to Syros common stock being taken into account in an "applicable financial statement" (as defined in the Code);
- persons who hold or received Syros common stock pursuant to the exercise of any employee stock option or otherwise as compensation;
- tax-qualified retirement plans; and
- U.S. Holders of warrants, options, or other stock rights.

U.S. Holders subject to particular U.S. or non-U.S. tax rules, including those that are described in this paragraph, are urged to consult their own tax advisors regarding the consequences to them of the proposed Syros reverse stock split.

If an entity that is treated as a partnership for U.S. federal income tax purposes holds Syros common stock, the U.S. federal income tax treatment of a partner in the partnership will generally depend upon the status of the partner, the activities of the partnership and certain determinations made at the partner level. Accordingly, partnerships holding Syros common stock and the partners in such partnerships should consult their tax advisors regarding the U.S. federal income tax consequences to them.

In addition, the following discussion does not address the tax consequences of the proposed Syros reverse stock split under state, local and foreign tax laws. Furthermore, the following discussion does not address any tax consequences of transactions effectuated before, after or at the same time as the proposed Syros reverse stock split, whether or not they are in connection with the proposed Syros reverse stock split.

SYROS STOCKHOLDERS SHOULD CONSULT THEIR TAX ADVISORS WITH RESPECT TO THE APPLICATION OF THE U.S. FEDERAL INCOME TAX LAWS TO THEIR PARTICULAR SITUATIONS AS WELL AS ANY TAX CONSEQUENCES OF THE PROPOSED SYROS REVERSE STOCK SPLIT ARISING UNDER THE U.S. FEDERAL ESTATE OR GIFT TAX LAWS OR UNDER THE LAWS OF ANY STATE, LOCAL OR NON-U.S. TAXING JURISDICTION OR UNDER ANY APPLICABLE INCOME TAX TREATY.

For purposes of this discussion, a "U.S. Holder" is a beneficial owner of Syros common stock that, for U.S. federal income tax purposes, is or is treated as:

- an individual who is a citizen or resident of the United States;
- a corporation or any other entity taxable as a corporation created or organized in or under the laws of the United States, any state thereof, or the District of Columbia;
- an estate, the income of which is subject to U.S. federal income tax regardless of its source; or
- a trust if either (i) a court within the United States is able to exercise primary supervision over the administration of such trust, and one or more United States persons (within the meaning of Section 7701(a)(30) of the Code) is authorized or has the authority to control all substantial decisions of such trust, or (ii) the trust was in existence on August 20, 1996 and has a valid election in effect under applicable Treasury Regulations to be treated as a United States person for U.S. federal income tax purposes.

Tax Consequences of the Proposed Syros Reverse Stock Split

The proposed Syros reverse stock split should constitute a "recapitalization" for U.S. federal income tax purposes pursuant to Section 368(a)(1)(E) of the Code. As a result, a U.S. Holder generally should not recognize gain or loss upon the proposed Syros reverse stock split, except with respect to cash received in lieu of a fractional share of Syros common stock, as discussed below. A U.S. Holder's aggregate adjusted tax basis in the shares of Syros common stock received pursuant to the proposed Syros reverse stock split should equal the aggregate adjusted tax basis of the shares of the Syros common stock surrendered (excluding any portion of such basis that is allocated to any fractional share of Syros common stock), and such U.S. Holder's holding period in the shares of Syros common stock received should include the holding period in the shares of Syros common stock surrendered. U.S. Treasury Regulations provide detailed rules for allocating the tax basis and holding period of the shares of Syros common stock surrendered to the shares of Syros common stock received in a recapitalization pursuant to the proposed Syros reverse stock split. U.S. Holders of shares of Syros common stock acquired on different dates and at different prices should consult their tax advisors regarding the allocation of the tax basis and holding period of such shares.

Cash in Lieu of Fractional Shares

A U.S. Holder that, pursuant to the proposed Syros reverse stock split, receives cash in lieu of a fractional share of Syros common stock generally should recognize capital gain or loss in an amount equal to the difference, if any, between the amount of cash received and the portion of the U.S. Holder's aggregate adjusted tax basis in the shares of Syros common stock surrendered that is allocated to such fractional share. Such capital gain or loss will be short term if the pre-split shares were held for one year or less at the effective time of the reverse stock split and long term if held for more than one year.

A U.S. Holder may be subject to information reporting and backup withholding on cash paid in lieu of a fractional share in connection with the reverse stock split. A U.S. Holder will be subject to backup withholding if such U.S. Holder is not otherwise exempt and such U.S. Holder does not provide its taxpayer identification number in the manner required or otherwise fails to comply with applicable backup withholding tax rules.

Backup withholding is not an additional tax and amounts withheld will be allowed as a credit against the holder's U.S. federal income tax liability and may entitle such holder to a refund, provided the required information is timely furnished to the IRS. U.S. Holders should consult their own tax advisors regarding the application of the information reporting and backup withholding rules to them.

SYROS' BOARD OF DIRECTORS RECOMMENDS A VOTE "FOR" THE APPROVAL OF THE AMENDMENT TO SYROS' RESTATED CERTIFICATE OF INCORPORATION TO EFFECT THE SYROS REVERSE STOCK SPLIT AND PROPORTIONATE REDUCTION IN THE NUMBER OF AUTHORIZED SHARES OF SYROS COMMON STOCK DESCRIBED ABOVE.

SYROS PROPOSAL NO. 4:

APPROVAL OF THE SYROS PHARMACEUTICALS, INC. 2022 EQUITY INCENTIVE PLAN

Why Syros is Requesting Syros Stockholder Approval of the 2022 Equity Incentive Plan

Syros is asking Syros stockholders to approve the Syros Pharmaceuticals, Inc. 2022 Equity Incentive Plan, or the 2022 Plan. Syros' board of directors believes that Syros' success depends, in large part, on Syros' ability to attract, retain and motivate key employees with experience and ability to efficiently advance its portfolio of clinical candidates and successfully prepare for a potential commercial launch, thereby creating value for all of Syros' stakeholders. Central to these objectives is Syros' equity-based compensation program, which Syros believes has been implemented prudently and consistent with the compensatory practices of other pharmaceutical companies in Syros' peer group and other companies that Syros' competes with for talent. Syros believes that the value of equity incentives granted to Syros' employees currently lags behind that of its compensation peer group and that the marketplace for experienced talent in the biopharmaceutical industry remains intense. Syros' attrition rate, a key human capital metric, has been higher during 2022 than in prior years as a result of a number of factors, and the loss of key employees or the inability to attract new talent is likely to have a material impact on Syros' future prospects. Syros and Syros' board of directors believe that approval of the 2022 Plan would provide an essential tool in meeting Syros' ambitious clinical and business objectives that have been enabled as a result of the merger and PIPE Financing and achieving Syros' ultimate mission of delivering meaningful new medicines to patients and delivering value to Syros' stockholders.

Syros and Syros' board of directors also understand that its equity-compensation needs must be balanced against the dilutive effect of such programs on Syros stockholders. To that end, and based on careful weighing of the considerations, as more fully described below, on July 14, 2022, upon the recommendation of the compensation committee of Syros' board of directors, or the compensation committee, and subject to approval by Syros stockholders, Syros' board of directors adopted the 2022 Plan.

The 2022 Plan is intended to replace Syros' 2016 Stock Incentive Plan, or the Syros 2016 Plan, which was put in place at the time of Syros' initial public offering and will expire by its terms on July 5, 2026. Syros intends to utilize the 2022 Plan as Syros has utilized the Syros 2016 Plan—specifically, to grant equity awards to its existing employees, officers, non-employee directors, and, upon rare occasion, its consultants and advisors, all in order to retain and award those who are critical to Syros' success. The number of shares remaining available for issuance under the Syros 2016 Plan is insufficient to meet these equity compensation needs, including those needs following the merger, thus impeding Syros' ability to properly compensate, motivate, incent and retain its employees, non-employee directors, and other critical advisors.

The Syros compensation committee determined the requested number of shares for the 2022 Plan based on projected annual equity awards to employees and Syros non-employee directors, employee recognition and promotion awards, and an assessment of the dilutive effect of the 2022 Plan in comparison to the peer group of 19 similarly situated companies that the Syros compensation committee currently uses to benchmark compensation. If Syros stockholders approve the 2022 Plan, subject to adjustment in the event of stock splits and other similar events, awards may be made under the 2022 Plan for up to a number of shares of Syros common stock equal to the sum of: (i) 30,000,000 shares of Syros common stock; and (ii) such additional number of shares of Syros common stock (up to 17,375,343 shares) as is equal to the sum of (x) the number of shares of Syros common stock reserved for issuance under the Syros 2016 Plan that remain available for grant immediately prior to the date that the 2022 Plan is approved by Syros stockholders and (y) the number of shares of Syros common stock subject to (A) awards granted under the Syros 2016 Plan and Syros' 2012 Equity Incentive Plan, or the 2012 Plan, that are outstanding as of such date and (B) stock options assumed by Syros pursuant to the merger as of the closing of the merger and which awards or stock options expire, terminate or are otherwise surrendered, cancelled, forfeited or repurchased by Syros at their original issuance price pursuant to a contractual repurchase right (subject, however, in the case of incentive stock options to any limitations under the Internal Revenue Code of 1986, as amended, or the Code, and any regulations thereunder).

The proposed 2022 Plan does not include an evergreen provision (which the Syros 2016 Plan contains) and includes several features that are consistent with protecting the interests of Syros stockholders and sound corporate governance practices, as described below. If Syros stockholders approve the 2022 Plan at the Syros special meeting, then Syros will not grant any new awards under the Syros 2016 Plan after the Syros special meeting. Awards outstanding under the Syros 2016 Plan will, however, remain in effect. If Syros stockholders do not approve the 2022 Plan, the Syros 2016 Plan will remain in effect pursuant to its terms, including the addition of up to 1,600,000 shares on January 1, 2023 under the current evergreen provision of the Syros 2016 Plan.

Syros has relied on the inducement grant exception under Nasdaq Listing Rule 5635(c)(4) to grant nonstatutory stock options as an inducement material to certain employee's acceptance of employment with Syros in accordance with Nasdaq Listing Rule 5635(c)(4). In furtherance of this approach and because the shares available for issuance under the Syros 2016 Plan have been (and continue to be) insufficient to meet Syros' needs, on January 25, 2022, Syros' board of directors approved the Syros 2022 Inducement Stock Incentive Plan, or the 2022 Inducement Plan, initially reserving 1,000,000 shares for issuance thereunder for inducement awards to be granted to persons who (a) were not previously an employee or director of Syros or (b) are commencing employment with Syros following a bona fide period of non-employment, in either case as an inducement material to the individual's entering into employment with Syros and in accordance with the requirements of Nasdaq Stock Market Rule 5635(c)(4). The 2022 Inducement Plan will remain in effect even if the 2022 Plan is approved.

The following table includes information regarding all of Syros' outstanding equity awards (under all of Syros' equity-based compensation plans or arrangements under which shares of Syros common stock may be issued, other than Syros' 2016 Employee Stock Purchase Plan) as of June 30, 2022, including any outstanding stock options granted under Tyme equity incentive plans, which Syros will assume as part of the merger on an as-converted basis (assuming the merger was consummated as of June 30, 2022 at an exchange ratio of 0.4312), shares available for future awards under the Syros 2016 Plan and 2022 Inducement Plan as of June 30, 2022 (assuming the 2022 Plan was approved as of such date) and the number of shares of Syros common stock outstanding as of June 30, 2022:

Number of outstanding options	7,631,678
Weighted average exercise price of outstanding options	$ 7.99
Weighted average remaining contractual term of outstanding options	6.73 years
Number of outstanding restricted stock units, or RSUs	4,587,725
Syros remaining shares available under the Syros 2016 Plan	466,410
Syros remaining shares available under the 2022 Inducement Plan	647,600
Estimated number of outstanding options under Tyme equity incentive plans	6,618,330
Weighted average exercise price of options under Tyme equity incentive plans	$ 3.36
Weighted average remaining contractual term of outstanding options under Tyme equity incentive plans (after giving effect to the extension of the post-termination exercise period of those options with an exercise price of less than $2.00 held by certain employees expected to enter into cooperation agreements)	1.71 years
Shares requested for approval pursuant to the 2022 Plan	30,000,000
Estimated total number of Syros shares available for issuance under all equity-incentive plans or arrangements	49,951,743
Number of shares of Syros common stock outstanding (not giving effect to the merger or the PIPE Financing)	62,989,020
Number of shares of Syros common stock outstanding giving effect to the issuance of an estimated 74,300,000 shares of common stock in the merger	137,289,020
Number of shares of Syros common stock outstanding giving effect to the PIPE Financing and issuance of an estimated 74,300,000 shares of common stock in the merger	201,160,798
Estimated number of shares of Syros common stock outstanding giving effect to the merger and the PIPE Financing assuming the exercise of all outstanding pre-funded warrants and the Pre-Funded PIPE Warrants, without giving effect to any beneficial ownership limitations applicable thereto	276,428,198

As of June 30, 2022, there were no outstanding shares of restricted stock, no stock appreciation rights, or SARs, nor any other stock-based awards.

Syros expects that the proposed share pool under the 2022 Plan will allow it to continue to grant market-competitive equity awards (other than to newly hired employees who will receive grants under the 2022 Inducement Plan to the extent eligible) for approximately two years, but the actual duration of the share pool may vary based on changes in participation and Syros' stock price.

Syros believes that its stock-based compensation programs have been integral to its success in the past and will be important to its ability to succeed in the future. If the 2022 Plan is not approved by Syros stockholders, Syros will not be able to make long-term equity incentive awards that are sufficient to meet its needs. The inability to make competitive equity awards to retain talented employees in a highly competitive market could have an adverse impact on Syros' business and future prospects. Further, if the 2022 Plan is not approved, Syros could be forced to increase cash compensation, which will reduce the resources Syros has allocated to meeting its clinical and business needs and objectives. Therefore, the approval of the 2022 Plan is vital to Syros' future success.

For purposes of this proposal and except where the context otherwise requires, the term "Syros" and similar terms shall include any of Syros' present or future parent or subsidiary corporations as defined in Sections 424(e) or (f) of the Code and any other business venture (including, without limitation, joint venture or limited liability company) in which Syros has a controlling interest, as determined by Syros' board of directors.

Accordingly, Syros' board of directors believes approval of the 2022 Plan is in the best interests of Syros and its stockholders and recommends a vote "FOR" the approval of the 2022 Plan.

The remainder of this Proposal No. 4 includes:

- Highlights of the 2022 Plan;
- Reasons Syros Stockholders Should Approve the 2022 Plan;
- Information Regarding Overhang and Dilution; and
- Description of the 2022 Plan.

Highlights of the 2022 Plan

The 2022 Plan includes several features that are consistent with protecting the interests of Syros stockholders and sound corporate governance practices. These features are highlighted below, and are more fully described in the summary of the 2022 Plan further below in this proposal as well as in the copy of the proposed 2022 Plan in *Annex J* to this joint proxy statement/prospectus.

No Evergreen. The 2022 Plan does not include an "evergreen" or other provision that provides for automatic increases in the number of shares available for grant under the plan. Therefore, Syros' stockholders will have a say in Syros' equity compensation programs because any increase to the maximum share reserve in the 2022 Plan is subject to approval by Syros stockholders.

Minimum Vesting Provisions. Minimum vesting provisions of one year generally apply to all awards to participants, with the exception of awards for up to 5% of Syros shares of common stock reserved under the 2022 Plan.

Clawback Policy. In accepting an award under the 2022 Plan, a participant agrees to be bound by any clawback policy that Syros has in effect or may adopt in the future.

No Automatic Vesting of Awards on a Change in Control Event The 2022 Plan does not provide for the automatic vesting of awards in connection with a change in control event.

No Liberal Share Recycling. The 2022 Plan prohibits there-granting of (i) Syros shares withheld or delivered to satisfy the exercise price of an award or to satisfy tax withholding obligations, (ii) Syros shares that were subject to a SAR and were not issued upon the net settlement or net exercise of such award, or (iii) Syros shares repurchased on the open market using proceeds from the exercise of an award.

No Repricing of Awards. The 2022 Plan prohibits the direct or indirect repricing of stock options or SARs without Syros stockholder approval.

No Discounted Options or SARs. All options and SARs must have an exercise or measurement price that is at least equal to the fair market value of the underlying Syros common stock on the date of grant.

No Reload Options or SARs. No options or SARs granted under the 2022 Plan may contain a provision entitling the award holder to the automatic grant of additional options or SARs in connection with any exercise of the original option or SAR.

No Dividend Equivalents on Options or SARs. No options or SARs granted under the 2022 Plan may provide for the payment or accrual of dividend equivalents.

Dividends and Dividend Equivalents on Restricted Stock, Restricted Stock Units and Other-Stock Based Awards Not Paid Until Award Vests. Any dividends or dividend equivalents paid with respect to restricted stock, RSUs or other stock-based awards will be subject to the same restrictions on transfer and forfeitability as the award with respect to which it is paid.

Limit on Non-Employee Director Compensation. The maximum aggregate amount of cash and value of awards (calculated based on grant date fair value for financial reporting purposes) granted to any non-employee director in any calendar year may not exceed $750,000 in the case of an incumbent director. However, such maximum aggregate amount shall not exceed $1,000,000 in any calendar year for any individual non-employee director in such non-employee director's initial year of election or appointment. Exceptions to these limitations may only be made by Syros' board of directors in extraordinary circumstances provided that the non-employee director receiving any additional compensation does not participate in the decision to award such compensation.

Material Amendments Require Syros Stockholder Approval. Syros stockholder approval is required prior to an amendment of the 2022 Plan that would (i) materially increase the number of Syros shares authorized (other than as provided under the 2022 Plan with respect to certain corporate events or substitute awards), (ii) expand the types of awards that may be granted, or (iii) materially expand the class of participants eligible to participate.

Administered by an Independent Committee. The 2022 Plan is administered by the Syros compensation committee, as delegated by Syros' board of directors. The Syros compensation committee is made up entirely of independent directors.

Reasons Syros Stockholders Should Approve the 2022 Plan

Incentivizes, Retains and Motivates Talent. It is critical to Syros' success that it incentivizes, retains and motivates the best talent in what is a tremendously competitive labor market. Syros' equity-based compensation program has always been and will continue to be a key component in its ability to pay market-competitive compensation to its employees.

Aligns with Syros Pay-for-Performance Compensation Philosophy. Syros believes that equity-based compensation is fundamentally performance-based. As the value of Syros' stock appreciates, its employees receive greater compensation at the same time that Syros stockholders are receiving a greater return on their investment. Conversely, if the stock price does not appreciate following the grant of an equity award, then Syros' employees would not realize any compensation benefit in respect of stock options and would receive lower than intended compensation in respect of RSUs.

Aligns Employee and Director Interests with Syros Stockholder Interests. Providing Syros' employees and non-employee directors with compensation in the form of equity directly aligns the interests of those employees and directors with the interests of Syros stockholders. If the 2022 Plan is approved by Syros stockholders, Syros will be able to continue fostering this alignment between its employees and non-employee directors and Syros stockholders by granting meaningful equity-based incentives.

Consistent with Syros Stockholder Interests and Sound Corporate Governance. As described under the heading "*Highlights of the 2022 Plan*" and more thoroughly below, the 2022 Plan was purposefully designed to include features that are consistent with the interests of Syros stockholders and sound corporate governance.

Information Regarding Overhang and Burn Rate

Overhang

In developing Syros' share request for the 2022 Plan and analyzing the impact of utilizing equity as a means of compensation on Syros stockholders, Syros considered both its "overhang" and its "burn rate".

Overhang is a measure of potential dilution which Syros defines as the sum of (i) the total number of Syros shares underlying all equity awards outstanding and (ii) the total number of Syros shares available for future award grants, divided by the number of shares of Syros common stock outstanding. Because the number of shares of Syros common stock outstanding will be affected by Syros' currently outstanding warrants, the merger and the PIPE Financing, the bullets below present the overhang calculation using various methods for determining the number of shares of Syros common stock outstanding. The overhang calculations presented do not give effect to any beneficial ownership limitations that may be applicable to the exercise of the pre-funded warrants included in such calculations.

As of June 30, 2022, there were 12,219,403 Syros shares underlying all Syros equity awards outstanding and 1,114,010 Syros shares available for issuance under the Syros 2016 Plan and the 2022 Inducement Plan.

- *Overhang Without Regard to the Merger and PIPE Financing* As of June 30, 2022, there were 63,989,020 shares of Syros common stock outstanding (assuming the exercise of the 1,000,000 outstanding pre-funded warrants, or the Pre-Funded 2020 Warrants). Syros believes measuring overhang assuming the exercise of pre-funded warrants, a vehicle used by certain of its investors to invest in Syros while maintaining beneficial ownership below certain thresholds, is appropriate because, having already been paid for, it is reasonable to assume that the pre-funded warrants will ultimately be exercised in the future. Based on these facts and assumptions, Syros' overhang at June 30, 2022 was 20.8% (and would be 21.2% if the Pre-Funded 2020 Warrants were not included in such calculation).
- *Overhang Including Shares Issued in the Merger.* As of June 30, 2022, there were 63,989,020 shares of Syros common stock outstanding (assuming the exercise of the 1,000,000 Pre-Funded 2020 Warrants). Assuming the issuance of an estimated 74,300,000 shares of Syros common stock in the merger and the assumption of outstanding Tyme stock options, which Syros currently estimates would convert into options to purchase 6,618,330 shares of Syros common stock (based on an assumed exchange ratio of 0.4312), Syros's overhang at June 30, 2022 would have been 14.4% (and would have been 14.5% if the Pre-Funded 2020 Warrants were not included in such calculation).
- *Overhang Including Shares Issued in the Merger and Reflecting the PIPE Financing* As of June 30, 2022, there were 63,989,020 shares of Syros common stock outstanding (assuming the exercise of the 1,000,000 Pre-Funded 2020 Warrants). Assuming the issuance of Syros common stock in the merger and assumption of outstanding Tyme stock options (based on an assumed exchange ratio of 0.4312) as described above, as well as the issuance of 63,871,778 shares of Syros common stock in the PIPE Financing and the issuance of 74,267,400 shares of common stock upon exercise of the Pre-Funded PIPE Warrants, Syros'

overhang on June 30, 2022 would have been 7.22% (and would have been 9.92% if the Pre-Funded 2020 Warrants and the Pre-Funded PIPE Warrants were not included in such calculation).

While approval of the 2022 Plan is not contingent on the closing of the merger or the PIPE Financing, the number of shares proposed to be authorized for grant under the 2022 Plan was developed on the assumption that both transactions would occur. If the 30,000,000 shares proposed to be authorized for grant under the 2022 Plan were included in this scenario calculation, Syros' overhang on June 30, 2022 would have been 18.1% (and would have been 24.8% if the Pre-Funded 2020 Warrants and the Pre-Funded PIPE Warrants were not included in such calculation). Syros believes that the approval of the 2022 Plan would not materially change share overhang from current levels in the event of the closing of the merger and the PIPE Financing, particularly in light of the elimination of the "evergreen" provision in the Syros 2016 Plan, and that an 18.1% overhang rate is at approximately the median for Syros' compensation peer group. Even if the Pre-Funded 2020 Warrants and Pre-Funded PIPE Warrants were excluded from the overhang calculation, the 24.8% overhang level is in the middle 50% of Syros' compensation peer group.

Burn Rate

Burn rate provides a measure of the potential dilutive impact of Syros' equity award program. which Syros calculates by dividing the number of Syros shares subject to equity awards granted during the year by the basic weighted average number of shares outstanding. Syros focuses primarily on a "net" burn rate, giving effect to cancellations and forfeitures, because it believes that this methodology more accurately reflects that actual dilutive effect of Syros' equity compensation program. Set forth below is a table that reflects Syros' burn rate for the 2021, 2020 and 2019 calendar years, calculated on both a "gross" and "net" basis, as well as an average over those years.

Calendar Year	Awards Granted (#)	Awards Cancelled or Forfeited (#)	Weighted Average Common Shares Outstanding (basic) (#)	Gross Burn Rate(1)	Net Burn Rate(2)
2021	4,165,154(3)	1,716,416	62,534,978	6.67%	3.92%
2020	2,054,550	306,256	46,051,617	4.46%	3.80%
2019	2,343,924	281,607	40,222,182	5.83%	5.13%
3-Year Average				5.65%	4.28%

(1) "Gross burn rate" is defined as the number of equity awards granted in the year divided by the basic weighted average number of shares of Syros common stock outstanding.

(2) "Net burn rate" is defined as the number of equity awards granted in the year*less* the number of shares subject to awards returned to the Syros 2016 Plan through cancellations or forfeitures, divided by the basic weighted average number of shares of Syros common stock outstanding.

(3) Includes 1,110,000 shares of Syros common stock subject to stock options granted during the year as an inducement material to the acceptance by Syros' Chief Financial Officer and Chief Commercial Officer of employment with Syros. Excluding these grants, the gross and net burn rates for 2021 would be 4.89% and 2.14%, respectively.

Over the last three years, Syros' headcount has increased by over 50% as it has expanded its portfolio of clinical candidates, advanced its programs into pivotal clinical development, begun building commercial capabilities, and entered into a strategic partnership for one of its discovery-stage programs. Even though Syros' stock price has declined over this three-year period, thus creating challenges in delivering market-competitive value from equity incentives, Syros believes it has responsibly managed dilution in its equity compensation program to date.

Description of the 2022 Plan

The following is a brief summary of the 2022 Plan, a copy of which is attached as *Annex J* to this joint proxy statement/prospectus. References to Syros' board of directors in this summary shall include the Syros compensation committee or any similar committee or sub-committee or the officers of Syros to the extent that Syros' board of directors' powers or authority under the 2022 Plan have been delegated to such committee or officers, in accordance with the 2022 Plan.

Types of Awards; Shares Available for Awards; Share Counting Rules

The 2022 Plan provides for the grant of incentive stock options intended to qualify under Section 422 of the Code,non-statutory stock options, SARs, restricted stock, RSUs, other stock-based awards and cash awards as described below (collectively, for purposes of this proposal, "awards").

Subject to adjustment in the event of stock splits, stock dividends and other similar events, awards may be made under the 2022 Plan (any or all of which awards may be in the form of incentive stock options) for up to a number of shares of Syros common stock equal to the sum of: ((i) 30,000,000 shares of Syros common stock; and (ii) such additional number of shares of Syros common stock (up to 17,375,343 shares) as is equal to the sum of (x) the number of shares of Syros common stock reserved for issuance under the Syros 2016 Plan that remain available for grant immediately prior to the date that the 2022 Plan is approved by Syros stockholders and (y) the number of shares of Syros common stock subject to awards granted under the Syros 2016 Plan and the 2012 Plan that are outstanding as of such date and the number of shares of Syros common stock subject to stock options assumed by Syros pursuant to the merger as of the closing of the merger and which awards expire, terminate or are otherwise surrendered, cancelled, forfeited or repurchased by Syros at their original issuance price pursuant to a contractual repurchase right (subject, however, in the case of incentive stock options to any limitations under the Code). Shares of Syros common stock issued under the 2022 Plan may consist in whole or in part of authorized but unissued shares or treasury shares.

The 2022 Plan provides that the maximum aggregate amount of cash and value of awards (calculated based on grant date fair value for financial reporting purposes) granted to any individual non-employee director in any calendar year may not exceed $750,000 in the case of an incumbent director. However, such maximum aggregate amount shall not exceed $1,000,000 in any calendar year for any individual non-employee director in such non-employee director's initial year of election or appointment. Moreover, fees paid by Syros on behalf of any non-employee director in connection with regulatory compliance and any amounts paid to a non-employee director as reimbursement of an expense will not count against this limit. Exceptions to this limitation may only be made by Syros' board of directors in extraordinary circumstances provided that any non-employee director receiving additional compensation does not participate in the decision to award such compensation. This limitation does not apply to cash or awards granted to a non-employee director in his or her capacity as an advisor or consultant to Syros.

For purposes of counting the number of Syros shares available for the grant of awards under the 2022 Plan, all shares of Syros common stock covered by SARs will be counted against the number of shares available for the grant of awards. However, SARs that may be settled only in cash will not be so counted. Similarly, to the extent that an RSU award may be settled only in cash, no Syros shares will be counted against the Syros shares available for the grant of awards under the 2022 Plan. In addition, if Syros grants a SAR in tandem with an option for the same number of shares of Syros common stock and provides that only one such award may be exercised, or tandem SAR, only the Syros shares covered by the option, and not the Syros shares covered by the tandem SAR, will be so counted, and the expiration of one in connection with the other's exercise will not restore Syros shares to the 2022 Plan.

Syros shares covered by awards under the 2022 Plan that expire or are terminated, surrendered, or cancelled without having been fully exercised or are forfeited in whole or in part (including as the result of Syros shares

subject to such award being repurchased by Syros at the original issuance price pursuant to a contractual repurchase right) or that result in any Syros shares not being issued (including as a result of a SAR or an RSU that was settleable either in cash or in stock actually being settled in cash) will again be available for the grant of awards under the 2022 Plan (subject, in the case of incentive stock options, to any limitations under the Code). In the case of the exercise of a SAR, the number of Syros shares counted against the Syros shares available for the grant of awards under the 2022 Plan will be the full number of Syros shares subject to the SAR multiplied by the percentage of the SAR actually exercised, regardless of the number of Syros shares actually used to settle the SAR upon exercise, and the Syros shares covered by a tandem SAR will not again become available for grant upon the expiration or termination of the tandem SAR.

Shares of Syros common stock that are delivered (by actual delivery, attestation, or net exercise) to Syros by a participant to purchase shares of Syros common stock upon exercise of an award or to satisfy tax withholding obligations (including shares retained from the award creating the tax obligation) will not be added back to the number of Syros shares available for the future grant of awards under the 2022 Plan. Syros shares repurchased by Syros on the open market using proceeds from the exercise of an award will not increase the number of Syros shares available for future grant of awards under the 2022 Plan.

In connection with a merger or consolidation of an entity with Syros or Syros' acquisition of property or stock of an entity, Syros' board of directors may grant awards under the 2022 Plan in substitution for any options or other stock or stock-based awards granted by such entity or an affiliate thereof on such terms as Syros' board of directors determines appropriate in the circumstances, notwithstanding any limitation on awards contained in the 2022 Plan. No such substitute awards shall count against the overall share limit, except as required by reason of Section 422 and related provisions of the Code.

Descriptions of Awards

Options. A participant who is awarded an option receives the right to purchase a specified number of Syros shares of common stock at a specified exercise price and subject to the other terms and conditions that are specified in connection with the award agreement. An option that is not intended to be an "incentive stock option" is a "non-statutory stock option." Options may not be granted at an exercise price that is less than 100% of the fair market value of Syros' common stock on the date of grant. If Syros' board of directors approves the grant of an option with an exercise price to be determined on a future date, the exercise price may not be less than 100% of the fair market value of Syros' common stock on that future date. Under present law, incentive stock options may not be granted at an exercise price less than 110% of the fair market value in the case of stock options granted to participants who hold more than 10% of the total combined voting power of all classes of Syros' stock or any of Syros' subsidiaries. Under the terms of the 2022 Plan, options may not be granted for a term in excess of ten years (and, under present law, five years in the case of incentive stock options granted to participants who hold greater than 10% of the total combined voting power of all classes of Syros stock or any of Syros' subsidiaries).

The 2022 Plan permits participants to pay the exercise price of options using one or more of the following manners of payment: (i) payment by cash or by check, (ii) except as may otherwise be provided in the applicable award agreement or approved by Syros' board of directors, in connection with a "cashless exercise" through a broker, (iii) to the extent provided in the applicable award agreement or approved by Syros' board of directors, and subject to certain conditions, by delivery to Syros (either by actual delivery or attestation) of shares of Syros common stock owned by the participant valued at their fair market value, (iv) to the extent provided in an applicable non-statutory stock option award agreement or approved by Syros' board of directors, by delivery of a notice of "net exercise" as a result of which Syros will retain a number of shares of Syros common stock otherwise issuable pursuant to the stock option equal to the aggregate exercise price for the portion of the option being exercised divided by the fair market value of Syros common stock on the date of exercise, (v) to the extent permitted by applicable law and provided for in the applicable award agreement or approved by Syros' board of directors, by any other lawful means, or (vi) by any combination of these forms of payment. No option granted

under the 2022 Plan may contain a provision entitling the participant to the automatic grant of additional options in connection with any exercise of the original option. No options granted under the 2022 Plan may provide for the payment or accrual of dividend equivalents.

Stock Appreciation Rights. A participant who is awarded a SAR receives, upon exercise, a number of shares of Syros common stock, or cash (or a combination of shares of Syros common stock and cash) determined by reference to appreciation, from and after the date of grant, in the fair market value of a share of Syros common stock over the measurement price. The 2022 Plan provides that the measurement price of a SAR may not be less than 100% of the fair market value of Syros common stock on the date the SAR is granted (provided, however, that if Syros' board of directors approves the grant of a SAR effective as of a future date, the measurement price shall not be less than 100% of the fair market value on such future date) and that SARs may not be granted with a term in excess of 10 years. No SARs granted under the 2022 Plan may contain a provision entitling the participant to the automatic grant of additional SARs in connection with any exercise of the original SAR. No SARs granted under the 2022 Plan may provide for the payment or accrual of dividend equivalents.

Limitation on Repricing of Options or SARs. With respect to options and SARs, unless such action is approved by Syros stockholders or otherwise permitted under the terms of the 2022 Plan in connection with certain changes in capitalization and reorganization events, Syros may not (i) amend any outstanding option or SAR granted under the 2022 Plan to provide an exercise price or measurement price per share that is lower than the then-current exercise price or measurement price per share of such outstanding option or SAR, (ii) cancel any outstanding option or SAR (whether or not granted under the 2022 Plan) and grant in substitution therefor new awards under the 2022 Plan (other than certain substitute awards issued in connection with a merger or consolidation of an entity with Syros or an acquisition by Syros, described above) covering the same or a different number of shares of Syros common stock and having an exercise price or measurement price per share lower than the then-current exercise price or measurement price per share of the cancelled option or SAR, (iii) cancel in exchange for a cash payment any outstanding option or SAR with an exercise price or measurement price per share above the then-current fair market value of Syros common stock, or (iv) take any other action under the 2022 Plan that constitutes a "repricing" within the meaning of the rules of The Nasdaq Stock Market or any other exchange or marketplace on which Syros' stock is listed or traded.

Restricted Stock Awards. A participant who is granted a restricted stock award is entitled to acquire shares of Syros common stock, subject to Syros' right to repurchase all or part of such shares at their issue price or other stated or formula price (or to require forfeiture of such shares if issued at no cost) in the event that the conditions specified in the applicable award are not satisfied prior to the end of the applicable restriction period established for such award. Any dividends (whether paid in cash, stock or property) declared and paid by Syros with respect to shares of restricted stock will be paid to the participant only if and when such shares become free from the restrictions on transferability and forfeitability that apply to such shares. No interest will be paid on unvested dividends.

Restricted Stock Unit Awards. A participant who is granted an RSU award is entitled to receive shares of Syros common stock, or cash equal to the fair market value of such shares or a combination thereof, to be delivered at the time such award vests or on a deferred basis pursuant to the terms and conditions established by Syros' board of directors. Syros' board of directors may provide that settlement of RSUs will be deferred, on a mandatory basis or at the election of the participant, in a manner that complies with Section 409A of the Code. A participant has no voting rights with respect to any RSU. An RSU award agreement may provide the applicable participant with the right to receive an amount equal to any dividends or other distributions declared and paid on an equal number of outstanding shares of Syros common stock. Any such dividend equivalents may be settled in cash and/or shares of Syros common stock and will be subject to the same restrictions on transfer and forfeitability as the RSUs with respect to which such dividend equivalents are awarded. No interest will be paid on dividend equivalents.

Other Stock-Based Awards. Under the 2022 Plan, Syros' board of directors may grant other awards of shares of Syros common stock, and other awards that are valued in whole or in part by reference to, or are otherwise based

on, shares of Syros common stock or other property, having such terms and conditions as Syros' board of directors may determine. Syros refers to these types of awards as other stock-based awards. Other stock-based awards may be available as a form of payment in settlement of other awards granted under the 2022 Plan or as payment in lieu of compensation to which a participant is otherwise entitled. Other stock-based awards may be paid in shares of Syros common stock or in cash, as Syros' board of directors may determine. The award agreement of an other stock-based award may provide the participant who receives that award of an other stock-based award with the right to receive dividend equivalents. Dividend equivalents may be settled in cash and/or shares of Syros common stock and will be subject to the same restrictions on transfer and forfeitability as the other stock-based award with respect to which they are awarded. No interest will be paid on dividend equivalents.

Cash Awards. Under the 2022 Plan, Syros' board of directors has the right to grant cash-based awards including awards subject to performance conditions.

Performance Conditions. Awards under the 2022 Plan may be made subject to the achievement of performance goals. Syros' board of directors may specify that the degree of granting, vesting and/or payout of any award subject to performance-based vesting conditions will be subject to the achievement of one or more of the following performance measures established by Syros' board of directors, which may be based on the relative or absolute attainment of specified levels of one or any combination of the following measures (and which may be determined pursuant to GAAP or on a non-GAAP basis, as determined by Syros' board of directors): (i) the entry into an arrangement or agreement with a third party for the development, commercialization, marketing or distribution of products, services or technologies, or for conducting a research program to discover and develop a product, service or technology, and/or the achievement of milestones under such arrangement or agreement, including events that trigger an obligation or payment right; (ii) achievement of domestic and international regulatory milestones, including the submission of filings required to advance products, services and technologies in clinical development and the achievement of approvals by regulatory authorities relating to the commercialization of products, services and technologies; (iii) the achievement of discovery, preclinical and clinical stage scientific objectives, discoveries or inventions for products, services and technologies under research and development; (iv) the entry into or completion of a phase of clinical development for any product, service or technology, such as the entry into or completion of Phase 1, 2 and/or 3 clinical trials; (v) the consummation of debt or equity financing transactions, or acquisitions of business, technologies and assets; (vi) new product or service releases; (vii) the achievement of qualitative or quantitative performance measures set forth in operating plans approved by Syros' board of directors from time to time; (viii) specified levels of product sales, net income, earnings before or after discontinued operations, interest, taxes, depreciation and/or amortization, operating profit before or after discontinued operations and/or taxes, sales, sales growth, earnings growth, cash flow or cash position, gross margins, stock price, market share, return on sales, assets, equity or investment; (ix) improvement of financial ratings; (x) achievement of balance sheet or income statement objectives; (xi) total stockholder return or stock price; (xii) other comparable measures of financial and operational performance; and/ or (xiii) any other measure selected by Syros' board of directors. Such goals may reflect absolute entity or business unit performance or a relative comparison to the performance of a peer group of entities or other external measure of the selected performance criteria and may be absolute in their terms or measured against or in relationship to other companies comparably, similarly or otherwise situated. Syros' board of directors may specify that such performance measures will be adjusted to exclude any one or more of: (I) extraordinary items; (II) gains or losses on the dispositions of discontinued operations; (III) the cumulative effects of changes in accounting principles; (IV) the write-down of any asset; (V) fluctuation in foreign currency exchange rates; (VI) charges for restructuring and rationalization programs; (VII) non-cash, mark-to-market adjustments on derivative instruments; (VIII) amortization of purchased intangibles; (IX) the net impact of tax rate changes; (X) non-cash asset impairment charges; (XI) gains on extinguishment of the tax receivable agreement; and (XII) any other factors as Syros' board of directors may determine. Such performance measures: (A) may vary by participant and may be different for different awards; (B) may be particular to a participant or the department, branch, line of business, subsidiary or other unit in which the participant works and (C) may cover such period as may be specified by Syros' board of directors. Syros' board of directors will have the

authority to make equitable adjustments to the performance goals in recognition of unusual or non-recurring events affecting Syros or the financial statements of Syros, in response to changes in applicable laws or regulations or to account for items of gain, loss or expense determined to be extraordinary or unusual in nature or infrequent in occurrence or related to the disposal of a segment of a business or related to a change in accounting principles. Syros' board of directors may adjust the cash or number of shares payable pursuant to a performance award, and Syros' board of directors may, at any time, waive the achievement of the applicable performance measures. Notwithstanding its designation as a performance award, no option or SAR will provide for the payment or accrual of dividend equivalents, any dividends declared and paid by Syros with respect to shares of restricted stock will be subject to the same dividend rules for restricted stock awards not designated as a performance award and any right to receive dividend equivalents on an award of RSUs and other stock-based awards will be subject to the same dividend equivalent rules for such awards that are not designated as a performance award.

Eligibility to Receive Awards

All of Syros' employees, officers, and directors, as well as Syros' consultants and advisors, are eligible to receive awards under the 2022 Plan. However, incentive stock options may only be granted to Syros' employees, employees of Syros' present or future parent or subsidiary corporations as defined in Sections 424(e) or (f) of the Code, and employees of any other entities the employees of which are eligible to receive incentive stock options under the Code.

Transferability of Awards

Awards may not be sold, assigned, transferred, pledged or otherwise encumbered by a participant, either voluntarily or by operation of law, except by will or the laws of descent and distribution or, other than in the case of an incentive stock option, pursuant to a qualified domestic relations order. During the life of the participant, awards are exercisable only by the participant. However, except with respect to awards that are subject to Section 409A of the Code and incentive stock options, Syros' board of directors may permit or provide in an award for the gratuitous transfer of the award by the participant to or for the benefit of any immediate family member, family trust or other entity established for the benefit of the participant and/or an immediate family member thereof if Syros would be eligible to use a Form S-8 under the Securities Act for the registration of the sale of Syros common stock subject to such award to the proposed transferee. Further, Syros is not required to recognize any such permitted transfer until such time as the permitted transferee has, as a condition to the transfer, delivered to Syros a written instrument in form and substance satisfactory to Syros confirming that such transferee will be bound by all of the terms and conditions of the award. None of the restrictions described in this paragraph prohibit a transfer from the participant to Syros.

No Rights as a Stockholder; Clawback

No participant or designated beneficiary shall have any rights as a stockholder with respect to any shares of Syros common stock to be distributed with respect to an award granted under the 2022 Plan until becoming a record holder of such shares, subject to the terms of an award agreement. In accepting an award under the 2022 Plan, a participant agrees to be bound by any clawback policy that Syros has in effect or may adopt in the future.

Plan Benefits

As of June 30, 2022, approximately 217 persons would be eligible to receive awards under the 2022 Plan, including all three of Syros' named executive officers who are current employees, the three other Syros executive officers who are not named executive officers (all of whom are also current employees), 123 employees who are not executive officers, nine Syros non-employee directors, and 79 active Syros consultants and advisors.

On August 8, 2022, the last reported sale price of Syros common stock on The Nasdaq Stock Market was .

New Plan Benefits Table

The granting of awards under the 2022 Plan is discretionary, and Syros cannot now determine the number or type of awards to be granted in the future to any particular person or group, other than as set forth below. Under Syros' director compensation program, immediately following each annual meeting of Syros stockholders, Syros grants each of its non-employee directors who has served on the Syros board of directors for at least six months an option to purchase 17,500 shares of Syros common stock. Based upon the current Syros director compensation program, future awards of options to purchase shares will be made to non-employee directors in years subsequent to 2023. If Syros stockholders do not approve the 2022 Plan, Syros will grant the options to the non-employee directors under the Syros 2016 Plan.

Name and Position	Dollar Value	Number of Shares of Common Stock Underlying Option Awards
Peter Wirth, Chair of the Syros Board of Directors	—	17,500
Srinivas Akkaraju, M.D., Ph.D., Director	—	17,500
Mark J. Alles, Director	—	17,500
Deborah Dunsire, M.D., Director	—	17,500
S. Gail Eckhardt, M.D., Director	—	17,500
Marsha H. Fanucci, Director	—	17,500
Amir Nashat, Ph.D., Director	—	17,500
Phillip A. Sharp, Ph.D., Director	—	17,500
Richard A. Young, Ph.D., Director	—	17,500
All current executive officers as a group	—	—
All current directors who are not executive officers as a group(1)	—	157,500
All employees, including all current officers who are not executive officers, as a group	—	—

(1) Represents the annual stock option award to purchase shares of common stock to be granted in 2023 to each non-employee director who has served on the Syros board of directors for at least six months. The value of a stock option to be granted under this policy will be determined using the same method Syros uses to calculate the grant-date fair value of share options in its financial statements included in its 2022 Annual Report. Excludes (i) options that the non-employee directors will be entitled to receive under the current Syros director compensation program for subsequent years following 2023 and (ii) any discretionary awards that any non-employee director may be awarded under the 2022 Plan. Under the current Syros director compensation program, immediately following each annual meeting of Syros stockholders, Syros will grant to each such non-employee director an option to purchase 17,500 shares of Syros common stock, with an exercise price equivalent to fair market value of a share of Syros common stock at the time of grant, which option will vest as to 50% of the shares on the six-month anniversary of the date of grant and as to the remainder of the shares in equal monthly installments thereafter until the first anniversary of the date of grant, subject to continued service, with full acceleration upon a change in control of Syros. The option will have a term of ten years.

Administration

The 2022 Plan will be administered by Syros' board of directors. Syros' board of directors has the authority to grant awards and to adopt, amend and repeal the administrative rules, guidelines and practices relating to the 2022 Plan that it deems advisable and to construe and interpret the provisions of the 2022 Plan and any award agreements entered into under the 2022 Plan. Syros' board of directors may correct any defect, supply any omission or reconcile any inconsistency in the 2022 Plan or any award. All actions and decisions by Syros' board of directors with respect to the 2022 Plan and any awards made under the 2022 Plan will be made in Syros' board of directors' discretion and will be final and binding on all persons having or claiming any interest in the 2022 Plan or in any award.

Pursuant to the terms of the 2022 Plan, Syros' board of directors may delegate any or all of its powers under the 2022 Plan to one or more committees or subcommittees of Syros' board of directors. Syros' board of directors has authorized the Syros compensation committee to administer certain aspects of the 2022 Plan. Awards granted to non-employee directors must be granted and administered by a committee of Syros' board of directors, all of the members of which are independent directors as defined by Section 5605(a)(2) of the Nasdaq Marketplace Rules. Subject to any requirements of applicable law, Syros' board of directors may delegate to one or more officers the power to grant awards (subject to any limitations under the 2022 Plan) to employees or officers and to exercise such other powers under the 2022 Plan as Syros' board of directors may determine, provided that, Syros' board of directors shall fix the terms of awards to be granted by such officers, the maximum number of Syros shares subject to awards that the officers may grant, and the time period in which such awards may be granted; and provided further, that no officer shall be authorized to grant awards to any "executive officer" (as defined by Rule 3b-7 under the Exchange Act or to any "officer" (as defined by Rule16a-1(f) under the Exchange Act).

Subject to applicable limitations contained in the 2022 Plan, Syros' board of directors, the Syros compensation committee, or any other committee or subcommittee or officer to whom Syros' board of directors has delegated authority pursuant to the 2022 Plan, as the case may be, selects the recipients of awards and determines (i) the number of shares of Syros common stock, cash or other consideration covered by awards and the terms and conditions of such awards, including the dates upon which such awards become exercisable or otherwise vest, (ii) the exercise or measurement price of awards, if any, and (iii) the duration of awards.

Except as otherwise provided in the 2022 Plan, each award under the 2022 Plan may be made alone or in addition or in relation to any other award. The terms of each award need not be identical, and Syros' board of directors need not treat participants uniformly. Syros' board of directors will determine the effect on an award of the disability, death, termination or other cessation of employment or service, authorized leave of absence or other change in the employment or other service status of a participant, and the extent to which, and the period during which, the participant (or the participant's legal representative, conservator, guardian or designated beneficiary) may exercise rights or receive any benefits under an award.

Syros' board of directors may at any time provide that any award shall become immediately exercisable in whole or in part, free from some or all restrictions or conditions or otherwise realizable in whole or in part, as the case may be. Subject to the preceding sentence, no award under the 2022 Plan shall vest earlier than the first anniversary of its date of grant, unless such award is granted in lieu of salary, bonus or other compensation otherwise earned by or payable to the participant; provided, that, such limitation will not apply to awards granted, in the aggregate, for up to 5% of the maximum number of authorized Syros shares under the 2022 Plan.

In the event of any stock split, reverse stock split, stock dividend, recapitalization, combination of shares, reclassification of shares,spin-off or other similar change in capitalization or event, or any dividend or distribution to holders of Syros common stock, other than an ordinary cash dividend, Syros is required to make equitable adjustments (or make substituted awards, as applicable), in the manner determined by Syros' board of directors, to (i) the number and class of securities available under the 2022 Plan, (ii) the share counting rules set

forth in the 2022 Plan, (iii) the number and class of securities and exercise price per share of each outstanding option, (iv) the share- and per-share provisions and the measurement price of each outstanding SAR, (v) the number of shares subject to and the repurchase price per share subject to each outstanding award of restricted stock, and (vi) the share and per-share-related provisions and the purchase price, if any, of each outstanding RSU award and each outstanding other stock-based award. In the event Syros effects a split of Syros common stock by means of a stock dividend and the exercise price of and the number of Syros shares subject to an outstanding option are adjusted as of the date of the distribution of the dividend (rather than as of the record date for such dividend), then a participant who exercises an option between the record date and the distribution date for such stock dividend shall be entitled to receive, on the distribution date, the stock dividend with respect to the shares of Syros common stock acquired upon such option exercise, notwithstanding the fact that such shares were not outstanding as of the close of business on the record date for such stock dividend.

Syros will indemnify and hold harmless each director, officer, employee or agent to whom any duty or power relating to the administration or interpretation of the 2022 Plan has been or will be delegated against any cost or expense (including attorneys' fees) or liability (including any sum paid in settlement of a claim with Syros' board of directors' approval) arising out of any act or omission to act concerning the 2022 Plan unless arising out of such person's own fraud or bad faith.

Amendment of awards. Except as otherwise provided under the 2022 Plan with respect to repricing outstanding stock options or SARs and with respect to amendments to the 2022 Plan, Syros' board of directors may amend, modify or terminate any outstanding award, including but not limited to, substituting therefor another award of the same or a different type, changing the date of exercise or realization, and converting an incentive stock option to a non-statutory stock option, provided that the participant's consent to any such action will be required unless Syros' board of directors determines that the action, taking into account any related action, does not materially and adversely affect the participant's rights under the 2022 Plan or the change is otherwise permitted under the terms of the 2022 Plan in connection with certain corporate events.

Reorganization Events

The 2022 Plan contains provisions addressing the consequences of any reorganization event. A reorganization event is defined under the 2022 Plan as (a) any merger or consolidation of Syros with or into another entity as a result of which all of Syros common stock is converted into or exchanged for the right to receive cash, securities or other property, or is cancelled, (b) any transfer or disposition of all of Syros common stock for cash, securities or other property pursuant to a share exchange or other transaction or (c) Syros liquidation or dissolution.

Provisions Applicable to Awards Other than Restricted Stock. Under the 2022 Plan, if a reorganization event occurs, Syros' board of directors may take any one or more of the following actions as to all or any (or any portion of) outstanding awards other than restricted stock on such terms as Syros' board of directors determines (except to the extent specifically provided otherwise in an applicable award agreement or another agreement between a participant and Syros): (1) provide that such awards shall be assumed, or substantially equivalent awards shall be substituted, by the acquiring or succeeding corporation (or an affiliate thereof), (2) upon written notice to a participant, provide that all of the participant's unvested awards will be forfeited immediately before the reorganization event and/or that all of the participant's unexercised awards will terminate immediately prior to the consummation of such reorganization event unless exercised by the participant (to the extent then exercisable) within a specified period following the date of such notice, (3) provide that outstanding awards shall become exercisable, realizable, or deliverable, or restrictions applicable to an award shall lapse, in whole or in part prior to or upon such reorganization event, (4) in the event of a reorganization event under the terms of which holders of Syros common stock will receive upon consummation thereof a cash payment for each share surrendered in the reorganization event, or the Acquisition Price, make or provide for a cash payment to participants with respect to each award held by a participant equal to (A) the number of shares of Syros common stock subject to the vested portion of the award (after giving effect to any acceleration of vesting that occurs upon or immediately prior to such reorganization event) multiplied by (B) the excess, if any, of (I) the

Acquisition Price over (II) the exercise, measurement or purchase price of such award and any applicable tax withholdings, in exchange for the termination of such award, provided, that if the Acquisition Price per share (as determined by Syros' board of directors) does not exceed the exercise price of the award, then the award will be cancelled without any payment of consideration, (5) provide that, in connection with Syros' liquidation or dissolution, awards shall convert into the right to receive liquidation proceeds (if applicable, net of the exercise, measurement or purchase price thereof and any applicable tax withholdings) and (6) any combination of the foregoing.

Syros' board of directors is not obligated to treat all awards, all awards held by a participant, or all awards of the same type, identically. Certain RSU awards that are subject to Section 409A of the Code will be settled in accordance with the terms of the applicable award agreement or as otherwise specified in the 2022 Plan. Syros' board of directors, with reasonable notice to participants holding options or SARs, may impose a limitation on the ability these participants to exercise their awards for the minimum number of days prior to the closing of the reorganization event as is reasonably necessary to facilitate the orderly closing of the reorganization event.

Provisions Applicable to Restricted Stock. Upon the occurrence of a reorganization event other than Syros' liquidation or dissolution, Syros' repurchase and other rights with respect to outstanding restricted stock will inure to the benefit of Syros' successor and will, unless Syros' board of directors determines otherwise, apply to the cash, securities or other property which Syros common stock was converted into or exchanged for pursuant to such reorganization event in the same manner and to the same extent as they applied to such restricted stock. However, Syros' board of directors may either provide for termination or deemed satisfaction of such repurchase or other rights under the instrument evidencing any restricted stock or any other agreement between a participant and Syros, either initially or by amendment or provide for forfeiture of such restricted stock if issued at no cost. Upon the occurrence of a reorganization event involving Syros' liquidation or dissolution, except to the extent specifically provided to the contrary in the instrument evidencing any award of restricted stock or any other agreement between the participant and Syros, all restrictions and conditions on all restricted stock then outstanding shall automatically be deemed terminated or satisfied.

Provisions for Foreign Participants

Syros' board of directors may establish one or more sub-plans under the 2022 Plan to satisfy applicable securities, tax or other laws of various jurisdictions. Syros' board of directors will establish such sub-plans by adopting supplements to the 2022 Plan containing any limitations on Syros' board of directors' discretion under the 2022 Plan and any additional terms and conditions not otherwise inconsistent with the 2022 Plan as Syros' board of directors deems necessary or desirable. All supplements adopted by Syros' board of directors will be deemed to be part of the 2022 Plan, but each supplement will only apply to participants within the affected jurisdiction.

Withholding

The participant must satisfy all applicable federal, state, and local or other income and employment tax withholding obligations before Syros will deliver stock certificates or otherwise recognize ownership of Syros common stock under an award. Syros may elect to satisfy the withholding obligations through additional withholding on salary or wages. If Syros elects not to or cannot withhold from other compensation, the participant must pay Syros the full amount, if any, required for withholding or have a broker tender to Syros cash equal to the withholding obligations. Payment of withholding obligations is due before Syros will issue any shares on exercise, vesting or release from forfeiture of an award or at the same time as payment of the exercise or purchase price, unless Syros determines otherwise. If provided for in an award or approved by Syros' board of directors, a participant may satisfy the tax obligations in whole or in part by delivery (either by actual delivery or attestation) of shares of Syros common stock, including shares retained from the award creating the tax obligation, valued at their fair market value. However, except as otherwise provided by Syros' board of directors, that the total tax withholding where stock is being used to satisfy such tax obligations cannot exceed Syros'

minimum statutory withholding obligations (based on minimum statutory withholding rates for federal and state tax purposes, including payroll taxes, that are applicable to such supplemental taxable income), except that, to the extent that Syros is able to retain shares of Syros common stock having a fair market value that exceeds the statutory minimum applicable withholding tax without financial accounting implications or Syros is withholding in a jurisdiction that does not have a statutory minimum withholding tax, Syros may retain such number of Syros shares (up to the number of shares having a fair market value equal to the maximum individual statutory rate of tax) as Syros shall determine to be necessary to satisfy the tax liability associated with any award. Shares used to satisfy tax withholding requirements cannot be subject to any repurchase, forfeiture, unfulfilled vesting or other similar requirements.

Amendment or Termination

If Syros receives Syros stockholder approval of the 2022 Plan, no award may be granted under the 2022 Plan after September 14, 2032, but awards previously granted may extend beyond that date. Syros' board of directors may amend, suspend or terminate the 2022 Plan or any portion of the 2022 Plan at any time, except that (i) no amendment may be made to the plan to permit an option or SAR to be repriced without Syros stockholder approval and (ii) no amendment that would require Syros stockholder approval under the rules of the national securities exchange on which Syros maintains its primary listing may be made effective unless and until such amendment has been approved by Syros stockholders. If the national securities exchange on which Syros maintains its primary listing does not have rules regarding when Syros stockholder approval of amendments to equity compensation plans is required (or if Syros common stock is not then listed on any national securities exchange), no amendment of the 2022 Plan materially increasing the number of shares authorized under the plan (other than as provided under the 2022 Plan with respect to certain corporate events or substitute awards), expanding the types of awards that may be granted under the plan or materially expanding the class of participants eligible to participate in the plan will be effective unless and until Syros stockholders approve such amendment. If at any time the approval of Syros stockholders is required as to any other modification or amendment under Section 422 of the Code or any successor provision with respect to incentive stock options, Syros' board of directors may not effect such modification or amendment without such approval. Unless otherwise specified in the amendment, any amendment to the 2022 Plan adopted in accordance with the procedures described above will apply to, and be binding on the holders of, all awards outstanding under the 2022 Plan at the time the amendment is adopted, provided that Syros' board of directors determines that such amendment, taking into account any related action, does not materially and adversely affect the rights of participants under the 2022 Plan. No award will be made that is conditioned on Syros stockholder approval of any amendment to the 2022 Plan unless the award provides that (i) it will terminate or be forfeited if Syros stockholder approval of such amendment is not obtained within no more than 12 months from the date the award was granted and (ii) it may not be exercised or settled (or otherwise result in the issuance of shares of Syros common stock) prior to the receipt of such Syros stockholder approval.

If Syros stockholders do not approve the 2022 Plan, the 2022 Plan will not go into effect, and Syros will not grant any awards under the 2022 Plan. In this event, Syros' board of directors will consider whether to adopt alternative arrangements based on its assessment of its needs.

Federal Income Tax Consequences

The following is a summary of the United States federal income tax consequences that generally will arise with respect to awards granted under the 2022 Plan. This summary is based on the federal tax laws in effect as of the date of this joint proxy statement/prospectus. In addition, this summary assumes that all awards are exempt from, or comply with, the rules under Section 409A of the Code regarding nonqualified deferred compensation. Changes to these laws could alter the tax consequences described below.

Incentive Stock Options. A participant will not have income upon the grant of an incentive stock option. Also, except as described below, a participant will not have income upon exercise of an incentive stock option if the

participant has been employed by Syros or its corporate parent or 50% or majority-owned corporate subsidiary at all times beginning with the option grant date and ending three months before the date the participant exercises the option. If the participant has not been so employed during that time, then the participant will be taxed as described below under "Non-statutory Stock Options." The exercise of an incentive stock option may subject the participant to the alternative minimum tax.

A participant will have income upon the sale of the stock acquired under an incentive stock option at a profit (if sales proceeds exceed the exercise price). The type of income will depend on when the participant sells the stock. If a participant sells the stock more than two years after the option was granted and more than one year after the option was exercised, then all of the profit will be long-term capital gain. If a participant sells the stock prior to satisfying these waiting periods, then the participant will have engaged in a disqualifying disposition and a portion of the profit will be ordinary income and a portion may be capital gain. This capital gain will be long-term if the participant has held the stock for more than one year and otherwise will be short-term. If a participant sells the stock at a loss (sales proceeds are less than the exercise price), then the loss will be a capital loss. This capital loss will be long-term if the participant held the stock for more than one year and otherwise will be short-term.

Non-statutory Stock Options. A participant will not have income upon the grant of a non-statutory stock option. A participant will have compensation income upon the exercise of a non-statutory stock option equal to the value of the stock on the day the participant exercised the option less the exercise price. Upon sale of the stock, the participant will have capital gain or loss equal to the difference between the sales proceeds and the value of the stock on the day the option was exercised. This capital gain or loss will be long-term if the participant has held the stock for more than one year and otherwise will be short-term.

Stock Appreciation Rights. A participant will not have income upon the grant of a SAR. A participant generally will recognize compensation income upon the exercise of a SAR equal to the amount of the cash and the fair market value of any stock received. Upon the sale of the stock, the participant will have capital gain or loss equal to the difference between the sales proceeds and the value of the stock on the day the SAR was exercised. This capital gain or loss will be long-term if the participant held the stock for more than one year and otherwise will be short-term.

Restricted Stock Awards. A participant will not have income upon the grant of restricted stock unless an election under Section 83(b) of the Code is made within 30 days of the date of grant. If a timely 83(b) election is made, then a participant will have compensation income equal to the value of the stock less the purchase price, if any. When the stock is sold, the participant will have capital gain or loss equal to the difference between the sales proceeds and the value of the stock on the date of grant. If the participant does not make an 83(b) election, then when the stock vests the participant will have compensation income equal to the value of the stock on the vesting date less the purchase price, if any. When the stock is sold, the participant will have capital gain or loss equal to the sales proceeds less the value of the stock on the vesting date. Any capital gain or loss will be long-term if the participant held the stock for more than one year and otherwise will be short-term.

Restricted Stock Units. A participant will not have income upon the grant of an RSU. A participant is not permitted to make an election under Section 83(b) of the Code with respect to an RSU award. When the shares or common stock are delivered with respect to the RSUs (which may be upon vesting or may be at a later date), the participant will have income on the date of delivery in an amount equal to the fair market value of the stock on such date less the purchase price, if any. When the stock is sold, the participant will have capital gain or loss equal to the sales proceeds less the value of the stock on the delivery date. Any capital gain or loss will be long-term if the participant held the stock for more than one year and otherwise will be short-term.

Other Stock-Based Awards. The tax consequences associated with any other stock-based award granted under the 2022 Plan will vary depending on the specific terms of such award. Among the relevant factors are whether or not the award has a readily ascertainable fair market value, whether or not the award is subject to forfeiture

provisions or restrictions on transfer, the nature of the property to be received by the participant under the award, and the participant's holding period and tax basis for the award or underlying common stock.

Tax Consequences to Syros. There will be no tax consequences to Syros except that Syros will be entitled to a deduction when a participant has compensation income, subject to the limitations of Section 162(m) of the Code.

THE SYROS BOARD OF DIRECTORS UNANIMOUSLY RECOMMENDS THAT SYROS STOCKHOLDERS VOTE "FOR" THE APPROVAL OF THE SYROS PHARMACEUTICALS, INC. 2022 EQUITY INCENTIVE PLAN.

SYROS PROPOSAL NO. 5:

APPROVAL OF THE ADJOURNMENT OF THE SYROS SPECIAL MEETING, IF NECESSARY

Syros may seek to adjourn the Syros special meeting, if necessary or appropriate in the judgment of Syros management and subject to the terms of the Merger Agreement, either (1) for the purpose of soliciting additional proxies to approve Syros Proposal Nos. 1, 2 and 3, if Syros fails to receive a sufficient number of votes to approve such proposals, or (2) to ensure that any supplement or amendment to this joint proxy statement/prospectus is timely provided to holders of Syros common stock.

Required Vote

The affirmative vote of a majority of the total votes cast by the holders of Syros common stock entitled to vote on the matter at the Syros special meeting is required for approval of the adjournment of the Syros special meeting for the purpose of soliciting additional proxies to approve Syros Proposal Nos. 1, 2 and 3 or to ensure that any supplement or amendment to this joint proxy statement/prospectus is timely provided to holders of Syros common stock.

SYROS' BOARD OF DIRECTORS RECOMMENDS A VOTE "FOR" THIS SYROS PROPOSAL NO. 5 TO SO ADJOURN THE SYROS SPECIAL MEETING.

MATTERS BEING SUBMITTED TO A VOTE OF TYME STOCKHOLDERS

TYME PROPOSAL NO. 1

ADOPTION OF THE MERGER AGREEMENT

Tyme's board of directors is asking the Tyme stockholders to consider and vote upon a proposal to adopt the Merger Agreement, pursuant to which, at the effective time, Tack Acquisition Corp. will merge with and into Tyme, with Tyme surviving as a wholly owned subsidiary of Syros. At the effective time of the Merger, each share of Tyme Common Stock that is issued an outstanding immediately prior to the effective time will be converted into the right to receive a number of shares of Syros common stock based on the Exchange Ratio (as described below) together with cash in lieu of any fractional shares of Syros common stock.

The "Exchange Ratio" will be the quotient (rounded down to four decimal places) obtained by dividing (x) the Tyme Per Share Value by (y) $0.94 (the "Syros Per Share Price"). The "Tyme Per Share Value" will be determined by dividing (x) the sum of Tyme Net Cash plus $7.5 million by (y) the total number of outstanding shares of Tyme Common Stock as of the Closing. "Tyme Net Cash" will be determined in accordance with the definitions and procedures in the Merger Agreement shortly prior to closing of the Merger; it represents an estimate of the cash and cash equivalents of Tyme and its subsidiaries as of the Closing, net of substantially all of Tyme's liabilities and expenses. As such, the Exchange Ratio is not yet knowable. Based on estimates and expectations as of the date of the signing of the Merger Agreement, the Exchange Ratio is estimated to be approximately 0.4312. However, the final Exchange Ratio will depend on Tyme Net Cash and the number of shares of Tyme Common Stock outstanding at Closing and could be materially different.

After careful consideration, Tyme's board of directors unanimously: (a) determined that the Merger is fair to and in the best interests of Tyme and its stockholders; (b) approved and declared advisable the execution and delivery of the Merger Agreement, the performance by Tyme of its covenants and agreements contained therein and the transactions contemplated thereby, including the Merger, on the terms and subject to the conditions set forth in the Merger Agreement; (c) directed that the adoption of the Merger Agreement be submitted to a vote at a meeting of Tyme stockholders and (d) recommended that Tyme stockholders adopt the Merger Agreement.

The Merger and a summary of the terms of the Merger Agreement are described in more detail under "The Merger" and "The Merger Agreement," and Tyme stockholders are encouraged to read the full text of the Merger Agreement, which is attached as *Annex A* hereto. It is a condition to the completion of the Merger that Tyme stockholders approve the Tyme Merger Proposal.

Required Vote

The affirmative vote of the holders of a majority of the outstanding shares of Tyme common stock entitled to vote at the Tyme special meeting is required to approve the adoption of the Merger Agreement.

TYME'S BOARD OF DIRECTORS RECOMMENDS A VOTE "FOR" THE APPROVAL OF THE ADOPTION OF THE MERGER AGREEMENT.

TYME PROPOSAL NO. 2

ADVISORY VOTE TO APPROVE MERGER-RELATED EXECUTIVE COMPENSATION

Pursuant to Section 14A of the Exchange Act, Tyme is seeking a non-binding advisory vote from the Tyme stockholders to approve the payment of certain compensation to Tyme's Named Executive Officers that will or may become payable by Tyme to the Tyme Named Executive Officers in connection with the consummation of the Merger, as disclosed in the sections titled "*The Merger—Tyme Golden Parachute Compensation*" and "*The Merger—Tyme Golden Parachute Compensation Table*."

Upon the consummation of the Merger, it is expected that each of the Tyme's Named Executive Officers will cease to be employed by Tyme. Therefore, Tyme is asking stockholders to indicate their approval of the compensation that will or may become payable by Tyme to the Tyme Named Executive Officers in connection with the expected termination of the Tyme Named Executive Officers upon the consummation of the Merger. These payments are set forth in the sections titled "*The Tyme Golden Parachute Compensation*" and "*The Merger—Tyme Golden Parachute Compensation Table*," and the accompanying footnotes. In general, the employment agreements, equity awards and other arrangements pursuant to which compensation payments have previously been made to Tyme's Named Executive Officers have formed a part of Tyme's overall compensation program and previously have been disclosed to stockholders as part of Tyme's annual proxy statements or its other reports filed with the SEC. These historical employment agreements, equity awards and other arrangements were adopted and approved by the Compensation Committee of Tyme's board of directors, which is composed solely of non-employee directors, and are believed to be fair and equitable to Tyme's Named Executive Officers and stockholders.

Accordingly, Tyme is seeking approval of the following resolution at the Tyme special meeting:

"RESOLVED, that the Tyme stockholders approve, on an advisory basis, the compensation that will or may become payable by Tyme to the Tyme Named Executive Officers that is based on or otherwise relates to the Merger as disclosed pursuant to Item 402(t) of Regulation S-K in the sections titled "*The Tyme Golden Parachute Compensation*" and "*The Merger—Tyme Golden Parachute Compensation Table*."

Tyme stockholders should note that this proposal is not a condition to the closing of the merger, and as an advisory vote, the result will not be binding on Tyme, Tyme's board of directors or Tyme's Named Executive Officers. Further, the underlying employment agreements, equity awards, retention agreements and other arrangements are contractual in nature and not, by their terms, subject to stockholder approval. Accordingly, regardless of the outcome of the advisory vote, if the merger is consummated and the employment of Tyme's Named Executive Officers is terminated in connection with the merger, the Tyme Named Executive Officers will be eligible to receive the compensation that is based on or otherwise relates to the merger in accordance with the terms and conditions applicable to the underlying employment agreements, equity awards, retention agreements and other arrangements Tyme entered into with these Named Executive Officers.

Required Vote

The affirmative vote of the holders of a majority of the shares present in attendance or represented by proxy at the Tyme special meeting and entitled to vote on the matter, assuming a quorum is present, is required to approve the non-binding advisory vote on merger-related compensation that will or may become payable by Tyme to the Tyme Named Executive Officers in connection with the consummation of the merger.

TYME'S BOARD OF DIRECTORS RECOMMENDS A NON-BINDING VOTE "FOR" THE APPROVAL OF THE MERGER-RELATED COMPENSATION OF THE COMPANY'S NAMED EXECUTIVE OFFICERS AS DISCLOSED IN THIS JOINT PROXY STATEMENT/PROSPECTUS.

TYME PROPOSAL NO. 3

APPROVAL OF THE AMENDMENT TO THE AMENDED AND RESTATED CERTIFICATE OF INCORPORATION OF TYME TO EFFECT THE REVERSE STOCK SPLIT

General

At the Tyme special meeting, Tyme stockholders will be asked to approve an amendment to Tyme's Certificate of Incorporation that will implement a reverse stock split of the issued and outstanding shares of Tyme common stock, by a ratio of not less than 1-for-15 and not more than 1-for-75, with the exact ratio to be determined in the discretion of Tyme's board of directors and with such reverse stock split to be effected at such time and date as determined by Tyme's board of directors in its sole discretion, however, Tyme's board of directors intends to consider the implementation of the reverse stock split proposal only if the Tyme Merger Proposal is not approved by the Tyme stockholders or if the merger is not completed for any other reason. The purpose of the reverse stock split is for Tyme to attempt to regain compliance with the applicable continued listing standards of The Nasdaq Stock Market.

Upon the effectiveness of the amendment to the Tyme Certificate of Incorporation to effect the reverse stock split, or the reverse stock split effective time, the issued and outstanding shares of Tyme common stock immediately prior to the reverse stock split effective time will be reclassified into a smaller number of shares such that a Tyme stockholder will own one new share of Tyme common stock for not less than 15 shares and not more than 75 shares of issued common stock held by that Tyme stockholder immediately prior to the reverse stock split effective time, as specified.

By approving this Tyme Proposal No. 3, Tyme stockholders will: (a) approve an amendment to the Tyme Certificate of Incorporation pursuant to which any whole number of issued and outstanding shares of common stock not less than 15 shares of Tyme common stock and not more than 75 shares of Tyme common stock could be combined and reclassified into one share of Tyme common stock; and (b) authorize the Tyme's board of directors to file only one such amendment, as determined by the Tyme board of directors in its sole discretion, and only if the Tyme Merger Proposal is not approved by the Tyme stockholders or if the merger is not completed for any other reason. If Tyme receives the required stockholder approval for this Tyme Proposal No. 3, *provided that* the Tyme Merger Proposal is not approved by the Tyme stockholders or the merger is not completed for any other reason, and the Tyme's board of directors determines that effecting the reverse stock split is in the best interests of Tyme and its stockholders, the reverse stock split will become effective as specified in the amendment filed with the Secretary of State of the State of Delaware. The filed amendment thereby will contain the number of shares selected by the Tyme board of directors within the limits set forth in this Tyme Proposal No. 3 to be combined and reclassified into one share of Tyme common stock. Accordingly, upon the effectiveness of the amendment to the Tyme Certificate of Incorporation to effect the reverse stock split, or the reverse split effective time, not less than 15 shares of Tyme common stock and not more than 75 shares of Tyme common stock outstanding immediately prior to the split effective time will be combined and reclassified into one share of Tyme common stock.

The proposed form of certificate of amendment to the Tyme Certificate of Incorporation to effect the reverse stock split will reduce the number of issued and outstanding shares of Tyme common stock but ***will not*** change the number of authorized shares of Tyme common stock or preferred stock, or the par value of Tyme common stock or preferred stock.

A copy of the proposed form of certificate of amendment to the Tyme Certificate of Incorporation to effect the reverse stock split is attached as*Annex K* to this joint proxy statement/prospectus.

Notwithstanding approval of this Tyme Proposal No. 3 by Tyme stockholders, Tyme's board of directors may, in its sole discretion, abandon the proposed amendments and determine prior to the effectiveness of any filing with

the Secretary of State of the State of Delaware not to effect the reverse stock split, as permitted under Section 242(c) of the DGCL. If Tyme's board of directors does not implement the reverse stock split amendment prior to the one-year anniversary of the Tyme special meeting, stockholder approval would again be required prior to implementing any reverse stock split.

If Tyme stockholders do not approve this Tyme Proposal No. 3, Tyme will not be able to file a certificate of amendment to the Tyme Certificate of Amendment to effect the reverse stock split.

Purpose

The principal reason for the reverse stock split is to increase theper-share trading price of Tyme's common stock to help ensure a stock price high enough to satisfy the $1.00-per-share minimum bid price requirement for continued listing on Nasdaq.

On December 22, 2021, Tyme received notice from Nasdaq that the closing bid price of Tyme common stock had been below $1.00 per share for the previous 30 consecutive business days, and that Tyme was therefore not in compliance with the minimum bid price requirement for continued inclusion on The Nasdaq Capital Market under Nasdaq Listing Rule 5550(a)(2), or the Bid Price Rule. Pursuant to the original notice, Tyme had a 180-day period in which to regain compliance.

On June 21, 2022, Tyme received notice from Nasdaq that it had granted Tymea 180-day extension to regain compliance with the Nasdaq continued listing standards. Nasdaq informed Tyme that it granted the extension, in part, due to Tyme's intention to cure the deficiency during the extension period by effecting a reverse split, if necessary. The extension runs through December 19, 2022.

If the Tyme Merger Proposal is not approved by Tyme stockholders or if the merger is not completed for any other reason, Tyme will remain an independent public company, shares of Tyme common stock will continue to be registered under the Exchange Act and Tyme will continue to file periodic reports with the SEC. In addition, if Tyme is unable to demonstrate compliance with the Bid Price Rule on or before December 19, 2022, Tyme's common stock may be delisted from trading on The Nasdaq Capital Market. As a result, Tyme's board of directors may elect to implement the reverse stock split of Tyme common stock in an effort to regain compliance with the $1.00 bid price requirement as set forth in Bid Price Rule.

Tyme's board of directors also believes that the increased market price of Tyme common stock expected to result from implementing the reverse stock split will improve the marketability and liquidity of Tyme common stock and will encourage interest and trading in Tyme common stock. Because of the trading volatility often associated with low-priced stocks, many brokerage houses and institutional investors have internal policies and practices that either prohibit them from investing in low-priced stocks or tend to discourage individual brokers from recommending low-priced stocks to their customers. Some of those policies and practices may function to make the processing of trades in low-priced stocks economically unattractive to brokers. Additionally, because brokers' commissions on low-priced stocks generally represent a higher percentage of the stock price than commissions on higher-priced stocks, the current average price per share of Tyme common stock can result in individual Tyme stockholders paying transaction costs representing a higher percentage of their total share value than would be the case if the share price were substantially higher. It should be noted that the liquidity of Tyme common stock may be harmed by the proposed reverse stock split given the reduced number of shares that would be outstanding after the reverse stock split.

Further, Tyme's board of directors believes that a higher stock price could help Tyme attract and retain employees and other service providers. Tyme's board of directors believes that some potential employees and service providers are less likely to work for a company with a low stock price, regardless of the size of Tyme's market capitalization. If the reverse stock split successfully increases the per-share price of Tyme common stock, Tyme's board of directors believes this increase will enhance Tyme's ability to attract and retain employees and service providers.

Although Tyme's board of directors expects that a reverse stock split of Tyme common stock will increase the market price of Tyme common stock so that Tyme is able to maintain compliance with the relevant Nasdaq rules for the foreseeable future, there can be no assurance that (a) the market price per share following the reverse stock split would rise in proportion to the reduction in the number of pre-split shares of Tyme common stock outstanding before the reverse stock split; (b) the market price per share following the reverse stock split would remain in excess of the minimum price required for listing on Nasdaq for a sustained period of time; (c) the Tyme common stock will not be delisted from Nasdaq due to a failure to meet other continued listing requirements even if the market price per post-reverse split share of Tyme common stock remains in excess of such required minimum price; and (d) the reverse stock split would result in a per share price that would attract brokers and investors who do not trade in lower-priced stock. The market price of Tyme common stock will also be based on Tyme's performance and other factors, some of which are unrelated to the number of shares outstanding. If the reverse stock split is effected and the market price of Tyme's common stock declines, the percentage decline as an absolute number and as a percentage of Tyme's overall market capitalization may be greater than would occur in the absence of the proposed reverse stock split.

Nasdaq Requirements for Continued Listing on The Nasdaq Capital Market

Tyme common stock is currently listed on Nasdaq under the symbol "TYME."

According to the Nasdaq rules, an issuer must meet certain financial and liquidity standards for continued listing on The Nasdaq Capital Market. As described above, on December 22, 2021, Tyme fell out of compliance with Bid Price Rule for continued listing on The Nasdaq Capital Market, which requires that the common stock of a listed issuer not fall below the $1.00 per share minimum for 30 consecutive business days, and Tyme must cure its non-compliance by December 19, 2022.

If the Tyme Merger Proposal is not approved by Tyme stockholders, or if the merger is not completed for any other reason, and Tyme does not effect a reverse stock split to comply with Bid Price Rule, Tyme common stock will likely not increase to a price above $1.00 for a sufficient period of time to cure its non-compliance, and Tyme would be delisted from trading on The Nasdaq Capital Market. Given these factors and potential outcomes, Tyme's board of directors believes the reverse stock split is necessary to regain compliance with the listing standards.

In addition to regaining compliance with Bid Price Rule, Tyme would have to meet the other continued listing criteria as laid out in Nasdaq Listing Rules 5550(a) and 5550(b)(1), 5550(b)(2) or 5550(b)(3).

Principal Effects of the Reverse Stock Split

The reverse stock split will be realized simultaneously for all shares of Tyme common stock, options to purchase shares of Tyme common stock and warrants to purchase common stock outstanding immediately prior to the effective time of the reverse stock split. The reverse stock split will affect all holders of shares of Tyme common stock outstanding immediately prior to the effective time of the reverse stock split uniformly and each such Tyme stockholder will hold the same percentage of Tyme common stock outstanding immediately following the reverse stock split as that Tyme stockholder held immediately prior to the reverse stock split, except for immaterial adjustments that may result from the treatment of fractional shares as described below.

The reverse stock split will not change the par value of Tyme common stock or preferred stock and will not reduce the number of authorized shares of Tyme common stock or preferred stock. Tyme common stock issued pursuant to the reverse stock split will remain fully paid and nonassessable. The reverse stock split will not affect Tyme continuing to be subject to the periodic reporting requirements of the Exchange Act.

The reverse stock split will not affect the common stock capital account on Tyme's balance sheet. Because the par value of Tyme's common stock will remain unchanged as of the reverse split effective time, the components

that make up the common stock capital account will change, by offsetting amounts. The stated capital component will be reduced to its present amount multiplied by the reverse split ratio, and the additional paid in capital component will be increased with the amount by which the stated capital is reduced. The per share net loss and net book value of the Tyme common stock will be increased because there will be fewer shares of Tyme common stock outstanding. Prior periods per share amounts will reflect the reverse stock split.

Procedure for Effecting Reverse Stock Split and Exchange of Stock Certificates

If the Tyme stockholders approve the amendment to the Tyme Certificate of Incorporation effecting the reverse stock split, and if Tyme's board of directors still believes that a reverse stock split is in the best interests of Tyme and its stockholders, and provided that the Tyme Merger Proposal is not approved by the Tyme stockholders or the merger is not completed for any other reason, Tyme will file the amendment to the Tyme Certificate of Incorporation with the Secretary of State of the State of Delaware at the time Tyme's board of directors determines is appropriate. Tyme's board of directors may delay effecting the reverse stock split without resoliciting stockholder approval. Beginning at the reverse split effective time, each stock certificate representing pre-split shares will be deemed for all corporate purposes to evidence ownership of post-split shares.

As soon as practicable after the split effective time, Tyme stockholders will be notified that the reverse stock split has been effected. Tyme expects that the Tyme transfer agent will act as exchange agent for purposes of implementing the exchange of stock certificates. Holders of pre-split shares will be asked to surrender to the exchange agent stock certificates representing pre-split shares in exchange for stock certificates (or book-entry positions) representing post-split shares in accordance with the procedures to be set forth in a letter of transmittal to be sent by Tyme. No new certificates (or book-entry positions) will be issued to a Tyme stockholder until that Tyme stockholder has surrendered the stockholder's outstanding certificate(s) together with the properly completed and executed letter of transmittal to the exchange agent. Shares of Tyme common stock held in book-entry form will be automatically exchanged. Any pre-split shares submitted for transfer, whether pursuant to a sale or other disposition, or otherwise, will automatically be exchanged for post-split shares. **Tyme stockholders should not destroy any stock certificate(s) and should not submit any certificate(s) unless and until requested to do so.**

Fractional Shares

No fractional shares will be issued in connection with the reverse stock split. Tyme expects that after the Certificate of Amendment is filed, Continental Stock Transfer and Trust, its transfer agent, would aggregate all fractional shares of Tyme common stock and arrange for them to be sold at the then-prevailing prices on the open market on behalf of those shareholders who would otherwise be entitled to receive a fractional share of Tyme common stock. Tyme expects that the transfer agent would cause the sale to be conducted in an orderly fashion at a reasonable pace and that it may take several days to sell all of the aggregated fractional Common Shares. After completing the sale, Tyme stockholders would receive a cash payment from the transfer agent in an amount equal to their pro rata share of the total net proceeds of these sales. The proceeds would be subject to certain taxes and Tyme stockholders would not be entitled to receive interest for the the period of time between the filing of the Certificate of Amendment and the date a Tyme stockholder receives payment for the cashed-out fractional shares of Tyme common stock. For the foregoing purposes, all shares of common stock held by a holder will be aggregated (thus resulting in no more than one fractional share of Tyme common stock per holder). The ownership of a fractional interest will not give the holder thereof any voting, dividend or other rights except to receive payment therefor as described herein.

Tyme stockholders should be aware that, under the escheat laws of the various jurisdictions where stockholders reside, where Tyme is domiciled and where the funds will be deposited, sums due for fractional interests that are not timely claimed after the effective date of the split may be required to be paid to the designated agent for each such jurisdiction, unless correspondence has been received by Tyme or the exchange agent concerning ownership of such funds within the time permitted in such jurisdiction. Thereafter, Tyme stockholders otherwise entitled to receive such funds will have to seek to obtain them directly from the state to which they were paid.

No Appraisal Rights

Under the DGCL, Tyme's stockholders are not entitled to dissenter's rights or appraisal rights with respect to the Tyme reverse stock split and Tyme will not independently provide its stockholders with any such rights.

Interest of Certain Persons in Matters to be Acted Upon

No officer or director has any substantial interest, direct or indirect, by security holdings or otherwise, in the Tyme reverse stock split that is not shared by all of our other stockholders.

Potential Anti-Takeover Effect

Because the reverse stock split would result in a decrease in the number of shares of common stock outstanding but would not change the number of authorized shares, effecting the reverse stock split would result in an increased proportion of unissued authorized shares to issued shares. Under certain circumstances, this change could have an anti-takeover effect, for example, by permitting issuances that would dilute the stock ownership of a person seeking to effect a change in the composition of Tyme's board of directors or contemplating a tender offer or other transaction for the combination of Tyme with another company. The reverse stock split proposal is being contemplated as an alternative if the merger is not approved or does not close for any other reason; it is not being proposed in response to any effort of which Tyme is aware to accumulate shares of Tyme common stock or obtain control of Tyme, nor is it part of a plan by management to recommend a series of similar amendments to tTyme's board of directors and stockholders. Other than the proposals being submitted to the Tyme stockholders for their consideration at the Tyme special meeting, Tyme's board of directors does not currently contemplate recommending the adoption of any other actions that could be construed to affect the ability of third parties to take over or change control of Tyme.

Material U.S. Federal Income Tax Consequences of the Reverse Stock Split

The following is a discussion of the material U.S. federal income tax consequences of the reverse stock split that are applicable to U.S. Holders (as defined below) that hold shares of Tyme common stock as capital assets for U.S. federal income tax purposes (generally, property held for investment). This discussion does not purport to be a complete analysis of all potential tax effects to such a U.S. Holder. This discussion is based on the Code, existing Treasury Regulations promulgated thereunder, judicial decisions and published rulings and administrative pronouncements of the IRS, in each case in effect as of the date hereof. These authorities may change or be subject to differing interpretations. Any such change or differing interpretation, which may be retroactive, could impact the U.S. federal income tax consequences described herein in a manner that could adversely affect a U.S. Holder.

This discussion does not address all U.S. federal income tax consequences relevant to U.S. Holders. In addition, it does not address consequences relevant to U.S. Holders that are subject to particular U.S. or non-U.S. tax rules, including, without limitation, to holders of Tyme common stock that are:

- U.S. expatriates and former citizens or long-term residents of the United States;
- U.S. Holders whose functional currency is not the U.S. dollar;
- persons holding Tyme common stock as part of a hedge, straddle or other risk reduction strategy or as part of a conversion transaction or other integrated investment;
- banks, insurance companies, and other financial institutions;
- real estate investment trusts or regulated investment companies;
- brokers, dealers or traders in securities;
- "controlled foreign corporations," "passive foreign investment companies," and corporations that accumulate earnings to avoid U.S. federal income tax;

- S corporations, partnerships or other entities or arrangements treated as partnerships for U.S. federal income tax purposes (and investors therein);
- persons for whom Tyme common stock constitutes "qualified small business stock" within the meaning of Section 1202 of the Code or as "Section 1244 stock" for purposes of Section 1244 of the Code;
- tax-exempt organizations or governmental organizations;
- persons subject to special tax accounting rules as a result of any item of gross income with respect to Tyme common stock being taken into account in an "applicable financial statement" (as defined in the Code);
- persons who hold or received Tyme common stock pursuant to the exercise of any employee stock option or otherwise as compensation;
- tax-qualified retirement plans; and
- U.S. Holders of warrants, options, or other stock rights.

U.S. Holders subject to particular U.S. or non-U.S. tax rules, including those that are described in this paragraph, are urged to consult their own tax advisors regarding the consequences to them of the reverse stock split.

If an entity that is treated as a partnership for U.S. federal income tax purposes holds Tyme common stock, the U.S. federal income tax treatment of a partner in the partnership will generally depend upon the status of the partner, the activities of the partnership and certain determinations made at the partner level. Accordingly, partnerships holding Tyme common stock and the partners in such partnerships should consult their tax advisors regarding the U.S. federal income tax consequences to them.

In addition, the following discussion does not address the tax consequences of the reverse stock split under state, local and foreign tax laws. Furthermore, the following discussion does not address any tax consequences of transactions effectuated before, after or at the same time as the reverse stock split, whether or not they are in connection with the reverse stock split.

TYME STOCKHOLDERS SHOULD CONSULT THEIR TAX ADVISORS WITH RESPECT TO THE APPLICATION OF THE U.S. FEDERAL INCOME TAX LAWS TO THEIR PARTICULAR SITUATIONS AS WELL AS ANY TAX CONSEQUENCES OF THE REVERSE STOCK SPLIT ARISING UNDER THE U.S. FEDERAL ESTATE OR GIFT TAX LAWS OR UNDER THE LAWS OF ANY STATE, LOCAL OR NON-U.S. TAXING JURISDICTION OR UNDER ANY APPLICABLE INCOME TAX TREATY.

For purposes of this discussion, a "U.S. Holder" is a beneficial owner of Tyme common stock that, for U.S. federal income tax purposes, is or is treated as:

- an individual who is a citizen or resident of the United States;
- a corporation or any other entity taxable as a corporation created or organized in or under the laws of the United States, any state thereof, or the District of Columbia;
- an estate, the income of which is subject to U.S. federal income tax regardless of its source; or
- a trust if either (i) a court within the United States is able to exercise primary supervision over the administration of such trust, and one or more United States persons (within the meaning of Section 7701(a)(30) of the Code) is authorized or has the authority to control all substantial decisions of such trust, or (ii) the trust was in existence on August 20, 1996 and has a valid election in effect under applicable Treasury Regulations to be treated as a United States person for U.S. federal income tax purposes.

Tax Consequences of the Reverse Stock Split

The proposed reverse stock split should constitute a "recapitalization" for U.S. federal income tax purposes pursuant to Section 368(a)(1)(E) of the Code. As a result, a U.S. Holder generally should not recognize gain or loss upon the proposed reverse stock split, except with respect to cash received in lieu of a fractional share of Tyme common stock, as discussed below. A U.S. Holder's aggregate adjusted tax basis in the shares of Tyme common stock received pursuant to the proposed reverse stock split should equal the aggregate adjusted tax basis of the shares of the Tyme common stock surrendered (excluding any portion of such basis that is allocated to any fractional share of Tyme common stock), and such U.S. Holder's holding period in the shares of Tyme common stock received should include the holding period in the shares of Tyme common stock surrendered. U.S. Treasury Regulations provide detailed rules for allocating the tax basis and holding period of the shares of Tyme common stock surrendered to the shares of Tyme common stock received in a recapitalization pursuant to the proposed reverse stock split. U.S. Holders of shares of Tyme common stock acquired on different dates and at different prices should consult their tax advisors regarding the allocation of the tax basis and holding period of such shares.

Cash in Lieu of Fractional Shares

A U.S. Holder that, pursuant to the reverse stock split, receives cash in lieu of a fractional share of Tyme common stock generally should recognize capital gain or loss in an amount equal to the difference, if any, between the amount of cash received and the portion of the U.S. Holder's aggregate adjusted tax basis in the shares of Tyme common stock surrendered that is allocated to such fractional share. Such capital gain or loss will be short term if the pre-split shares were held for one year or less at the effective time of the reverse stock split and long term if held for more than one year.

A U.S. Holder may be subject to information reporting and backup withholding on cash paid in lieu of a fractional share in connection with the reverse stock split. A U.S. Holder will be subject to backup withholding if such U.S. Holder is not otherwise exempt and such U.S. Holder does not provide its taxpayer identification number in the manner required or otherwise fails to comply with applicable backup withholding tax rules.

Backup withholding is not an additional tax and amounts withheld will be allowed as a credit against the holder's U.S. federal income tax liability and may entitle such holder to a refund, provided the required information is timely furnished to the IRS. U.S. Holders should consult their own tax advisors regarding the application of the information reporting and backup withholding rules to them.

Required Vote

The affirmative vote of the holders of a majority of the outstanding shares of Tyme common stock is required to approve the Tyme Certificate of Incorporation to effect a reverse stock split of Tyme common stock.

TYME'S BOARD OF DIRECTORS UNANIMOUSLY RECOMMENDS A VOTE "FOR" THIS TYME PROPOSAL NO. 3 TO APPROVE THE TYME AMENDED AND RESTATED CERTIFICATE OF INCORPORATION TO EFFECT THE REVERSE STOCK SPLIT.

TYME PROPOSAL NO. 4

APPROVAL OF POSSIBLE ADJOURNMENT OF THE TYME SPECIAL MEETING

Tyme may seek to adjourn the Tyme special meeting, if necessary or appropriate in the judgment of Tyme management and subject to the terms of the Merger Agreement, either (1) for the purpose of soliciting additional proxies to approve Tyme Proposal Nos. 1, 2 and 3, if Tyme fails to receive a sufficient number of votes to approve such proposals, or (2) to ensure that any supplement or amendment to this joint proxy statement/prospectus is timely provided to holders of Tyme common stock.

Required Vote

The affirmative vote of the holders of a majority of the shares present in attendance or represented by proxy at the Tyme special meeting and entitled to vote on the matter, assuming a quorum is present, is required to approve the adjournment of the Tyme special meeting for the purpose of soliciting additional proxies to approve the Tyme Merger Proposal or to ensure that any supplement or amendment to this joint proxy statement/prospectus is timely provided to holders of Tyme common stock.

TYME'S BOARD OF DIRECTORS RECOMMENDS A VOTE "FOR" THIS TYME PROPOSAL NO. 4 TO SO ADJOURN THE TYME SPECIAL MEETING.

Overview

Syros is a biopharmaceutical company seeking to redefine the power of small molecules to control the expression of genes. Based on Syros' unique ability to elucidate regulatory regions of the genome, Syros aims to develop medicines that provide a profound benefit for patients with diseases that have eluded other genomics-based approaches. Syros is primarily focused on developing treatments for cancer and building a clinical stage pipeline of gene control medicines.

Syros' lead product candidates are:

- Tamibarotene, a selective retinoic acid receptor alpha, or RARα, agonist for which Syros is conducting SELECT-MDS-1, a Phase 3 clinical trial evaluating tamibarotene in combination with azacitidine in a genomically defined subset of patients with HR-MDS and for which Syros is conducting SELECT-AML-1, a randomized Phase 2 clinical trial evaluating tamibarotene in combination with venetoclax and azacitidine in a genomically defined subset of newly diagnosed patients with AML who are not suitable candidates for standard intensive chemotherapy;
- SY-2101, a novel oral form of ATO which Syros is evaluating in a dose confirmation study, and which Syros plans to follow with a Phase 3 clinical trial, in patients with newly diagnosed low-risk APL; and
- SY-5609, a highly selective and potent oral inhibitor of CDK7, which Syros is evaluating in combination with chemotherapy in pancreatic cancer patients in an expansion cohort of its existing Phase 1 clinical trial, and which is being evaluated in combination with atezolizumab, a PD-L1 inhibitor, in BRAF-mutant colorectal cancer in an arm of a Phase 1/1b clinical trial sponsored by Roche that is now open for enrollment.

Syros also has multiple preclinical and discovery programs in oncology, including programs targeting the inhibition of CDK12, CDK11, and WRN. Syros expects that its next development candidate will be nominated from its CDK12 program in the third quarter of 2022. Syros is seeking partnerships for its oncology discovery programs, including CDK12.

In December 2019, Syros entered into a collaboration with GBT to discover, develop and commercialize novel therapies for sickle cell disease and beta thalassemia. Syros also uses its gene control platform in collaboration with third parties to identify and validate targets in diseases beyond its current areas of focus. To this end, Syros entered into a target discovery, research collaboration and option agreement with Incyte in January 2018, under which Syros is using Syros' platform to identify novel therapeutic targets with a focus on myeloproliferative neoplasms. Syros expects to continue to execute on these existing collaborations with Incyte and GBT, for which its research efforts are fully funded externally.

Tamibarotene

At the 62nd American Society of Hematology Annual Meeting and Exposition held in December 2020, or ASH 2020, Syros presented data from its fully enrolled Phase 2 clinical trial evaluating the safety and efficacy of tamibarotene in combination with azacitidine in newly diagnosed AML patients who are not suitable candidates for standard chemotherapy, as well as in relapsed or refractory, or R/R, AML patients who have been prospectively selected using Syros' proprietary RARA, the gene that codes for RARα, biomarker. As of an October 1, 2020 data cut-off, 51 newly diagnosed unfit AML patients, including both RARA-positive and RARA-negative patients, were eligible for a safety analysis. Among these patients, tamibarotene in combination with azacitidine was generally well-tolerated, with no evidence of increased toxicity relative to either as a single agent, including rates of myelosuppression that were comparable to single-agent azacitidine. As of the data cut-off, of the 18 RARA-positive patients that were evaluable for clinical response, the overall response rate, or ORR, was 67%, with a composite complete response rate of 61%, with 50% of patients achieving complete

response, or CR, and 11% achieving a complete response with incomplete blood count recovery, or CRi. The median time to initial response was 1.2 months, the median duration of response was 10.8 months, and the median overall survival, or mOS, among patients who achieved a CR or CRi was 18 months. As of the data cut-off, of the 28 RARA-negative patients that were evaluable for clinical response, the ORR was 43%, with a composite complete response rate of 32%, with 25% of patients achieving CR and 7% achieving CRi. The median time to initial response was 3.0 months, and the median duration of response was 10.3 months. Syros also presented translational data demonstrating that most RARA-positive newly diagnosed unfit AML patients enrolled in Syros' Phase 2 study had a monocytic disease phenotype that is associated with resistance to venetoclax. These data suggest that the RARA biomarker not only selects for patients who are more likely to respond to treatment with tamibarotene but also for patients who may be less likely to benefit from treatment with venetoclax. Approximately 25,000 patients are diagnosed with unfit AML in the United States and Europe annually and Syros expects the overall total addressable market opportunity for all AML patients to grow to approximately $6.6 billion by 2025.

Based on these data and Syros' assessment of ongoing areas of high unmet need, Syros advanced tamibarotene in combination with azacitidine into a registration-enabling Phase 3 clinical trial in RARA-positive newly diagnosed HR-MDS patients, which Syros refers to as SELECT-MDS-1. HR-MDS is a hematologic malignancy that is closely related to AML, and Syros believes that approximately 50% of HR-MDS patients are RARA-positive. Syros believes that approximately 21,000 patients are diagnosed with HR-MDS in the United States and Europe annually and Syros expects the total addressable market opportunity for MDS patients of all risk groups to grow to approximately $3.3 billion by 2026. Syros plans to enroll approximately 190 RARA-positive newly diagnosed HR-MDS patients in the double-blind placebo-controlled trial, randomized 2:1 to receive tamibarotene in combination with azacitidine or placebo with azacitidine, respectively. The primary endpoint of the trial will be the CR rate. The trial is designed with 90% power and a one-sided alpha of 0.025 to detect a difference in CR rates between the experimental and control arms. Syros is currently dosing patients in SELECT-MDS-1, and Syros expects to report data from the SELECT-MDS-1 trial in the fourth quarter of 2023 or first quarter of 2024, with a potential submission to the FDA of an NDA expected in 2024. In addition, Syros is advancing tamibarotene in combination with venetoclax and azacitidine in RARA-positive newly diagnosed unfit AML patients. The trial, which Syros refers to as SELECT-AML-1, is designed with a single-arm safety lead-in of approximately 15 patients to confirm the dosing regimen of the triplet to be used in the randomized portion of the Phase 2 clinical trial, which will evaluate the safety and efficacy of tamibarotene in combination with venetoclax and azacitidine compared to venetoclax and azacitidine in approximately 80 patients randomized 1:1. The primary endpoint of the trial will be the composite CR rate. The trial will also evaluate the triplet as a salvage strategy for patients in the control arm who do not respond to venetoclax and azacitidine. Syros has begun dosing patients in the SELECT-AML-1 trial, and Syros expects to report clinical activity data from the safety lead-in portion of the trial in the second half of 2022. Syros also plans to initiate the randomized portion of the trial, with data expected in 2023 or 2024.

SY-2101

In December 2020, Syros acquired from Orsenix a novel oral form of ATO, which Syros refers toas SY-2101. SY-2101 is in development for the treatment of APL, a subtype of AML defined by a fusion of the RARA and promyelocytic leukemia, or PML, genes. APL represents approximately 10% of all AML cases, and approximately 2,000 patients are diagnosed with APL in the United States and Europe annually. An IV formulation of ATO is approved for use in combination with All-Trans-Retinoic-Acid, or ATRA, in patients with newly diagnosed low-risk APL and, while curative in more than 80% of patients, its administration requires up to 140 two- to four-hour infusions over the typical course of induction and consolidation treatment. If SY-2101 demonstrates comparable efficacy to IV ATO in Syros' clinical studies, Syros believes it has the potential to become the standard-of-care frontline therapy for APL by providing a substantially more convenient option that reduces the treatment burden on patients, improving access, and lowering costs to the healthcare system. In a Phase 1 clinical trial, SY-2101 demonstrated bioavailability, pharmacokinetic, or PK, exposures similar to IV ATO, and a generally well-tolerated safety profile. Syros has begun dosing patients in a dose confirmation study

of SY-2101. The ongoing dose confirmation study is evaluating the PK, food effect, safety and tolerability ofSY-2101 and is expected to enroll between six and 24 adult APL patients undergoing consolidation with IV ATO plus ATRA. Participants receive a single dose of 15 mg of SY-2101 in both the fasted and in the fed state, and a single dose of IV ATO for PK assessments, with flexibility to allow for other SY-2101 doses to be evaluated. Daily administration of SY-2101 is also being evaluated in a multiple-dose treatment module substituting for IV ATO during consolidation to assess steady state SY-2101 PK and safety. Syros anticipates reporting PK and safety data in mid-2022. The feedback from a Type C meeting to review Syros' Phase 3 study design with the FDA in November 2021 continues to support molecular complete response rate as the primary endpoint for accelerated approval and event free survival as the primary endpoint for full approval, in each case compared to historic IV ATO data. In addition, FDA feedback supports the inclusion of patients randomized to IV ATO for comparative safety assessments. Based on this feedback and following confirmation of a dose that demonstrates comparable PK exposures to IV ATO, Syros intends to initiate a registration-enabling Phase 3 clinical trial in approximately 215 patients with newly diagnosed low-risk APL, randomized 2:1 to receive SY-2101 or IV ATO, in the second half of 2023.

SY-5609

At the European Society for Medical Oncology Congress held in September 2021, or ESMO 2021, Syros presented data from the dose-escalation portion of the Phase 1 multi-center, open-label study of SY-5609 evaluating patients with advanced breast, colorectal, lung, ovarian and pancreatic cancers, as well as patients with solid tumors of any histology harboring Rb pathway alterations. Patients were treated in cohorts exploring continuous daily dosing as well as intermittent dosing regimens, including seven days on treatment and seven days off, or 7d on/7d off, and five days on treatment and two days off, or 5d on/2d off. As of a July 6, 2021 data cut-off, 54 patients treated with single-agentSY-5609 in the study were eligible for a safety analysis and 45 patients were evaluable for clinical response. The median age of patients enrolled in the study was 65.5. Patients had been heavily pre-treated with as many as eight prior therapies and a median of four prior therapies. Across all doses and schedules, the majority of AEs were low-grade and reversible, and there was a low rate of discontinuations due to AEs. The most common treatment-emergent AEs were gastrointestinal (nausea, diarrhea, decreased appetite, abdominal pain, vomiting), fatigue, thrombocytopenia, and anemia. Tolerability was optimized with the 7d on/7d off schedule, which had the lowest rates of treatment-emergent AEs relative to other regimens, while demonstrating comparable rates of stable disease, or SD, as seen with more dose-intense regimens, supporting the selection of this schedule for further development of SY-5609. The maximum tolerated dose of the 7d on/7d off schedule has not yet been reached as of the data cut-off date. Changes in POLR2A mRNA expression, a pharmacodynamic marker for CDK7 inhibition, were associated with anti-tumor activity and were sustained for at least three days following drug cessation, supporting intermittent dosing. As of the data cut-off date, thirteen response-evaluable patients (29%) had achieved SD, with tumor regressions of up to 20% in six of those patients, across multiple tumor types. The most substantial clinical activity was observed in heavily pre-treated patients with advanced pancreatic cancer, for which five of 13 (39%) evaluable patients achieved SD, with tumor reductions in two of those SD patients. Further, reductions in the CA 19-9 tumor marker, which is used in clinical practice to monitor tumor progression, were observed in three of four pancreatic cancer patients with serial CA 19-9 data, with these reductions ranging from 32% to 72%. Notably, one metastatic pancreatic cancer patient who had failed two prior lines of therapy and relapsed after a third line of treatment experienced prolonged SD of up to ten months. The analysis of clinical activity by tumor type and mutational status supported the mechanistic rationale for SY-5609 in Rb-altered and KRAS-mutant cancers.

Syros also presented preclinical data at ESMO 2021 evaluating the anti-tumor and PD activity of intermittent dosing regimens forSY-5609, as well as preclinical data evaluating SY-5609 as a single agent and in combination with chemotherapy in pancreatic cancer models. Taken together, these data further support Syros' dose expansion strategy, including the decision to use a 7d on/7d off dosing schedule and combine with chemotherapy in patients with pancreatic cancer.

Based on these data, Syros intends to further develop SY-5609 by exploring indications with compelling clinical and/or preclinical activity, as well as a strong mechanistic rationale and high unmet need. Syros has initiated an expansion cohort that includes two arms evaluating SY-5609 in combination with chemotherapy for the treatment of pancreatic cancer. The cohort is expected to enroll approximately 50 patients with metastatic pancreatic cancer in first or second relapse who have progressed following first-line treatment with the chemotherapy regimen known as FOLFIRINOX, with one arm exploring a doublet regimen of SY-5609 in combination with gemcitabine and the other arm exploring a triplet regimen of SY-5609 with gemcitabine and nab-paclitaxel. SY-5609 will be administered 7d on/7d off at a starting dose of 4 mg, and the combination agents will be administered at the approved doses. The study will evaluate safety and tolerability, as well as efficacy measures such as disease control rate and progression free survival. Syros expects to report safety and clinical activity data of SY-5609 in combination with chemotherapy from the safety lead-in portion of the trial in the second half of 2022. Based on the safety lead-in data, Syros will determine the best course for further development of SY-5609.

In addition, in August 2021, Syros announced entry into a clinical supply agreement with Roche, pursuant to which Syros agreed to supply SY-5609 for a combination dosing cohort with atezolizumab in Roche's ongoing Phase 1/1b INTRINSIC trial, which is evaluating multiple targeted therapies or immunotherapy, including atezolizumab, as single agents or in rational specified combinations in molecularly defined subsets of colorectal cancer patients. SY- 5609 is being evaluated in combination with atezolizumab in patients with BRAF-mutant disease, this arm of Roche's trial is now open for enrollment. Under the terms of the agreement, Roche will sponsor and conduct the Phase 1/1b study to evaluate the safety, tolerability and preliminary efficacy of the combination of SY-5609 and atezolizumab and will assume all costs associated with the study. In exchange for providing SY-5609, Syros will receive access to the data on SY-5609 in combination with atezolizumab. Syros retains all rights to SY-5609.

Syros' Strategic Priorities

Syros intends to achieve its goal of becoming an integrated biopharmaceutical company by focusing on three strategic priorities: building a leading portfolio of targeted therapies for hematologic disorders, which include two clinical stage product candidates, tamibarotene and SY-2101; building on Syros' leadership in CDK inhibition for difficult-to-treat cancers, which includes its clinical stage product candidate SY-5609; and partnering its discovery programs related to CDK12, CDK11 and WRN to better resource these programs and maximize potential value for shareholders and patients.

Syros' Targeted Hematology Portfolio

Syros is advancing two clinical-stage drug candidates, tamibarotene and SY-2101, across three genomically defined patient populations in HR-MDS, AML and APL. Together, Syros believes these programs provide us the opportunity to address high unmet medical needs of patients with targeted therapies for hematologic disorders.

Tamibarotene

Overview

Tamibarotene is an oral, potent and selective agonist of the transcription factor RARα. At ASH 2020, Syros presented data from its fully enrolled Phase 2 clinical trial assessing the safety and efficacy of tamibarotene in combination with azacitidine in 22 RARA-positive newly diagnosed AML patients who are "unfit," meaning that they are not suitable candidates for standard intensive chemotherapy, who were prospectively selected using Syros' proprietary RARA biomarker, as well as in 29 RARA-negative newly diagnosed unfit AML patients. The RARA-negative patients were enrolled to support the development of a commercial companion diagnostic test for tamibarotene. In addition, at ASH 2020, Syros presented data from its fully enrolled Phase 2 clinical trial assessing the safety and efficacy of tamibarotene in combination with azacitidine in 28 RARA-positive R/R

AML patients. Based on these data and Syros' assessment of ongoing areas of high unmet need, Syros is advancing tamibarotene in combination with azacitidine in SELECT-MDS-1, a registration-enabling Phase 3 clinical trial in RARA-positive newly diagnosed HR-MDS patients. Syros expects to report data from the ongoing SELECT-MDS-1 trial in the fourth quarter of 2023 or first quarter of 2024, with a potential NDA filing expected in 2024. Syros is also advancing tamibarotene in combination with venetoclax and azacitidine in SELECT-AML-1, a randomized Phase 2 clinical trial of RARA-positive newly diagnosed unfit AML patients, and expects to report clinical activity data from the safety lead-in portion of this trial in the second half of 2022.

Linking Tamibarotene to Novel Patient Populations

Syros leveraged its gene control platform to analyze regulatory regions of the genome in primary AML, MDS, and breast cancer patient tissue samples. Syros discovered that RARA was associated with a super-enhancer in some patients' tumors but not in others. A super-enhancer is a highly specialized regulatory region of non-coding DNA central to controlling the expression of genes most crucial to the function of a given cell. The function of RARα differs depending on whether it is bound to its ligand. In the absence of a ligand, RARα represses differentiation. Syros believes that the RARA-associated super-enhancer drives increased expression of RARα in tumors with the super-enhancer, which leads to an abundance of unliganded RARα that results in the repression of differentiation, thereby locking the cell in an immature, proliferative and undifferentiated state. Introducing a RARα agonist, such as tamibarotene, simulates the activity of a ligand, activating differentiation.

Tamibarotene Development Plan

Based on the clinical activity and favorable safety and tolerability profile of tamibarotene in combination with azacitidine as well as an assessment of ongoing areas of high unmet need within the evolving treatment landscape, Syros advanced tamibarotene in combination with azacitidine in SELECT-MDS-1, a registration-enabling Phase 3 clinical trial in RARA-positive newly diagnosed HR-MDS patients. HR-MDS is a hematologic malignancy that is closely related to AML, and Syros believes that approximately 50% of HR-MDS patients are RARA-positive. In an earlier clinical trial evaluating tamibarotene as a single agent, clinical activity was observed in ten of 23 (43%) evaluable patients with R/R AML and HR-MDS, including a marrow CR in a HR-MDS patient.

Informed by feedback from the FDA, Syros is enrolling RARA-positive newly diagnosed HR-MDS patients in a double-blind placebo-controlled, randomized study to receive tamibarotene in combination with azacitidine or placebo with azacitidine, respectively, with the CR rate as the primary endpoint. The study will enroll approximately 190 patients randomized 2:1 into the experimental vs. control arms, respectively, and depending on the data outcome, the CR endpoint could support accelerated or full approval in this patient population in the United States. Syros expects to report data from the ongoing SELECT-MDS-1 trial in the fourth quarter of 2023 or first quarter of 2024, with a potential NDA filing expected in 2024.

In addition, Syros advanced tamibarotene in combination with venetoclax and azacitidine in RARA-positive newly diagnosed unfit AML patients. Syros' ongoing Phase 2 clinical trial, known as SELECT-AML-1, is designed with a single-arm safety lead-in of approximately 15 patients to confirm the dosing regimen of the triplet to be used in the randomized portion of the trial, which will evaluate the safety and efficacy of tamibarotene in combination with venetoclax and azacitidine compared to venetoclax and azacitidine in approximately 80 patients randomized 1:1. The trial will also evaluate the triplet as a salvage strategy for patients in the control arm who do not respond to venetoclax and azacitidine in the control arm. Syros expects to report clinical activity data from the safety lead-in portion of SELECT-AML-1 in the second half of 2022. Syros also plans to initiate the randomized portion of the trial, with data expected in 2023 or 2024.

Syros has entered into an agreement with a third-party commercial provider to provide a validated laboratory test under Clinical Laboratory Improvement Amendment, or CLIA, guidelines using a diagnostic platform and approach that is being used to prospectively enroll RARA biomarker positive patients in its clinical trials. In

March 2022, Syros entered into a Master Collaboration Agreement and associated project work plan with Qiagen pursuant to which Qiagen will develop and commercialize a companion diagnostic for this biomarker.

Tamibarotene in Combination with Azacitidine

In October 2018, Syros published preclinical data in *Haematologica*, a peer-reviewed journal of the European Hematology Association, supporting the rationale for combining tamibarotene with hypomethylating agents such as azacitidine in AML with high RARA expression. These data showed that tamibarotene in combination with azacitidine resulted in synergistic anti-proliferative effects supported by evidence of DNA damage and apoptosis and, in patient-derived xenograft models of AML with high RARA expression, tamibarotene in combination with azacitidine showed both greater clearance of tumor cells in bone marrow and other tissues and greater duration of response, compared to either azacitidine or tamibarotene alone.

Syros presented data at ASH 2020 from its fully enrolled Phase 2 clinical trial evaluating the safety and efficacy of tamibarotene in combination with azacitidine in newly diagnosed AML patients who are not suitable candidates for standard chemotherapy, as well as in RARA-positive R/R AML patients.

As of October 1, 2020, 51 newly diagnosed unfit AML patients, including both RARA-positive and RARA-negative patients, were eligible for a safety analysis. Eighteen RARA-positive were evaluable for clinical response. In those patients, the data showed that:

- The ORR was 67% (12/18), with a composite CR rate of 61% (11/18), including nine patients (50%) achieving CR and two patients (11%) achieving CRi.
- 89% (8/9) of CRs were deep molecular or cytogenetic CRs.
- Responses were seen across AML risk groups, including patients with mutations that are typically associated with poor outcomes.
- The median time to initial response was 1.2 months.
- The median duration of response was 10.8 months, and median OS among patients who achieved a CR or CRi was 18 months.
- 86% (6/7) of patients who were transfusion dependent at baseline became transfusion independent, and 67% (12/18) of patients achieved or maintained transfusion independence.

As of October 1, 2020, in the 28 RARA-negative patients that were evaluable for clinical response, the data showed that the ORR was 43% (12/28), with a composite complete response rate of 32% (9/28), including seven patients (25%) achieving CR and two patients (7%) achieving CRi. The median time to initial response was 3.0 months, and the median duration of response was 10.3 months.

Tamibarotene in combination with azacitidine was generally well-tolerated with no evidence of increased toxicity relative to either as a single agent, including rates of myelosuppression that were comparable to single-agent azacitidine.

Syros also presented translational data demonstrating that most RARA-positive newly diagnosed unfit AML patients enrolled in its Phase 2 study had a monocytic disease phenotype that is associated with resistance to venetoclax. These data suggest that the RARA biomarker not only selects for patients who are more likely to respond to treatment with tamibarotene but also for patients who may be less likely to benefit from treatment with venetoclax.

Tamibarotene as a Single Agent

At the American Society of Hematology Annual Meeting held in December 2017, or ASH 2017, Syros presented clinical data from cohorts of its Phase 2 clinical trial evaluating tamibarotene as a single agent in 29 patients with

R/R AML or relapsed HR-MDS, and in 29 patients with lower-risk transfusion-dependent MDS. In these cohorts of the trial, Syros observed that chronic daily dosing of tamibarotene administered at 6 mg/m2 orally divided in two doses was generally well-tolerated, with a median treatment duration of 80 days and patients treated up to eight months and remaining on study. The majority of adverse events observed in the trial were low grade. At the time of the data cut-off for presenting data at ASH 2017, 48 patients were evaluable for response assessment, including 23 patients in the R/R AML or relapsed HR-MDS cohort and 25 patients in the lower-risk transfusion-dependent MDS cohort. Myeloid differentiation was observed in the bone marrow, consistent with the underlying mechanism of action. Clinical activity and hematologic improvement were observed in ten of 23 (43%) evaluable patients with R/R AML or HR-MDS, including three out of seven (43%) evaluable patients with HR-MDS, which included a marrow CR in a HR-MDS patient. Syros is no longer evaluating tamibarotene as a single agent in patients with AML or MDS, but Syros believes that these data support its decision to advance tamibarotene in combination with azacitidine into a registration enabling Phase 3 clinical trial in RARA-positive newly diagnosed HR-MDS patients.

Tamibarotene Market Opportunity

Syros believes that tamibarotene has the potential to address significant unmet medical need across a range of RARA-positive cancer populations and, despite a significant number of new product approvals in AML since 2018, that there continues to be a significant unmet medical need in that indication.

Syros believes that approximately 21,000 patients are diagnosed with HR-MDS in the United States and Europe annually and Syros expects the total addressable market opportunity for MDS patients of all risk groups to grow to approximately $3.3 billion by 2026. In addition, Syros believes that approximately 25,000 patients are diagnosed with unfit AML in the United States and Europe annually and Syros expects the overall total addressable market opportunity for all AML patients (fit and unfit for treatment with standard intensive chemotherapy) to grow to be approximately $6.6 billion by 2025. Based on data from patients screened in Syros' clinical trials, Syros believes approximately 50% of MDS patients and approximately 30% of AML patients are positive for the RARA biomarker.

There have been no new drug approvals for HR-MDS since 2006 other than HMAs, which represent the current standard of care but offer low CR rates with mOS in the range of 15 to 25 months. Based on current treatment guidelines, a majority of HR-MDS patients receive hypomethylating agents upon diagnosis, but those treatments are believed to have modest efficacy, with an estimated survival of less than 1.6 years for higher-risk, newly diagnosed patients and less than six months for patients who have relapsed or become refractory to front-line treatment.

It is estimated that more than half of newly diagnosed AML patients are elderly or unfit for treatment with intensive therapies, underscoring the need for well-tolerated therapies that can be used in combination. Despite initial responses to therapy in select patients, the majority of AML patients relapse or become refractory to current treatment options. Syros believes that tamibarotene has the potential to provide a meaningful benefit for newly diagnosed unfit AML patients who are RARA-positive.

SY-2101

Overview

In December 2020, Syros acquired from Orsenix a novel oral form of ATO, which Syros refers toas SY-2101. SY-2101 is in development for the treatment of APL, a subtype of AML defined by a fusion of the RARA and PML genes. An IV formulation of ATO is approved for use in combination with ATRA in patients with newly diagnosed lower-risk APL and, while curative in more than 80% of patients, its administration requires up to 140 two- to four-hour infusions over the typical course of induction and consolidation treatment. IfSY-2101 demonstrates comparable efficacy to IV ATO in Syros' clinical studies, Syros believes it has the

potential to become the standard-of-care frontline therapy for APL by providing a substantially more convenient option that reduces the treatment burden on patients, improving access, and lowering costs to the healthcare system. In a Phase 1 clinical trial, SY-2101 demonstrated bioavailability PK exposures similar to IV ATO, and a generally well-tolerated safety profile. Syros anticipates reporting PK and safety data from its ongoing Phase 1 clinical trial of SY-2101 in mid-2022. Following confirmation of a dose that demonstrates suitable PK, Syros intends to initiate a registration-enabling Phase 3 clinical trial in patients with newly diagnosed lower-risk APL in the second half of 2023.

SY-2101 Clinical Development Plan

Syros has begun dosing patients in a dose confirmation study of SY-2101. The ongoing dose confirmation study is evaluating the PK, food effect, safety and tolerability of SY-2101 and is expected to enroll between six and 24 adult APL patients undergoing consolidation with IV ATO plus ATRA. Participants receive a single dose of 15 mg of SY-2101 in both the fasted and in the fed state, and a single dose of IV ATO for PK assessments, with flexibility to allow for other SY-2101 doses to be evaluated. Daily administration of SY-2101 is also being evaluated in a multiple-dose treatment module substituting for IV ATO during consolidation to assess steady state SY-2101 PK and safety. Syros anticipates reporting PK and safety data in mid-2022. The feedback from a Type C meeting to review Syros' Phase 3 study design with the FDA in November 2021 continues to support molecular complete response rate as the primary endpoint for accelerated approval and event free survival as the primary endpoint for full approval, in each case compared to historic IV ATO data. In addition, FDA feedback supports the inclusion of patients randomized to IV ATO for comparative safety assessments. Based on this feedback and following confirmation of a dose that demonstrates comparable PK exposures to IV ATO, Syros intends to initiate a registration-enabling Phase 3 clinical trial in approximately 215 patients with newly diagnosed low-risk APL, randomized 2:1 to receive SY-2101 or IV ATO, in the second half of 2023.

SY-2101 Clinical Data

To-date, SY-2101 has been evaluated in a Phase 1 PK study, which included three dose cohorts of 5 mg, 10 mg and 15 mg, given once daily. The study enrolled 12 patients with advanced hematologic malignancies, including six patients with R/R MDS, four patients with R/R AML, and two patients with chronic myelomonocytic leukemia. The median age of these patients was 76.5 years (with patients ranging from 45 to 81 years), and patients had a median of two prior therapies (with patients ranging from one to five prior therapies). The study showed that SY-2101 is bioavailable and achieves exposure levels in the range of the approved IV dose. It was generally well-tolerated at all doses, with the majority of adverse events being low-grade. Specifically, investigators reported preliminary responses in two MDS patients, observing one patient with marrow remission at two and five months after start of dosing, and another patient had bone marrow response and became eligible for transplant. Steady-state plasma concentration was reached on day 15. Exposure levels of SY-2101 at the 15 mg dose were comparable to the IV ATO approved dose (0.15 mg/kg) for adult patients, based on IV ATO historical data.

SY-2101 Market Opportunity

APL is a subtype of AML, defined by a genetic fusion of the RARA and PML genes, and represents about 10% of AML cases. In APL, promyelocytes are overproduced and accumulate in the bone marrow and blood, resulting in signs and symptoms of the disease.

Approximately 2,000 patients are diagnosed with APL in the United States and Europe annually. Syros does not believe there are any oral formulations of ATO in development or on the market for the treatment of APL in the United States or Europe.

Contingent Obligations to Orsenix

In December 2020, Syros entered into an Asset Purchase Agreement with Orsenix, pursuant to which Syros acquired all of Orsenix's assets related to SY-2101. Under the terms of the Asset Purchase Agreement, Syros paid Orsenix an upfront fee of $12.0 million. In addition, Syros is required to pay Orsenix single-digit million milestone payments related to the development of SY-2101 in indications other than APL, $6.0 million following the achievement of a regulatory milestone related to the development of SY-2101 in APL, and up to $10.0 million upon the achievement of certain commercial milestones with respect to SY-2101. Syros' obligation to pay the commercial milestone payments expires following the tenth anniversary of the first commercial sale of SY-2101. The Asset Purchase Agreement requires Syros to use commercially reasonable efforts to develop and commercialize SY-2101 for APL in the United States during such period, and to use commercially reasonable efforts to dose the first patient in a Phase 3 clinical trial of SY-2101 on or before the third anniversary of the closing of the transaction; however, Syros retains sole discretion to operate the acquired assets as it determines.

Selective CDK Inhibition

CDK is a family of kinases that have emerged as potentially important drug targets in cancer because of their roles in transcription, the process by which genes express proteins, and by interfering with cancer's ability to progress unchecked through the cell cycle. Syros intends to build on its leadership in selective CDK inhibition for difficult-to-treat cancers by continuing to develop SY-5609, which is currently in the dose escalation portion of a Phase 1 clinical trial in patients with select advanced solid tumors. Syros also has selective CDK12 and CDK11 inhibitor programs in cancer, and Syros expects that its next development candidate will be nominated from its CDK12 program in the third quarter of 2022.

SY-5609

Overview

SY-5609 is a highly potent and selective small molecule CDK7 inhibitor that can be administered orally. CDK7, a member of the CDK family, is a transcriptional kinase that plays a central role in two processes that cancer cells use to survive and thrive: increased expression of cancer-promoting genes, and uncontrolled cell cycle progression. CDK7 activity has been implicated in a range of solid tumors and blood cancers. Syros believes that inhibiting CDK7 preferentially lowers the expression of disease-driving transcription factors and anti-apoptotic proteins, resulting in the preferential killing of cancer cells over non-cancerous cells. Syros also believes that selective inhibition of CDK7 interferes with cancer-driving adaptations at multiple points in the cell cycle, promoting the induction of apoptosis, or cell death. Using Syros' platform, Syros has generated several potent and selective small molecule CDK7 inhibitors, including SY-5609.

SY-5609 Clinical Development Plan

At ESMO 2021, Syros presented data from its Phase 1 clinical trial of SY-5609 in patients with breast, colorectal, lung, ovarian or pancreatic cancer, or with solid tumors of any histology having Rb pathway alterations. These data demonstrated proof of activity and proof of mechanism in refractory solid tumor patient populations, with a generally favorable tolerability profile. Based on these data, Syros intends to further develop SY-5609 in three tumor settings, focusing initially on indications with compelling clinical and/or preclinical activity, as well as a strong mechanistic rationale and high unmet need. Syros is currently evaluating SY-5609 in combination with chemotherapy in relapsed/refractory metastatic pancreatic cancer patients in an expansion cohort of its existing Phase 1 clinical trial. Syros also plans to evaluate SY-5609 in combination with atezolizumab, a PD-L1 inhibitor, in BRAF-mutant colorectal cancer in a Phase 1/1b clinical trial sponsored by Roche that is now open for enrollment.

Phase 1 Dose Escalation Study of SY-5609 in Patients with Select Solid Tumors

At ESMO 2021, Syros presented data from its ongoing dose-escalation portion of the Phase 1 multi-center, open-label study of SY-5609 evaluating patients with advanced breast, colorectal, lung, ovarian and pancreatic cancers, as well as patients with solid tumors of any histology harboring Rb pathway alterations.

Patients were treated in cohorts exploring continuous daily dosing as well as intermittent dosing regimens, including 7d on/7d off 5d on/2d off schedules. As of a July 6, 2021 data cut-off, 54 patients treated with single-agent SY-5609 in the study were eligible for a safety analysis and 45 patients were evaluable for clinical response. The median age of patients enrolled in the study was 65.5. Patients had been heavily pre-treated with as many as eight prior therapies and a median of four prior therapies.

Across all doses and schedules, the majority of AEs were low-grade and reversible, and there was a low rate of discontinuations due to AEs (7%). The most common treatment-emergent AEs were gastrointestinal (nausea, diarrhea, decreased appetite, abdominal pain, vomiting), fatigue, thrombocytopenia, and anemia. Tolerability was optimized with the 7d on/7d off schedule, which had the lowest rates of treatment-emergent AEs relative to other regimens, while demonstrating comparable rates of SD as seen with more dose-intense regimens, supporting the selection of this schedule for further development of SY-5609. The maximum tolerated dose of the 7d on/7d off schedule has not yet been reached as of the data cut-off date, with dosing up to 6 mg. Changes in POLR2A mRNA expression, a pharmacodynamic marker for CDK7 inhibition, in patients treated with 3 mg and above were associated with anti-tumor activity and were sustained for at least three days following drug cessation, supporting intermittent dosing. The data further showed that:

- Thirteen response-evaluable patients (29%) had achieved SD, with tumor regressions of up to 20% in six of those patients, across multiple tumor types.
- The most substantial clinical activity was observed in heavily pre-treated patients with advanced pancreatic cancer.
- Five of 13 (39%) evaluable patients achieved SD, with tumor reductions in two of those SD patients.
- Reductions in the CA 19-9 tumor marker, which is used in clinical practice to monitor tumor progression, were observed in three of four pancreatic cancer patients with serial CA 19-9 data, with these reductions ranging from 32% to 72%.
- Notably, one metastatic pancreatic cancer patient who had failed two prior lines of therapy and relapsed after a third line of treatment experienced prolonged SD of up to ten months.
- The analysis of clinical activity by tumor type and mutational status supported the mechanistic rationale for SY-5609 in Rb-altered and KRAS-mutant cancers.

Based on these data, Syros intends to further develop SY-5609 by exploring three combination regimens, focusing initially on pancreatic cancer and BRAF-mutant colorectal cancer, each of which are indications with compelling clinical and/or preclinical activity, as well as a strong mechanistic rationale and high unmet need.

Expansion Cohort in Metastatic Pancreatic Cancer

Syros presented preclinical data at ESMO evaluating the anti-tumor and PD activity of intermittent dosing regimens for SY-5609, as well as preclinical data evaluating SY-5609 as a single agent and in combination with chemotherapy in pancreatic cancer models. Taken together, these data further support Syros' dose expansion strategy, including the decision to use a 7d on/7d off dosing schedule and combine with chemotherapy in patients with pancreatic cancer. The data showed that SY-5609:

- Induced robust anti-tumor activity as a single agent in ovarian cancer models that was maintained at higher doses on intermittent schedules, including a 7d on/7d off schedule. POLR2A PD effects were sustained in tumor tissue through 72 hours post-dosing, consistent with what was observed in patients in the dose-escalation study.

- Induced regressions as a single agent in half (4/8) of the pancreatic cancer models that were studied, including models derived from heavily pre-treated patients.
- Resulted in deeper responses when combined on 7d on/7d off schedule with gemcitabine in KRAS-mutant pancreatic models than either agent alone.

Based on these preclinical data, along with the data showing clinical activity in pancreatic cancer presented at ESMO 2021, Syros has initiated an expansion cohort that includes two arms evaluating SY-5609 in combination with chemotherapy for the treatment of pancreatic cancer. The cohort is expected to enroll approximately 50 patients with metastatic pancreatic cancer in first or second relapse who have progressed following first-line treatment with the chemotherapy regimen known as FOLFIRINOX, with one arm exploring a doublet regimen of SY-5609 in combination with gemcitabine and the other arm exploring a triplet regimen of SY-5609 with gemcitabine and nab-paclitaxel. SY-5609 will be administered 7d on/7d off at a starting dose of 4 mg, and the combination agents will be administered at the approved doses. The study will evaluate safety and tolerability, as well as efficacy measures such as disease control rate and progression free survival. Syros expects to report clinical activity data of SY-5609 in combination with chemotherapy from the safety lead-in portion of the trial in the second half of 2022. Based on the safetylead-in data, Syros will determine the best course for further development of SY-5609.

BRAF-Mutant Colorectal Cancer

BRAF mutations, present in 10% of colorectal cancer patients, are powerful activators of cell signaling and transcriptional programs. At the 2020 American Society of Clinical Oncology Virtual Scientific Program, or ASCO 2020, Syros reported the results of a series of preclinical studies of SY-5609 in colorectal cancer cell lines, as well as in 30 independent patient-derived xenograft, or PDX, models of colorectal cancer, including BRAF-mutant, KRAS-mutant and wild-type models. The data showed that SY-5609:

- Potently inhibited proliferation and induced G2/M cell cycle arrest in KRAS- and BRAF-mutant colorectal cancer cell lines in vitro.
- Induced dose-dependent tumor growth inhibition, including complete regressions that were sustained after treatment discontinuation, with repeated daily dosing at well-tolerated doses that were associated with dose-dependent expression changes in cell cycle markers E2F1 and CCNB1 and the transcriptional marker POLR2A in a BRAF-mutant PDX model.
- Resulted in at least 50% tumor growth inhibition in 67% (20/30) of PDX models, and at least 90% tumor growth inhibition in 23% (7/30) of PDX models, including in models derived from heavily pre-treated patients, at well-tolerated doses.
- Deeper responses, defined as at least 90% tumor growth inhibition, were observed more frequently in models with BRAF mutations (50%, or 5/10) relative to KRAS-mutant or wild-type models (10%, or 1/10 each).
- Regressions were seen in two BRAF-mutant models and one KRAS-mutant model.

Preclinical studies have also demonstrated that CDK7 inhibition enhances anti-tumor activity of PD1 inhibition, inducing DNA replication stress and genome instability in cancer cells and triggering immune-response signaling. In animal models, CDK7 inhibitors have been shown to enhance tumor response to anti-PD1 immunotherapy, prolonging overall survival, or OS, and increasing immune cell infiltrates.

Syros believes that these preclinical data support the exploration of SY-5609 in BRAF-mutant colorectal cancer in combination with a PDL1 inhibitor as part of Roche’s Phase 1/1b INTRINSIC trial. Syros has entered into a clinical supply agreement with Roche, pursuant to which Syros agreed to supply SY-5609 for a combination dosing cohort with atezolizumab in Roche’s ongoing Phase 1/1b INTRINSIC trial, which is evaluating multiple targeted therapies or immunotherapy, including atezolizumab, as single agents or in rational specified

combinations in molecularly defined subsets of colorectal cancer patients. SY-5609 is being evaluated in combination with atezolizumab in patients with BRAF-mutant disease, and this arm of the trial is now open for enrollment. Under the terms of the agreement, Roche will sponsor and conduct the Phase 1/1b study to evaluate the safety, tolerability and preliminary efficacy of the combination of SY-5609 and atezolizumab and will assume all costs associated with the study. In exchange for providing SY-5609, Syros will receive access to the data on SY-5609 in combination with atezolizumab. Syros retains all rights to SY-5609.

SY-5609 Market Opportunity

With SY-5609, Syros believes that it has the opportunity to address significant unmet medical needs across a range of cancers. Syros' clinical development program for SY-5609 is currently focused on patients with pancreatic cancer and BRAF-mutant colorectal cancer.

Pancreatic cancer is a particularly aggressive and difficult-to-treat form of cancer. This is in part because most patients do not exhibit symptoms until the cancer has reached an advanced stage. In 2022, there are predicted to be over 62,000 newly diagnosed cases in the United States and over 49,000 deaths from the disease. Syros believes that there are approximately 27,500 patients with relapsed/refractory metastatic pancreatic cancer in the United States. Currently, pancreatic cancer is treated with surgery, chemotherapy, radiation, and, more recently, targeted therapies and immunotherapies. The only approved second-line therapy in the United States and Europe (Onivyde® in combination with fluorouracil and leucovorin) has demonstrated a progression free survival of only 3.1 months. There continues to be a need for better treatment options to improve the prognosis for patients with pancreatic cancer, with a focus on new therapies that target specific genetic mutations and pathway alterations that contribute to the cancer-causing processes in cells.

Colorectal cancer is the third most commonly diagnosed cancer in men and women but is the second leading cause of death in the United States. The number of colorectal cancer cases in 2021 is estimated to be 500,000 across the developed pharmaceutical markets. In the United States, it is estimated that there will be 160,000 new cases, and approximately 55,000 metastatic stage patients, diagnosed this year. Chemotherapeutic regimens are the standard of care for initial treatment of metastatic colorectal cancer. Mutations in the BRAF gene, which are found in about 10% of patients with metastatic colorectal cancer, are associated with a poor prognosis, underscoring the need for better treatment options for these patients. Therapies targeted towards specific mutations such as BRAF are currently being investigated in clinical trials.

Syros' Gene Control Platform and Discovery Programs

There are approximately 200 different cell types in the human body. Despite having identical genomes, each of these cell types has a different function. For example, a skin cell functions differently than a muscle cell despite sharing the exact same DNA. What determines cell type and function is the specific set of genes that is expressed, or turned "on" or "off," in that given cell. Transcription factors, transcriptional kinases, other transcriptional and regulatory proteins, and RNA play a critical role in this coordinated activation and repression of genes, and therefore, represent important points for therapeutic intervention. Because this biology is fundamental to the function of all cells, it applies across diseases.

Although researchers have long believed that alterations innon-coding regions of DNA, which account for 98% of the genome, play a key role in driving disease, the scientific community has lacked the tools to study these regions of the genome, rendering them poorly understood. As a result, the discovery and development of targeted therapies to date has focused almost exclusively on abnormal proteins resulting from genetic alterations found in regions of DNA that encode for proteins, which represent less than 2% of the entire genome.

Syros' Gene Control Platform

Syros' proprietary gene control platform consists of two fundamental pillars:

- identifying gene control targets that, when modulated with a drug, may provide a therapeutic benefit to defined patient populations; and
- drugging gene control targets.

Syros develops product candidates to modulate gene control targets through internal drug discovery efforts focused on creating small molecule drugs targeting transcription factors, transcriptional kinases and other transcriptional and regulatory proteins. Syros has also used its platform to link existing drugs to novel genomically defined patient populations, and seek to in-license, acquire or use those drugs as starting points for its own drug discovery programs to accelerate its development path, as Syros did with tamibarotene.

Syros has developed significant core internal capabilities in small molecule chemistry, biochemistry and structural biology to characterize the structure and function of transcription factors such as transcriptional kinases, chromatin regulators, and other transcriptional and regulatory proteins in order to generate novel chemical matter, including SY-5609, and multiple molecules across other programs in Syros' pipeline. Syros has also developed a sophisticated suite of proprietary assays, which are internally developed tests to measure the biochemical, biophysical, cellular and genomic activity of known and novel compounds against gene control targets.

Oncology Programs

Syros currently has several oncology programs in its preclinical and discovery pipeline targeting the inhibition of CDK12, CDK11, and WRN. Syros is seeking partnerships for these oncology programs.

Syros' CDK12 inhibitor program builds on its capabilities to discover potent and selective small molecule inhibitors to specific members of the CDK family. In preclinical studies, Syros has observed that inhibiting CDK7 results in different transcriptional effects than inhibiting CDK12, pointing to distinct therapeutic opportunities to benefit patients with difficult-to-treat cancers. Specifically, Syros believes that a selective CDK12 inhibitor presents a therapeutic opportunity in cancers that have a dependency on DNA repair. Syros expects that its next development candidate will be nominated from its CDK12 program in the third quarter of 2022.

CDK11 is a transcriptional kinase like CDK7 and CDK12. Utilizing Syros' expertise in designing selective CDK inhibitors, Syros believes it can identify a potent and selective CDK11 inhibitor. Syros' work in understanding the role of CDK11 in specific tumor types and identification of synthetic lethal relationships supports the thesis that it will identify specific tumors that have a dependency on CDK11.

WRN is a recently identified helicase of the recQ family that has been shown to be important for the survival of microsatellite instability, or MSI, colon cancer cells. Syros is leveraging its small molecule drug discovery capabilities to identify small molecule WRN inhibitors. Syros is also using its platform to analyze regulatory regions of the genome across various cancers and monogenic diseases to identify points of therapeutic intervention in specific subsets of patients and to create a pipeline of novel product candidates targeting transcriptional and regulatory proteins. Syros is also using its platform in collaboration with third parties to identify and validate targets in diseases beyond its current areas of focus. To this end, Syros entered a target discovery, research collaboration and option agreement with Incyte in January 2018, under which Syros is using its platform to identify novel therapeutic targets with a focus on myeloproliferative neoplasms. See "*—License and Collaboration Agreements—Incyte Corporation*" below.

Sickle Cell Disease and Beta Thalassemia

Syros' objective is to provide a functional cure for sickle cell disease patients by switching on the gamma-globin gene with an oral medicine. Using Syros' gene control platform to elucidate mechanisms controlling gamma-

globin gene expression, Syros has focused its efforts to date on LRF (leukemia/lymphoma-related factor) and the NuRD (nucleosome remodeling and histone deacetylation) complex as potential targets to switch on the gamma-globin gene, which is normally silenced a few months after birth. By turning on gamma-globin expression, Syros aims to induce the production of fetal hemoglobin, which is known to exert protective effects on the red blood cells of patients with sickle cell disease and beta thalassemia and to mitigate the clinical manifestations of those diseases.

At the American Society of Hematology Annual Meeting held in December 2019, or ASH 2019, Syros highlighted a portion of its sickle cell disease work by reporting that Syros had discovered and validated a novel fetal hemoglobin repressor, Nuclear Factor I X, or NFIX, that could serve as a potential target for therapeutic intervention. The preclinical data presented at ASH 2019 showed that knockdown of NFIX:

- increased expression of gamma-globin mRNA comparable to increases observed by decreasing the level of previously identified gamma-globin repressors;
- resulted in detectable levels of fetal hemoglobin in nearly 100% of cells, compared to 16% of cells when the NFIX gene was not knocked down; and
- increased total fetal hemoglobin levels to 40%, exceeding levels that are associated in the published literature with a functional cure in a subset of sickle cell patients.

In December 2019, Syros entered into a collaboration with GBT to discover, develop and commercialize novel therapies for sickle cell disease and beta thalassemia. See "*—License and Collaboration Agreements—Global Blood Therapeutics*" below.

Intellectual Property

Syros files patent applications directed to various compositions of matter, formulations and methods related to its product candidates and compounds in earlier stages of development, methods related to its gene control platform, and other commercially relevant inventions. As of December 31, 2021, Syros owns 19 issued U.S. patents and 15 pending U.S. utility patent applications. Syros is pursuing or maintaining 97 corresponding patent applications that are pending or granted in various jurisdictions outside the United States, including Europe, Japan, Australia, Canada and China, and Syros owns five applications that are pending in accordance with the Patent Cooperation Treaty, or PCT. In addition, as of December 31, 2021, Syros has field-limited exclusive licenses to six issued U.S. patents and 11 corresponding applications that are pending or granted in various jurisdictions outside the United States, including Europe, Japan and Canada. A significant portion of the patents and applications Syros owns or licenses pertain to its product candidates that are in clinical or pre-clinical development, to methods of using them in the treatment of disease, and to methods of selecting patients for treatment based on biomarker expression.

Syros' IP portfolio as of December 31, 2021 is further described below. For some of Syros' pending patent applications, prosecution has yet to commence. Prosecuting patent applications to allowance is often a lengthy process, during which the scope of the claims initially submitted for examination by various patent offices is often significantly narrowed, and some claims may never be granted. It is possible that Syros will amend the claims of its pending patent applications to limit their scope. Syros may also elect to abandon some of its pending patent applications, particularly those pending outside of the United States, if Syros determines these applications do not have strategic significance to its programs or platform.

Tamibarotene

The patent portfolio Syros owns for tamibarotene contains six issued U.S. patents, two pending U.S. utility patent applications, 26 applications pending or granted in countries other than the United States, including Europe, Japan, Australia, Canada, China, Russia, Israel and Mexico, and two pending PCT applications. Generally, these

patents and applications disclose methods of identifying and treating patients who are sensitive to RARα agonists, including tamibarotene, based on the expression of certain biomarkers, including RARA. The applications disclose methods of treating selected patients with tamibarotene alone or with a combination of tamibarotene and a second agent, such as azacitidine. One of Syros' issued patents, U.S. Patent No. 9,845,508, covers methods of diagnosing and treating human patients suffering from non-APL AML by administering tamibarotene; the patients are diagnosed based on the level of RARA messenger RNA, or mRNA, previously determined to be present in a sample of diseased cells from the subject. The granted claims of a second patent, U.S. Patent No. 10,167,518, cover methods of treating human subjects suffering from MDS. Selection of subjects for treatment is again based on the level of RARA mRNA expression, and RARA-positive subjects are treated with tamibarotene. A third patent, U.S. Patent No. 9,868,994, covers methods of treating non-APL AML or MDS by administering tamibarotene to a patient when a defined sample obtained from the patient is determined to have an elevated level of IRF8 mRNA or elevated levels of both IRF8 and RARA mRNA. A fourth patent, U.S. Patent No. 10,240,210, covers methods of treating non-APL AML or MDS with a combination of tamibarotene and azacitidine when a defined sample from the subject has been determined to have an elevated RARA mRNA level or an elevated IRF8 mRNA level. A fifth patent, U.S. Patent No. 10,697,025, covers methods of treating subjects who have non-APL AML with tamibarotene; treatment proceeds when a sample of diseased cells from the subject was determined to have a super enhancer associated with a RARA gene or a level of primary RNA transcripts form the RARA gene that is equal to or above a pre-determined threshold. A sixth patent, U.S. Patent No. 11,053,552, covers methods of treating non-APL AML or MDS by administering a combination of tamibarotene and a second therapeutic agent, with further specification of the analysis of an IRF8 biomarker and/or a RARA biomarker. Syros believes these six U.S. patents are eligible for listing in the Orange Book. These patents, as well as any additional patents that may grant from applications claiming the benefit of the same filing date as the currently granted patents, have statutory expiration dates no earlier than March 2036. Patent term extensions could result in later expiration dates.

In addition, Syros has an exclusive license from TMRC to practice the inventions claimed in two U.S. patents and five corresponding patents granted in Canada and Europe. The claims of the U.S. patents are directed to a tamibarotene capsule preparation, to a crystal form of tamibarotene, medicaments comprising that form, and methods of making it. The U.S. patent covering capsule preparations has a statutory expiration date in April 2028, and the U.S. patent related to the crystalline form has a statutory expiration date in August 2021. Syros does not have composition of matter patent protection with respect to tamibarotene.

SY-2101

The patent portfolio Syros owns for SY-2101 contains five issued patents, three of which were obtained in the U.S., one of which was granted in Europe, and one of which was granted in Japan. In addition, applications remain pending in the U.S. and ten other jurisdictions, including Europe, Japan, Australia, Canada and China. Generally, these patents and applications disclose methods of making lyophilized compositions comprising arsenic and formulations containing the lyophilized arsenic that can be orally administered to patients having APL and other hematological malignancies. One of Syros' issued patents, U.S. Patent No. 10,111,836, covers methods of preparing an oral pharmaceutical formulation comprising a lyophilized composition comprising arsenic or lyophilized ATO. A second patent, U.S. Patent No. 10,272,045, covers distinct methods of preparing a lyophilized composition comprising arsenic. A third patent, U.S. Patent No. 10,653,628, covers a solution for use in the lyophilization of a pharmaceutical compound comprising ATO. These patents, as well as any additional patents that may grant from applications claiming the benefit of the same filing date as the currently granted patents, have statutory expiration dates no earlier than February 2036. Patent term extensions could result in later expiration dates.

SY-5609 and Other CDK7 Inhibitors

The patent portfolio Syros owns for SY-5609 and its other CDK7 inhibitors, including SY-1365, contains patents and patent applications generally directed to the inhibitors, pharmaceutical formulations containing them, and

methods of making and using them, including their use in treating various biomarker-selected patient populations. As of December 31, 2021, Syros owns seven issued U.S. patents, eight pending U.S. patent applications, 55 corresponding applications pending or granted in countries outside the United States, including Europe, Japan, Australia, Canada and China, and three pending applications filed in accordance with the PCT. Any patent that has issued or will issue and that claims the benefit of the priority date of one or more of these patents or patent applications will have a statutory expiration date ranging from October 2034 to October 2041. Patent term adjustments or patent term extensions could result in later expiration dates.

Of the seven issued U.S. patents Syros owns, U.S. Patent No. 10,106,526 covers compounds and pharmaceutical compositions generically describing SY-1365; U.S. Patent No. 10,059,690 specifically claims SY-1365 and pharmaceutical compositions containing SY-1365; U.S. Patent No. 10,519,135 covers pharmaceutical compositions containing stereoisomers of SY-1365; U.S. Patent No. 10,336,760 covers CDK7 inhibitors conforming to the structural formula provided; U.S. Patent No. 10,308,648 covers CDK7 inhibitors conforming to the structural formula provided as well as pharmaceutically acceptable salts, solvates, hydrates, tautomers, and stereoisomers thereof; U.S. Patent No. 10,865,206 covers pharmaceutical compositions comprising a pharmaceutically acceptable excipient and a therapeutically effective amount of a CDK7 inhibitor conforming to the structural formula provided or a pharmaceutically acceptable salt, isotopically labeled derivative, or stereoisomer thereof; and U.S. Patent No. 10,738,067 covers SY-5609 and pharmaceutical compositions comprising a therapeutically effective amount thereof. The first six of these patents have statutory expiration dates in 2035, not including available patent term extensions. The seventh patent, covering SY-5609 and pharmaceutical compositions containing SY-5609, has a statutory expiration date in November 2039, not including available patent term adjustments or patent term extensions.

Sickle Cell Disease

As of December 31, 2021, Syros owns one PCT application directed to methods of treating hemoglobinopathies such as sickle cell disease.

Other Programs

The IP portfolio Syros owns that relates to programs other than those described above contains patents and patent applications directed to compositions of matter for inhibiting transcription factors and immuno-oncology targets in multiple compound families, and methods of treating various diseases, including cancer and immunological diseases, through inhibition of specific transcription factor(s) or gene products. As of December 31, 2021, Syros owns three U.S. patents and four U.S. patent applications. Syros' issued patents numbered 10,787,444 and 11,124,527 cover compounds conforming to the structures provided as well as pharmaceutically acceptable salts thereof, which are intended for use as inhibitors of Myc. These patents have statutory expiration dates in June 2036. Syros' issued patent, U.S. Patent No. 11,040,981, covers compounds conforming to the structures provided as well as pharmaceutically acceptable salts thereof that are intended for use as inhibitors of TAM kinases. This patent has a statutory expiration date in October 2038.

Platform

Syros' platform technology relates to super-enhancers, their detection, and uses thereof to identify novel disease targets. As of December 31, 2021, Syros has a field-limited exclusive license to three issued U.S. patents (U.S. Patent Nos. 9,155,724; 9,181,580; and 10,160,977) and one granted patent in Europe directed to these technologies. These patents have a statutory expiration date in October 2033.

In most countries, including the United States, a patent expires 20 years from its earliest effective filing date. In the United States, a patent's term may be lengthened to compensate for delays by the or USPTO in examining and granting a patent or may be shortened if a patent is terminally disclaimed over an earlier filed patent. A patent that covers a therapeutic agent may also be eligible for patent term extension when FDA approval is

granted, provided statutory and regulatory requirements are met. See "*—Government Regulation and Product Approvals—Marketing Authorization*" below for additional information on such exclusivity. If and when Syros' products receive approval by the FDA or regulatory agencies in other countries, Syros expects to apply for a patent term extension on an issued patent covering a given product, depending upon the length of the clinical trials for each product and other factors. There can be no assurance that any of Syros' pending patent applications will issue or that Syros will benefit from any patent term extension or favorable adjustment to the terms of any of its patents.

As with other biotechnology and pharmaceutical companies, Syros' ability to exclude others from making, using, or selling its product candidates and other inventions will depend on its success in obtaining valid patent claims and enforcing those claims. One or more of Syros' pending patent applications, and any that Syros may file or license from third parties in the future may not, however, proceed to grant as an issued patent. Syros also cannot predict the breadth of claims that may be allowed or enforced in its patents. Any patent may be challenged, invalidated or circumvented. For example, Syros cannot be certain of the priority of inventions covered by pending third-party patent applications. If third parties prepare and file patent applications in the United States that also claim technology or therapeutics to which Syros has rights, it may have to participate in interference proceedings in the USPTO to determine priority of invention, which could result in substantial costs to us, even if the eventual outcome is favorable to Syros, which is highly unpredictable. In addition, because of the extensive time required for clinical development and regulatory review of a product candidate Syros may develop, it is possible that, before any of its product candidates can be commercialized, any related patent may expire or remain in force for only a short period following commercialization, thereby limiting protection such patent would afford the respective product and any competitive advantage such patent may provide.

In addition to patents and pending patent applications, Syros relies upon unpatentable know-how and continuing technological innovation to develop and maintain its competitive position. Syros seeks to protect its proprietary information, in part, by executing non-competition, non-solicitation, confidentiality, and invention assignment agreements with its employees, collaborators, scientific advisors and consultants as appropriate. The confidentiality agreements Syros enters into are designed to protect its proprietary information and the agreements or clauses requiring assignment of inventions to it are designed to grant it ownership of technologies that are developed through its relationship with the respective counterparty. Syros cannot guarantee, however, that these agreements will afford it adequate protection of its IP and proprietary information rights.

License and Collaboration Agreements

Syros is a party to collaborations in which it aims to use its platform to benefit patients with diseases beyond its current areas of focus, or that Syros believes will contribute to its ability to advance development and ultimately commercialize its product candidates. Syros expects to enter into additional collaborations in the future. For instance, Syros intends to seek to enter into collaborations where Syros believes that realizing the full commercial value of its development programs will require access to broader geographic markets or the pursuit of broader patient populations or indications. Syros' existing collaborations impose, and any collaborations Syros may enter into in the future are likely to impose, certain performance obligations on it.

In addition, Syros is a party to a number of license agreements under which Syros licenses patents, patent applications and other IP from third parties. Syros enters into these agreements to augment its proprietary IP portfolio. This licensed IP covers some of the compounds that Syros is researching and developing and some of the scientific processes that it uses. These licenses impose various diligence and financial payment obligations on it. Syros expect to continue to enter into these types of license agreements in the future.

Global Blood Therapeutics

In December 2019, Syros entered into a license and collaboration agreement with GBT with respect to a research collaboration to discover novel targets that induce fetal hemoglobin, in order to develop new small molecule

treatments for sickle cell disease and beta thalassemia. Under the terms of the collaboration agreement, parties will use commercially reasonable efforts to identify at least one compound for the commencement of studies that are reasonably required to meet the requirements for filing an IND. Each party will be solely responsible for its own costs incurred to conduct its activities under the research plan, except that GBT will reimburse us for full-time employee and out-of-pocket costs and expenses that Syros incurs in accordance with the agreed upon research budget. Unless earlier terminated or extended, the research program will end in December 2022. The term of the research program may be extended by one or two one-year extensions as mutually agreed upon.

Under the terms of the collaboration agreement, Syros granted to GBT an option to obtain an exclusive, worldwide license, with the right to sublicense, under relevant IP rights and know-how of Syros arising from the collaboration to develop, manufacture and commercialize any compounds or products resulting from the collaboration. GBT may exercise this option at any time during the period (i) commencing on the earlier of (a) the date of GBT's designation of the first IND candidate, or (b) if no IND candidate is so designated as of the expiration of the research term, the date of expiration of the research term, and (ii) ending on the 180th day after the date of expiration or earlier termination of the research term. GBT's exercise of the option will be subject to any required filings with the applicable antitrust authority as required by the antitrust laws and satisfaction of any applicable antitrust conditions.

After any exercise of the option, GBT will be solely responsible, at its own expense, for all development, manufacturing, regulatory activities and commercialization of licensed compounds and products worldwide. Under the collaboration agreement, GBT is required to use commercially reasonable efforts to develop (including to seek and obtain regulatory approval of) and, if regulatory approval is obtained, commercialize at least one product in any and all uses in the United States and any of the United Kingdom, Germany, France, Italy and Switzerland. In addition, Syros has an option to co-promote the first product in the United States.

GBT made an upfront payment of $20.0 million to Syros in January 2020. Should GBT exercise its license option, Syros could receive up to $315 million in option exercise, development, regulatory, commercialization and sales-based milestones per product candidate and product resulting from the collaboration. Syros is also entitled to receive, subject to certain reductions, tiered mid-to-high single digit royalties as percentages of calendar year net sales on any licensed product. GBT's obligation to pay royalties, on a licensed product-by-licensed product and country-by-country basis, will commence on the date of the first commercial sale of such licensed product in such country and end on the later of (a) the tenth anniversary of the first commercial sale of such licensed product in such country, (b) the expiration of the last to expire valid claim in Syros' patent rights, the jointly-owned patent rights or certain other specified patent rights that cover such licensed product in such country, and (c) the expiration of regulatory exclusivity for such licensed product in such country.

Either party may terminate the collaboration agreement for the other party's uncured material breach or insolvency, and in certain other specified circumstances, subject to specified notice and cure periods. GBT may unilaterally terminate the collaboration agreement in its entirety, for any or no reason, upon nine-months' prior written notice to Syros if such notice is delivered during the research term, or 90 days' prior written notice to Syros if such notice is delivered after the expiration or termination of the research term. Upon the termination of the collaboration agreement in certain specified cases (including any unilateral termination by GBT), GBT has agreed to grant Syros, effective as of the effective date of such termination, a worldwide, exclusive, royalty-bearing license, with the right to grant sublicenses, under specified IP necessary or useful for the development, manufacture or commercialization of licensed compounds and products for any and all uses, as well as engage in other customary technology transfer activities.

Incyte Corporation

In January 2018, Syros entered into a target discovery, research collaboration and option agreement with Incyte. Under this agreement, Syros will use its gene control platform to identify novel therapeutic targets with a

focus on myeloproliferative neoplasms, and Incyte has received options to obtain exclusive worldwide rights to IP resulting from the collaboration for the development and commercialization of therapeutic products directed to up to seven validated targets. For each option exercised by Incyte, Incyte will have the exclusive worldwide right to use the licensed IP to develop and commercialize therapeutic products that modulate the target as to which the option was exercised.

Under the terms of the collaboration agreement, Incyte paid Syros $10.0 million in up-front consideration, consisting of $2.5 million in cash and $7.5 million in pre-paid research funding, or the pre-paid research amount. Syros' activities under this agreement are subject to a joint research plan and, subject to certain exceptions, Incyte is responsible for funding Syros' activities under the research plan, including amounts in excess of the pre-paid research amount. Under the collaboration agreement, Syros is required to use commercially reasonable efforts to conduct the research services over a period commencing on the effective date of the collaboration agreement and ending upon the completion of specified target validation activities.

Syros is eligible to receive target selection milestone payments and option exercise fees of up to an aggregate of $54.0 million if Incyte selects the maximum number of targets for validation and exercises its options to obtain exclusive rights to collaboration IP for therapeutic products directed to all seven validated targets. Should any therapeutic product be developed by Incyte against a target as to which Incyte has exercised its option to obtain exclusive rights to collaboration IP, Syros will be eligible to receive milestone payments and, if approved and commercialized, royalty payments from Incyte. For each of the seven validated targets, Syros would become eligible to receive from Incyte a total of up to $50.0 million in development and regulatory milestone payments. If products arising from the collaboration are approved, Syros would become eligible to receive from Incyte, for each validated target, a total of up to $65.0 million in commercial milestone payments. Upon approval and commercialization of any therapeutic product resulting from the collaboration, Syros would become eligible to receive low single-digit royalties on net sales of such product.

The term of the collaboration agreement with Incyte will, unless terminated by a party early, expire when all royalty obligations for products arising from the collaboration expire. The agreement may be terminated by Incyte for convenience on sixty (60) days' prior written notice to Syros, or by Syros on thirty (30) days' written notice in the event Incyte or one of its affiliates or sublicensees challenges the validity or enforceability of certain patent rights controlled by Syros. The agreement may also be terminated by either of the parties on thirty (30) days' prior written notice in the event of an uncured material breach of the agreement by the other party or immediately in the case of certain bankruptcy events. If the collaboration agreement is terminated by Incyte for material breach, then Syros must refund any unexpended pre-paid research amount. Incyte's right to terminate for convenience and each party's right to terminate for uncured material breach may be exercised either with respect to the agreement in its entirety or, as applicable, in relation to the relevant validated target and associated therapeutic products.

In connection with the collaboration agreement, Syros sold 793,021 shares of Syros common stock to Incyte for an aggregate purchase price of $10.0 million in cash, or $12.61 per share, in a private placement. In addition, from the closing of this sale until the earlier of the second anniversary of such closing or the expiration or termination of the collaboration agreement, Syros has granted to Incyte the right to purchase up to its *pro rata* share of the securities offered in certain subsequent offerings of Syros common stock or common stock equivalents, subject to the terms and conditions set forth in the stock purchase agreement. In February 2018, Syros sold 144,505 additional shares of Syros common stock to Incyte at a price of $9.55 per share, resulting in proceeds to Syros of $1.4 million.

TMRC

In September 2015 Syros entered into, and in April 2016 Syros amended and restated, a license agreement with TMRC, which Syros refers to as the TMRC license agreement, pursuant to which TMRC granted Syros an exclusive license, with the right to sublicense, under TMRC patent rights, data, regulatory filings and other IP for

the North American and European development and commercialization of tamibarotene products for the treatment of human cancer indications. In January 2021, Syros further amended the TMRC license agreement to expand the territory under which Syros is licensed to include Central and South America, Australia, Israel, and Russia. Under the TMRC license agreement, Syros has agreed to pay TMRC single-digit royalties based on net sales if TMRC's patents cover its product and low single-digit royalties based on net sales with respect to know-how licensed by TMRC during a predefined royalty term, and to make payments to TMRC upon meeting specified clinical and regulatory milestones in an aggregate amount of approximately $13.0 million per indication. Syros paid to TMRC $1.0 million in the third quarter of 2016 upon successful dosing of the first patient in Syros' Phase 2 clinical trial of tamibarotene, $2.0 million in the second quarter of 2021 upon the successful dosing of the first patient in Syros' Phase 3 clinical trial of tamibarotene in MDS patients, and $1.0 million in the third quarter of 2021 upon the successful dosing of the first patient in Syros' Phase 2 clinical trial of tamibarotene in AML patients. Under the TMRC license agreement, Syros must use commercially reasonable efforts to, among other things, commence development activities within one year, to develop tamibarotene in at least one cancer indication, and, following marketing approval, to market the product. The license agreement expires on the expiration of the subject patent rights or 15 years after the date of first commercial sale of product, whichever is later. The TMRC license agreement may be terminated by either party if the other party is in breach and the breach is not cured within a required amount of time or if the other party is in bankruptcy. If Syros has reason to do so, it may also terminate the agreement after one year from the original effective date at its sole discretion.

In connection with the TMRC license agreement, in April 2016 Syros entered into a supply management agreement with TMRC. Pursuant to the supply management agreement, Syros and TMRC have agreed to establish a joint manufacturing committee to discuss strategy for supply of tamibarotene. In addition, Syros has agreed to pay TMRC a fee for each kilogram of tamibarotene Syros procures for clinical trial or commercial use. The supply management agreement terminates on the expiration or termination of the TMRC license agreement, and Syros' obligation to pay these fees survives the termination of the supply management agreement. In April 2016, Syros also entered into a standby license with TMRC and Toko, the owner of the patent rights licensed to TMRC from which Syros' license agreement with TMRC derives its rights, pursuant to which Syros obtains a standby license from Toko if Toko's license with TMRC is terminated.

Syros has developed its own patent portfolio related to tamibarotene, which generally discloses methods of identifying and treating patients who are sensitive to RARα agonists, including tamibarotene, based on the expression of certain biomarkers, including RARA. In January 2021, Syros entered into a license agreement with TMRC, which Syros refers to as the biomarker license agreement, under which Syros granted TMRC an exclusive license, with the right to grant sublicenses, under these patent rights and certain know-how that it controls related to the RARA biomarker for the development and commercialization of tamibarotene for human cancer indications in Japan, China, South Korea, India and Taiwan. Under the biomarker license agreement, TMRC will be obligated to pay Syros a low single-digit royalty on net sales of tamibarotene in these territories during a pre-specified royalty term to the extent the manufacture, use or sale of tamibarotene infringes a valid claim of the patent rights or is developed using know-how licensed to TMRC under the biomarker license agreement.

Qiagen

In March 2022, Syros entered into a master collaboration agreement and a project schedule with Qiagen. Pursuant to this agreement, Qiagen has agreed to develop and commercialize an assay as a companion diagnostic test to determine the expression level of Syros' proprietary RARA biomarker for use with tamibarotene in newly diagnosed HR-MDS patients.

Under the agreement, Qiagen is responsible for developing, and obtaining and maintaining regulatory approvals for the companion diagnostic test in the United States and, at Syros' request and subject to the negotiation of mutually agreed payments, in the following additional markets: Canada, the United Kingdom, the member states

of the EEA, Switzerland, Mexico, Australia, Russia, Israel and Brazil. In addition, Qiagen has agreed to use commercially reasonable efforts to manufacture the companion diagnostic test and, upon negotiation of mutually agreed terms, to make the companion diagnostic test commercially available in the United States, the additional markets described above, and such other countries as the parties may mutually agree. Qiagen has agreed to undertake specified actions to minimize the risk of an inability of supply occurring for the manufacture of the companion diagnostic test.

Subject to the terms of the agreement and upon achievement of specified technical and development milestones, Syros is obligated to pay Qiagen up to a high single-digit million dollar payment in the agreement over the term of the initial project schedule in connection with developing and obtaining and maintaining regulatory approval for the companion diagnostic in the United States. In addition, Syros must reimburse Qiagen for certain pass-through costs. These amounts are subject to adjustment if the parties determine that changes in the scope of the development program are required. In addition, Qiagen will retain all proceeds from the commercialization of the companion diagnostic test. Syros has no financial obligations to Qiagen under the agreement on the commercialization of tamibarotene.

The initial term of the agreement expires on the later to occur of (i) the fifth anniversary of the agreement and (ii) the expiration or termination of all project schedules executed under the agreement. Thereafter, the agreement automatically renews for additional periods of one year. Syros may terminate the agreement or a project schedule executed under the agreement for convenience upon 90 day's prior written notice to Qiagen. Either party may terminate the agreement or any project schedule executed under the agreement, as applicable, upon a material breach of the other party that is not cured within 30 days after written notice of such breach, immediately upon the bankruptcy or insolvency of the other party, or in certain other circumstances described in the agreement. In the event that Syros terminates the agreement for reasons other than Qiagen's material breach or bankruptcy, Syros will be obligated to pay Qiagen wind-down and other costs and other final payments.

Competition

The pharmaceutical and biotechnology industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. While Syros believes that its technology, development experience, and scientific knowledge provide Syros with competitive advantages, it faces potential competition from many different sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions and governmental agencies and public and private research institutions. Any product candidates that Syros successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future.

Syros competes in the segments of the pharmaceutical, biotechnology and other related markets that address gene control and cancer. There are other companies working to develop therapies in the fields of gene control and cancer. These companies include divisions of large pharmaceutical companies and biotechnology companies of various sizes.

The most common methods of treating patients with cancer are surgery, radiation and drug therapy, including chemotherapy, hormone therapy and targeted drug therapy. There are a variety of available drug therapies marketed for cancer. In many cases, these drugs are administered in combination to enhance efficacy. While Syros' product candidates may compete with many existing drug and other therapies, they may also be used in combination with or as an adjunct to these therapies. Some of the currently approved drug therapies are branded and subject to patent protection, and others are available on a generic basis. Many of these approved drugs are well-established therapies and are widely accepted by physicians, patients andthird-party payors. In general, although there has been considerable progress over the past few decades in the treatment of cancer and the currently marketed therapies provide benefits to many patients, these therapies all are limited to some extent in their efficacy and frequency of adverse events. As a result, the level of morbidity and mortality from cancer remains high.

In addition to currently marketed therapies, there are also a number of medicines in late stage clinical development to treat cancer. These medicines in development may provide efficacy, safety, convenience and other benefits that are not provided by currently marketed therapies. As a result, they may provide significant competition for any of Syros' product candidates for which it obtains market approval.

Many of Syros' competitors may have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved medicines than Syros does. Mergers and acquisitions in the pharmaceutical, biotechnology and diagnostic industries may result in even more resources being concentrated among a smaller number of Syros competitors. These competitors also compete with Syros in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, Syros' programs. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies.

The key competitive factors affecting the success of all of Syros' product candidates, if approved, are likely to be their efficacy, safety, convenience, price, the effectiveness of companion diagnostics in guiding the use of related therapeutics, the level of generic competition and the availability of reimbursement from government and other third-party payors.

Syros' commercial opportunity could be reduced or eliminated if its competitors develop and commercialize medicines that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any medicines that Syros may develop. Syros' competitors also may obtain FDA or other regulatory approval for their medicines more rapidly than Syros may obtain approval for its, which could result in Syros' competitors establishing a strong market position before Syros is able to enter the market. In addition, Syros' ability to compete may be affected in many cases by insurers or other third-party payors seeking to encourage the use of generic medicines. There are many generic medicines currently on the market for the indications that Syros is pursuing, and additional medicines are expected to become available on a generic basis over the coming years. If Syros' therapeutic product candidates are approved, Syros expects that they will be priced at a significant premium over competitive generic medicines.

If the product candidates of Syros' priority programs are approved for the indications for which Syros is currently planning clinical trials, they will compete with the drugs discussed below and will likely compete with other drugs currently in development.

Tamibarotene

Syros is developing tamibarotene, its RARα agonist, for patients with AML and MDS. Syros is selecting patients for its clinical trials based onhigh-levels of RARα as measured by its proprietary RARA biomarker. Syros is aware of several new drugs approved by the FDA since 2018 for the treatment of newly diagnosed AML or patient subsets within newly diagnosed AML (including ivosidenib, venetoclax, and glasdegib), and one new drug approved by the FDA in 2020 for the treatment of MDS or patient subsets within MDS (decitabine/cedazuridine). Tamibarotene may also face competition from other agents currently in clinical development for AML and MDS, including those in late-stage development from Gilead Sciences, Inc., Abbvie Inc., Novartis AG, Astex Pharmaceuticals, Inc., and Pfizer Inc. Syros is not aware of any selective RARα agonist programs that are in active clinical development.

SY-2101

Syros is developing SY-2101, a novel oral form of ATO, in patients with newly diagnosed APL.SY-2101 may face competition from Trisenox® or any of the generic forms of Trisenox, an intravenously administered ATO product approved by the FDA for the treatment of APL. Syros is also aware of a traditional Chinese medicine

(TCM)-based formulation of oral arsenic commercially available in China. In addition, Syros is aware of an oral formulation of ATO in clinical development by Phebra, an Australian based specialty pharmaceutical group. Phebra has entered into an agreement with Medsenic SAS, a European biopharmaceutical company, for the investigation of their oral ATO compound for the treatment of autoimmune diseases. Syros is also aware of an oral formulation of ATO being studied in an academic setting in Hong Kong.

SY-5609

Syros is conducting a Phase 1 clinical trial of SY-5609 in patients with select advanced solid tumors. Syros is aware of selective CDK7 inhibitors being developed in early clinical trials by Carrick Therapeutics Ltd. and Exelixis, Inc., and three other selective CDK7 inhibitor programs that Syros believes are in preclinical development from Qurient Co. Ltd., Yungjin Pharma Co., Ltd., and The Translational Genomics Research Institute, and a collaboration between Exscientia Ltd. and GT Apeiron Therapeutics Ltd. focused on developing novel CDK inhibitors, including selective CDK7 inhibitors. SY-5609 may face competition from these CDK7 inhibitors. There is also significant competition from products with mechanisms other than CDK7 inhibition in pancreatic cancer and BRAF-mutant colorectal cancer, the disease areas where Syros is currently focusing its development of SY-5609.

Government Regulation and Product Approvals

Government authorities in the United States, at the federal, state and local level, and in other countries and jurisdictions such as the European Union extensively regulate, among other things, the research, development, testing, manufacture, pricing, quality control, approval, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, post-approval monitoring and reporting, and import and export of biopharmaceutical products. The processes for obtaining marketing approvals in the United States and in foreign countries and jurisdictions, along with compliance with applicable statutes and regulations and other regulatory authorities, require the expenditure of substantial time and financial resources.

Approval and Regulation of Drugs in the United States

In the United States, drug products are approved and regulated under the FDCA and applicable implementing regulations and guidance. A company, institution or organization which takes responsibility for the initiation and management of a clinical development program for such products, and for their regulatory approval, is typically referred to as a sponsor. The failure of a sponsor to comply with the applicable regulatory requirements at any time during the product development process may result in delays to the conduct of a study, regulatory review and approval and/or administrative or judicial sanctions.

Specifically, a sponsor seeking approval to market and distribute a new drug in the United States generally must satisfactorily complete each of the following steps before the product candidate will be approved by the FDA:

- preclinical testing including laboratory tests, animal studies and formulation studies, which must be performed in accordance with the FDA's good laboratory practice, or GLP, regulations and standards;
- design of a clinical protocol and submission to the FDA of an IND for human clinical testing, which must become effective before human clinical trials may begin;
- approval by an independent IRB representing each clinical site before each clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trials to establish the safety, potency and purity of the product candidate for each proposed indication, in accordance with current good clinical practices, or GCP;
- preparation and submission to the FDA of an NDA for a drug product which includes not only the results of the clinical trials, but also, detailed information on the chemistry, manufacture and quality controls for the product candidate and proposed labelling for one or more proposed indication(s);

- review of the product candidate by an FDA advisory committee, where appropriate or if applicable;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities, including those of third parties, at which the product candidate or components thereof are manufactured to assess compliance with cGMP requirements and to assure that the facilities, methods and controls are adequate to preserve the product's identity, strength, quality and purity;
- satisfactory completion of any FDA audits of the non-clinical and clinical trial sites to assure compliance with GCP and the integrity of clinical data in support of the NDA;
- payment of user fees and securing FDA approval of the NDA to allow marketing of the new drug product; and
- compliance with any post-approval requirements, including the potential requirement to implement a REMS and the potential requirement to conduct any post-approval studies required by the FDA.

Preclinical Studies

Before a sponsor begins testing a product candidate with potential therapeutic value in humans, the product candidate enters the preclinical testing stage. Preclinical tests include laboratory evaluations of product chemistry, formulation and stability, as well as other studies to evaluate, among other things, the toxicity of the product candidate. The conduct of the preclinical tests and formulation of the compounds for testing must comply with federal regulations and requirements, including GLP regulations and standards and the United States Department of Agriculture's Animal Welfare Act, if applicable. Some long-term preclinical testing, such as animal tests of reproductive adverse events and carcinogenicity, and long-term toxicity studies, may continue after the IND is submitted.

The IND and IRB Processes

An IND is a request for FDA authorization to administer such investigational product to humans. Such authorization must be secured prior to interstate shipment and administration of any product candidate that is not the subject of an approved NDA. In support of a request for an IND, sponsors must submit a protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. In addition, the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical trials, among other things, must be submitted to the FDA as part of an IND. The FDA requires a 30-day waiting period after the filing of each IND before clinical trials may begin. This waiting period is designed to allow the FDA to review the IND to determine whether human research subjects will be exposed to unreasonable health risks. At any time during this 30-day period, or thereafter, the FDA may raise concerns or questions about the conduct of the trials as outlined in the IND and impose a clinical hold or partial clinical hold. In this case, the IND sponsor and the FDA must resolve any outstanding concerns before clinical trials can begin.

Following commencement of a clinical trial under an IND, the FDA may also place a clinical hold or partial clinical hold on that trial. A clinical hold is an order issued by the FDA to the sponsor to delay a proposed clinical investigation or to suspend an ongoing investigation. A partial clinical hold is a delay or suspension of only part of the clinical work requested under the IND. For example, a specific protocol or part of a protocol is not allowed to proceed, while other protocols may do so. No more than 30 days after imposition of a clinical hold or partial clinical hold, the FDA will provide the sponsor a written explanation of the basis for the hold. Following issuance of a clinical hold or partial clinical hold, an investigation may only resume after the FDA has notified the sponsor that the investigation may proceed. The FDA will base that determination on information provided by the sponsor correcting the deficiencies previously cited or otherwise satisfying the FDA that the investigation can proceed.

A sponsor may choose, but is not required, to conduct a foreign clinical study under an IND. When a foreign clinical study is conducted under an IND, all FDA IND requirements must be met unless waived. When a foreign

clinical study is not conducted under an IND, the sponsor must ensure that the study complies with certain regulatory requirements of the FDA in order to use the study as support for an IND or application for marketing approval. The FDA's regulations are intended to help ensure the protection of human subjects enrolled in non-IND foreign clinical studies, as well as the quality and integrity of the resulting data. They further help ensure that non-IND foreign studies are conducted in a manner comparable to that required for IND studies.

In addition to the foregoing IND requirements, an IRB representing each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution, and the IRB must conduct continuing review and reapprove the study at least annually. The IRB must review and approve, among other things, the study protocol and informed consent information to be provided to study subjects. An IRB must operate in compliance with FDA regulations. An IRB can suspend or terminate approval of a clinical trial at its institution, or an institution it represents, if the clinical trial is not being conducted in accordance with the IRB's requirements or if the product candidate has been associated with unexpected serious harm to patients.

Additionally, some trials are overseen by an independent group of qualified experts organized by the trial sponsor, known as a DSMB. This group provides a recommendation as to whether or not a trial may move forward at designated check points based on access that only the group maintains to available data from the study. Suspension or termination of development during any phase of clinical trials can occur if it is determined that the participants or patients are being exposed to an unacceptable health risk. Other reasons for suspension or termination may be made by Syros based on evolving business objectives and/or competitive climate.

Expanded Access to an Investigational Drug for Treatment Use

Expanded access, sometimes called "compassionate use," is the use of investigational new drug products outside of clinical trials to treat patients with serious or immediately life-threatening diseases or conditions when there are no comparable or satisfactory alternative treatment options. The rules and regulations related to expanded access are intended to improve access to investigational drugs for patients who may benefit from investigational therapies. FDA regulations allow access to investigational drugs under an IND by the company or the treating physician for treatment purposes on a case-by-case basis for: individual patients (single-patient IND applications for treatment in emergency settings and non-emergency settings); intermediate-size patient populations; and larger populations for use of the drug under a treatment protocol or Treatment IND Application.

When considering an IND application for expanded access to an investigational product with the purpose of treating a patient or a group of patients, the sponsor and treating physicians or investigators will determine suitability when all of the following criteria apply: patient(s) have a serious or immediately life-threatening disease or condition, and there is no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the disease or condition; the potential patient benefit justifies the potential risks of the treatment and the potential risks are not unreasonable in the context or condition to be treated; and the expanded use of the investigational drug for the requested treatment will not interfere with the initiation, conduct, or completion of clinical investigations that could support marketing approval of the product or otherwise compromise the potential development of the product.

There is no obligation for a sponsor to make its investigational products available for expanded access. Sponsors of one or more investigational drugs for the treatment of a serious disease(s) or condition(s) must, however, make publicly available their policy for evaluating and responding to requests for expanded access for individual patients.

In addition, on May 30, 2018, the Right to Try Act, was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational new drug products that have completed a Phase 1 clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program.

There is no obligation for a drug manufacturer to make its drug products available to eligible patients as a result of the Right to Try Act, but the manufacturer must develop an internal policy and respond to patient requests according to that policy.

Human Clinical Trials in Support of an NDA

Clinical trials involve the administration of the investigational product candidate to human subjects under the supervision of a qualified investigator in accordance with GCP requirements which include, among other things, the requirement that all research subjects provide their informed consent in writing before their participation in any clinical trial. Clinical trials are conducted under written clinical trial protocols detailing, among other things, the objectives of the study, inclusion and exclusion criteria, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated.

Human clinical trials are typically conducted in three sequential phases, but the phases may overlap or be combined. Additional studies may also be required after approval.

Phase 1 clinical trials are initially conducted in a limited population to test the product candidate for safety, including AEs, dose tolerance, absorption, metabolism, distribution, excretion and pharmacodynamics in healthy humans or in patients. During Phase 1 clinical trials, information about the investigational drug product's pharmacokinetics and pharmacological effects may be obtained to permit the design of well-controlled and scientifically valid Phase 2 clinical trials.

Phase 2 clinical trials are generally conducted in a limited patient population to identify possible AEs and safety risks, evaluate the efficacy of the product candidate for specific targeted indications and determine dose tolerance and optimal dosage and dosage schedule. Multiple Phase 2 clinical trials may be conducted by the sponsor to obtain information prior to beginning larger and more costly Phase 3 clinical trials. Phase 2 clinical trials are well controlled, closely monitored and conducted in a limited patient population.

Phase 3 clinical trials proceed if the Phase 2 clinical trials demonstrate that a dose range of the product candidate is potentially effective and has an acceptable safety profile. Phase 3 clinical trials are undertaken within an expanded patient population to further evaluate dosage, provide substantial evidence of clinical efficacy and further test for safety in an expanded and diverse patient population at multiple, geographically dispersed clinical trial sites. A well-controlled, statistically robust Phase 3 clinical trial may be designed to deliver the data that regulatory authorities will use to decide whether to approve, and, if approved, how to appropriately label a drug: such Phase 3 studies are referred to as "pivotal."

In some cases, the FDA may approve an NDA for a product candidate but require the sponsor to conduct additional clinical trials to further assess the product candidate's safety and effectiveness after approval. Such post-approval trials are typically referred to as Phase 4 clinical trials. These studies are used to gain additional experience from the treatment of a larger number of patients in the intended treatment group and to further document a clinical benefit in the case of drugs approved under accelerated approval regulations. Failure to exhibit due diligence with regard to conducting Phase 4 clinical trials could result in withdrawal of approval for products.

In August 2018, the FDA released a draft guidance entitled "Expansion Cohorts: Use in First-In-Human Clinical Trials to Expedite Development of Oncology Drugs and Biologics," which outlines how sponsors can utilize an adaptive trial design in the early stages of oncology product development (i.e., the FIH clinical trial) to compress the traditional three phases of trials into one continuous trial called an expansion cohort trial. Information to support the design of individual expansion cohorts are included in IND applications and assessed by the FDA. Expansion cohort trials can potentially bring efficiency to product development and reduce developmental costs and time. Progress reports detailing the status and a brief description of available results of the clinical trials must be submitted at least annually to the FDA. In addition, IND safety reports must be submitted to the FDA for any

of the following: serious and unexpected suspected adverse reactions; findings from other studies or animal or *in vitro* testing that suggest a significant risk in humans exposed to the product; and any clinically important increase in the case of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. The FDA will typically inspect one or more clinical sites to assure compliance with GCP and the integrity of the clinical data submitted.

Sponsors of clinical trials are required to register and disclose certain clinical trial information on a public registry (clinicaltrials.gov) maintained by the U.S. National Institutes of Health, or NIH. In particular, information related to the product, patient population, phase of investigation, study sites and investigators and other aspects of the clinical trial is made public as part of the registration of the clinical trial. The failure to submit clinical trial information to clinicaltrials.gov, as required, is a prohibited act under the FDCA with violations subject to potential civil monetary penalties of up to $10,000 for each day the violation continues.

Concurrent with clinical trials, companies often complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the investigational drug as well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, must develop methods for testing the identity, strength, quality, purity, and potency of the final drug. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life.

Review and Approval of an NDA

In order to obtain approval to market a drug product in the United States, a marketing application must be submitted to the FDA that provides sufficient data establishing the safety, purity and potency of the proposed drug product for its intended indication. The application includes all relevant data available from pertinent preclinical and clinical trials, together with detailed information relating to the product's chemistry, manufacturing, controls and proposed labeling, among other things. Data can come from company-sponsored clinical trials intended to test the safety and effectiveness of a use of a product, or from a number of alternative sources, including studies initiated by investigators. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety, purity and potency of the drug product to the satisfaction of the FDA.

The NDA is a vehicle through which sponsors formally propose that the FDA approve a new product for marketing and sale in the United States for one or more indications. Every new drug product candidate must be the subject of an approved NDA before it may be commercialized in the United States. Under federal law, the submission of most NDAs is subject to an application user fee, which for federal fiscal year 2022 is $3,117,218 for an application requiring clinical data. The sponsor of an approved NDA is also subject to an annual program fee, which for federal fiscal year 2022 is $369,413. Certain exceptions and waivers are available for some of these fees, such as an exception from the application fee for products with orphan designation and a waiver for certain small businesses.

Following submission of an NDA, the FDA conducts a preliminary review of the application within 60 days of receipt and must inform the sponsor by that time whether the application is sufficiently complete to permit substantive review. If not, the FDA will issue a Refuse to File, or RTF, determination to the sponsor. The FDA may request additional information rather than accept the application for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA has agreed to specified performance goals in the review process of NDAs, but the review process and the Prescription Drug User Fee Act, or PDUFA, goal date may be extended by the FDA for three additional months to consider new information or clarification provided by the sponsor to address an outstanding deficiency identified by the FDA following the original submission.

In connection with its review of an application, the FDA typically will inspect the facility or facilities where the product is or will be manufactured. These pre-approval inspections may cover all facilities associated with an NDA submission, including component manufacturing, finished product manufacturing and control testing laboratories. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP.

In addition, as a condition of approval, the FDA may require a sponsor to develop a REMS. REMS use risk minimization strategies beyond the professional labeling to ensure that the benefits of the product outweigh the potential risks. To determine whether a REMS is needed, the FDA will consider the size of the population likely to use the product, seriousness of the disease, expected benefit of the product, expected duration of treatment, seriousness of known or potential adverse events and whether the product is a new molecular entity.

The FDA may refer an application for a novel product to an advisory committee or explain why such referral was not made. Typically, an advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Fast Track, Breakthrough Therapy and Priority Review

The FDA is authorized to designate certain products for expedited review if they are intended to address an unmet medical need in the treatment of a serious or life-threatening disease or condition. These programs, as applicable to Syros' business, are referred to as fast track designation, breakthrough therapy designation and priority review designation. None of these programs changes the standards for approval but each may help expedite the development or approval process governing product candidates.

Specifically, the FDA may designate a product for Fast Track review if it is intended, whether alone or in combination with one or more other products, for the treatment of a serious or life-threatening disease or condition, and it demonstrates the potential to address unmet medical needs for such a disease or condition. For Fast Track products, sponsors may have greater interactions with the FDA and the FDA may initiate review of sections of a Fast Track product's application before the application is complete. This rolling review may be available if the FDA determines, after preliminary evaluation of clinical data submitted by the sponsor, that a Fast Track product may be effective. The sponsor must also provide, and the FDA must approve, a schedule for the submission of the remaining information and the sponsor must pay applicable user fees. However, the FDA's time period goal for reviewing a Fast Track application does not begin until the last section of the application is submitted. In addition, the Fast Track designation may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

Second, a product may be designated as a Breakthrough Therapy if it is intended, either alone or in combination with one or more other products, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The FDA may take certain actions with respect to Breakthrough Therapies, including holding meetings with the sponsor throughout the development process; providing timely advice to the product sponsor regarding development and approval; involving more senior staff in the review process; assigning a cross-disciplinary project lead for the review team; and taking other steps to design the clinical trials in an efficient manner.

Third, the FDA may designate a product for priority review if it is a product that treats a serious condition and, if approved, would provide a significant improvement in safety or effectiveness. The FDA determines, on a

case-by-case basis, whether the proposed product represents a significant improvement when compared with other available therapies. Significant improvement may be illustrated by evidence of increased effectiveness in the treatment of a condition, elimination or substantial reduction of a treatment-limiting product reaction, documented enhancement of patient compliance that may lead to improvement in serious outcomes, and evidence of safety and effectiveness in a new subpopulation. A priority designation is intended to direct overall attention and resources to the evaluation of such applications, and to shorten the FDA's goal for taking action on a marketing application from ten months to six months.

Accelerated Approval Pathway

The FDA may grant accelerated approval to a product for a serious orlife-threatening condition that provides meaningful therapeutic advantage to patients over existing treatments based upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit. The FDA may also grant accelerated approval for such a condition when the product has an effect on an intermediate clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality, or IMM, and that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity or prevalence of the condition and the availability or lack of alternative treatments. Products granted accelerated approval must meet the same statutory standards for safety and effectiveness as those granted traditional approval.

For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign or other measure that is thought to predict clinical benefit but is not itself a measure of clinical benefit. Surrogate endpoints can often be measured more easily or more rapidly than clinical endpoints. An intermediate clinical endpoint is a measurement of a therapeutic effect that is considered reasonably likely to predict the clinical benefit of a drug, such as an effect on IMM. The FDA has limited experience with accelerated approvals based on intermediate clinical endpoints but has indicated that such endpoints generally may support accelerated approval where the therapeutic effect measured by the endpoint is not itself a clinical benefit and basis for traditional approval, if there is a basis for concluding that the therapeutic effect is reasonably likely to predict the ultimate clinical benefit of a product.

The accelerated approval pathway is most often used in settings in which the course of a disease is long, and an extended period of time is required to measure the intended clinical benefit of a product, even if the effect on the surrogate or intermediate clinical endpoint occurs rapidly. Thus, accelerated approval has been used extensively in the development and approval of products for treatment of a variety of cancers in which the goal of therapy is generally to improve survival or decrease morbidity and the duration of the typical disease course requires lengthy and sometimes large trials to demonstrate a clinical or survival benefit. Thus, the benefit of accelerated approval derives from the potential to receive approval based on surrogate endpoints sooner than possible for trials with clinical or survival endpoints, rather than deriving from any explicit shortening of the FDA approval timeline, as is the case with priority review.

The accelerated approval pathway is usually contingent on a sponsor's agreement to conduct, in a diligent manner, additionalpost-approval confirmatory studies to verify and describe the product's clinical benefit. As a result, a product candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of Phase 4 or post-approval clinical trials to confirm the effect on the clinical endpoint. Failure to conduct required post-approval studies, or confirm a clinical benefit duringpost-marketing studies, would allow the FDA to initiate expedited proceedings to withdraw approval of the product. All promotional materials for product candidates approved under accelerated regulations are subject to prior review by the FDA.

The FDA's Decision on an NDA

On the basis of the FDA's evaluation of the application and accompanying information, including the results of the inspection of the manufacturing facilities, the FDA may issue an approval letter or a complete response letter,

or CRL. A CRL generally outlines the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. If and when those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the NDA, the FDA will issue an approval letter. The FDA has committed to reviewing such resubmissions in two or six months depending on the type of information included. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

An approval letter authorizes commercial marketing of the product with specific prescribing information for each indication. If the FDA approves a new product, it may limit the approved indications for use of the product. The agency may also require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution restrictions or other risk management mechanisms, including REMS, to help ensure that the benefits of the product outweigh the potential risks. REMS can include medication guides, communication plans for health care professionals, and elements to assure safe use, or ETASU. ETASU can include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring and the use of patent registries. The FDA may prevent or limit further marketing of a product based on the results of post-market studies or surveillance programs. After approval, many types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Post-Approval Regulation

If regulatory approval for marketing of a product or new indication for an existing product is obtained, the sponsor will be required to comply with all regular post-approval regulatory requirements as well as any post-approval requirements that the FDA may have imposed as part of the approval process. The sponsor will be required to report, among other things, certain adverse reactions and manufacturing problems to the FDA, provide updated safety and efficacy information and comply with requirements concerning advertising and promotional labeling requirements. Manufacturers and certain of their subcontractors are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with ongoing regulatory requirements, including cGMP regulations, which impose certain procedural and documentation requirements upon manufacturers.

A product may also be subject to official lot release, meaning that the manufacturer is required to perform certain tests on each lot of the product before it is released for distribution. If the product is subject to official release, the manufacturer must submit samples of each lot, together with a release protocol showing a summary of the history of manufacture of the lot and the results of all of the manufacturer's tests performed on the lot, to the FDA. The FDA may in addition perform certain confirmatory tests on lots of some products before releasing the lots for distribution. Finally, the FDA will conduct laboratory research related to the safety, purity, potency and effectiveness of pharmaceutical products.

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending applications or supplements to approved applications, or suspension or revocation of product license approvals;

- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates the marketing, labeling, advertising and promotion of prescription drug products placed on the market. This regulation includes, among other things, standards and regulations for direct-to-consumer advertising, communications regarding unapproved uses, industry-sponsored scientific and educational activities, and promotional activities involving the Internet and social media. Promotional claims about a drug's safety or effectiveness are prohibited before the drug is approved. After approval, a drug product generally may not be promoted for uses that are not approved by the FDA, as reflected in the product's prescribing information. In September 2021, the FDA published final regulations which describe the types of evidence that the agency will consider in determining the intended use of a drug product.

In the United States, health care professionals are generally permitted to prescribe drugs for such uses not described in the drug's labeling, known as off-label uses, because the FDA does not regulate the practice of medicine. However, FDA regulations impose rigorous restrictions on manufacturers' communications, prohibiting the promotion of off-label uses. It may be permissible, under very specific, narrow conditions, for a manufacturer to engage in nonpromotional, non-misleading communication regarding off-label information, such as distributing scientific or medical journal information.

If a company is found to have promoted off-label uses, it may become subject to adverse public relations and administrative and judicial enforcement by the FDA, the DOJ, or the Office of the Inspector General of HHS, as well as state authorities. This could subject a company to a range of penalties that could have a significant commercial impact, including civil and criminal fines and agreements that materially restrict the manner in which a company promotes or distributes drug products. The federal government has levied large civil and criminal fines against companies for alleged improper promotion, and has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed.

Pediatric Studies

Under the Pediatric Research Equity Act of 2003, or PREA, an NDA or supplement thereto must contain data that are adequate to assess the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. Sponsors must also submit pediatric study plans prior to the assessment data. Those plans must contain an outline of the proposed pediatric study or studies the sponsor plans to conduct, including study objectives and design, any deferral or waiver requests and other information required by regulation. The sponsor, the FDA, and the FDA's internal review committee must then review the information submitted, consult with each other and agree upon a final plan. The FDA or the sponsor may request an amendment to the plan at any time.

The FDA Reauthorization Act of 2017 established new requirements to govern certain molecularly targeted cancer indications. Any company that submits an NDA three years after the date of enactment of that statute must submit pediatric assessments with the NDA if the drug is intended for the treatment of an adult cancer and is directed at a molecular target that the FDA determines to be substantially relevant to the growth or progression of a pediatric cancer. The investigation must be designed to yield clinically meaningful pediatric study data regarding the dosing, safety and preliminary efficacy to inform pediatric labeling for the product.

The law now requires the FDA to send a PREANon-Compliance letter to sponsors who have failed to submit their pediatric assessments required under PREA, have failed to seek or obtain a deferral or deferral extension or have failed to request approval for a required pediatric formulation. Unless otherwise required by regulation, the pediatric data requirements do not apply to products with orphan designation, although FDA has recently taken

steps to limit what it considers abuse of this statutory exemption in PREA by announcing that it does not intend to grant any additional orphan drug designations for rare pediatric subpopulations of what is otherwise a common disease.

Orphan Drug Designation and Exclusivity

Under the Orphan Drug Act, the FDA may designate a drug product as an "orphan drug" if it is intended to treat a rare disease or condition, generally meaning that it affects fewer than 200,000 individuals in the United States, or more in cases in which there is no reasonable expectation that the cost of developing and making a product available in the United States for treatment of the disease or condition will be recovered from sales of the product. A company must seek orphan drug designation before submitting an NDA for the product candidate. If the request is granted, the FDA will disclose the identity of the therapeutic agent and its potential use. Orphan drug designation does not shorten the PDUFA goal dates for the regulatory review and approval process, although it does convey certain advantages such as tax benefits and exemption from the PDUFA application fee.

If a product with orphan designation receives the first FDA approval for the disease or condition for which it has such designation or for a select indication or use within the rare disease or condition for which it was designated, the product generally will receive orphan drug exclusivity. Orphan drug exclusivity means that the FDA may not approve another sponsor's marketing application for the same drug for the same condition for seven years, except in certain limited circumstances. Orphan exclusivity does not block the approval of a different product for the same rare disease or condition, nor does it block the approval of the same product for different conditions. If a drug designated as an orphan drug ultimately receives marketing approval for an indication broader than what was designated in its orphan drug application, it may not be entitled to exclusivity.

Orphan drug exclusivity will not bar approval of another product under certain circumstances, including if a subsequent product with the same drug for the same condition is shown to be clinically superior to the approved product on the basis of greater efficacy or safety, or providing a major contribution to patient care, or if the company with orphan drug exclusivity is not able to meet market demand. Under Omnibus legislation signed by former President Trump on December 27, 2020, the requirement for a product to show clinical superiority applies to drug products that received orphan drug designation before enactment of amendments to the FDCA in 2017 but have not yet been approved by the FDA.

In September 2021, the Court of Appeals for the 11th Circuit held that, for the purpose of determining the scope of market exclusivity, the term "same disease or condition" in the statute means the designated "rare disease or condition" and could not be interpreted by the FDA to mean the "indication or use." It is unclear how this court decision will be implemented by the FDA.

Pediatric Exclusivity

Pediatric exclusivity is another type of non-patent marketing exclusivity in the United States and, if granted, provides for the attachment of an additional six months of marketing protection to the term of any existing patent or regulatory exclusivity, including the non-patent and orphan exclusivity. This six-month exclusivity may be granted if an NDA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. The data do not need to show the product to be effective in the pediatric population studied; rather, if the clinical trial is deemed to fairly respond to the FDA's request, the additional protection is granted. If reports of requested pediatric studies are submitted to and accepted by the FDA within the statutory time limits, whatever statutory or regulatory periods of exclusivity or patent protection cover the product are extended by six months.

Section 505(b)(2) NDAs

NDAs for most new drug products are based on two full clinical studies that must contain substantial evidence of the safety and efficacy of the proposed new product for the proposed use. These applications are submitted under

Section 505(b)(1) of the FDCA. The FDA is, however, authorized to approve an alternative type of NDA under Section 505(b)(2) of the FDCA. This type of application allows the sponsor to rely, in part, on the FDA's previous findings of safety and efficacy for a similar product, or published literature. Specifically, Section 505(b)(2) applies to NDAs for a drug for which the investigations made to show whether or not the drug is safe for use and effective in use and relied upon by the sponsor for approval of the application "were not conducted by or for the sponsor and for which the sponsor has not obtained a right of reference or use from the person by or for whom the investigations were conducted."

Thus, Section 505(b)(2) authorizes the FDA to approve an NDA based on safety and effectiveness data that were not developed by the sponsor. NDAs filed under Section 505(b)(2) may provide an alternate and potentially more expeditious pathway to FDA approval for new or improved formulations or new uses of previously approved products. If the 505(b)(2) applicant can establish that reliance on the FDA's previous approval is scientifically appropriate, the applicant may eliminate the need to conduct certain preclinical or clinical studies of the new product. The FDA may also require companies to perform additional studies or measurements to support the change from the approved product. The FDA may then approve the new product candidate for all or some of the label indications for which the referenced drug has been approved, as well as for any new indication sought by the Section 505(b)(2) applicant.

Abbreviated New Drug Applications for Generic Drugs

In 1984, with passage of the Hatch-Waxman Amendments to the FDCA, Congress established an abbreviated regulatory scheme authorizing the FDA to approve generic drugs that are shown to contain the same active ingredients as, and to be bioequivalent to, drugs previously approved by the FDA pursuant to NDAs.

Specifically, in order for an ANDA to be approved, the FDA must find that the generic version is identical to the RLD with respect to the active ingredients, the route of administration, the dosage form, the strength of the drug and the conditions of use of the drug. At the same time, the FDA must also determine that the generic drug is "bioequivalent" to the innovator drug.

Under the Hatch-Waxman Amendments, the FDA may not approve an ANDA until any applicable period ofnon-patent exclusivity for the RLD has expired. The FDCA provides a period of five years of non-patent data exclusivity for a new drug containing an NCE. For the purposes of this provision, an NCE is a drug that contains no active moiety that has previously been approved by the FDA in any other NDA. An active moiety is the molecule or ion responsible for the physiological or pharmacological action of the drug substance. This interpretation of the FDCA by the FDA was confirmed with enactment of the Ensuring Innovation Act in April 2021. In cases where such NCE exclusivity has been granted, an ANDA may not be filed with the FDA until the expiration of five years unless the submission is accompanied by a Paragraph IV certification, in which case the applicant may submit its application four years following the original product approval.

Hatch-Waxman Patent Certification and the 30-Month Stay

Upon approval of an NDA or a supplement thereto, NDA sponsors are required to list with the FDA each patent with claims that cover the applicant's product or an approved method of using the product. Each of the patents listed by the NDA sponsor is published in the Orange Book. The FDA's regulations governing patient listings were largely codified into law with enactment of the Orange Book Modernization Act in January 2021. When an ANDA or 505(b)(2) applicant files its application with the FDA, the applicant is required to certify to the FDA concerning any patents listed for the reference product in the Orange Book, except for patents covering methods of use for which the ANDA applicant is not seeking approval. To the extent that the Section 505(b)(2) applicant is relying on studies conducted for an already approved product, the applicant is required to certify to the FDA concerning any patents listed for the approved product in the Orange Book to the same extent that an ANDA applicant would.

Specifically, the applicant must certify with respect to each patent that:

- the required patent information has not been filed;
- the listed patent has expired;
- the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or
- the listed patent is invalid, unenforceable or will not be infringed by the new product.

A certification that the new product will not infringe the already approved product's listed patents or that such patents are invalid or unenforceable is called a Paragraph IV certification. If the applicant does not challenge the listed patents or indicates that it is not seeking approval of a patented method of use, the application will not be approved until all the listed patents claiming the referenced product have expired (other than method of use patents involving indications for which the applicant is not seeking approval).

To the extent that the Section 505(b)(2) applicant is relying on studies conducted for an already approved product, the applicant is required to certify to the FDA concerning any patents listed for the approved product in the Orange Book to the same extent that an ANDA applicant would. As a result, approval of a Section 505(b)(2) NDA can be stalled until all the listed patents claiming the referenced product have expired, until any non-patent exclusivity, such as exclusivity for obtaining approval of an NCE, listed in the Orange Book for the referenced product has expired, and, in the case of a Paragraph IV certification and subsequent patent infringement suit, until the earlier of 30 months, settlement of the lawsuit or a decision in the infringement case that is favorable to the Section 505(b)(2) applicant.

Patent Term Restoration and Extension

A patent claiming a new drug product may be eligible for a limited patent term extension under the Hatch-Waxman Act, which permits a patent restoration of up to five years for patent term lost during product development and the FDA regulatory review. The restoration period granted on a patent covering a product is typically one-half the time between the effective date of the IND and the submission date of an application, plus the time between the submission date of an application and the ultimate approval date. Patent term restoration cannot be used to extend the remaining term of a patent past a total of 14 years from the product's approval date. Only one patent applicable to an approved product is eligible for the extension, and the application for the extension must be submitted prior to the expiration of the patent in question. A patent that covers multiple products for which approval is sought can only be extended in connection with one of the approvals. The USPTO reviews and approves the application for any patent term extension or restoration in consultation with the FDA.

FDA Approval and Regulation of Companion Diagnostics

If safe and effective use of a therapeutic depends on an *in vitro* diagnostic, then the FDA generally will require approval or clearance of that diagnostic, known as a companion diagnostic, at the same time that the FDA approves the therapeutic product. In August 2014, the FDA issued final guidance clarifying the requirements that will apply to approval of therapeutic products and *in vitro* companion diagnostics. According to the guidance, if the FDA determines that a companion diagnostic device is essential to the safe and effective use of a novel therapeutic product or indication, the FDA generally will not approve the therapeutic product or new therapeutic product indication if the companion diagnostic device is not approved or cleared for that indication.

Under the FDCA, *in vitro* diagnostics, including companion diagnostics, are regulated as medical devices. In the United States, the FDCA and its implementing regulations, and other federal and state statutes and regulations govern, among other things, medical device design and development, preclinical and clinical testing, premarket clearance or approval, registration and listing, manufacturing, labeling, storage, advertising and promotion, sales and distribution, export and import, and post-market surveillance. Unless an exemption applies, diagnostic tests

require marketing clearance or approval from the FDA prior to commercial distribution. The two primary types of FDA marketing authorization applicable to a medical device are premarket notification, also called 510(k) clearance, and PMA approval.

The FDA previously has required in vitro companion diagnostics intended to select the patients who will respond to the product candidate to obtain pre-market approval, or PMA, simultaneously with approval of the therapeutic product candidate. The PMA process, including the gathering of clinical and preclinical data and the submission to and review by the FDA, can take several years or longer. It involves a rigorous premarket review during which the sponsor must prepare and provide the FDA with reasonable assurance of the device's safety and effectiveness and information about the device and its components regarding, among other things, device design, manufacturing and labeling. PMA applications are subject to an application fee. For federal fiscal year 2022, the standard fee is $374,858 and the small business fee is $93,714.

Healthcare Law and Regulation

Health care providers and third-party payors play a primary role in the recommendation and prescription of drug products that are granted marketing approval. Arrangements with providers, consultants, third-party payors and customers are subject to broadly applicable fraud and abuse, anti-kickback, false claims laws, patient privacy laws and regulations and other health care laws and regulations that may constrain business and/or financial arrangements. Restrictions under applicable federal and state health care laws and regulations, include the following:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, paying, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made, in whole or in part, under a federal health care program such as Medicare and Medicaid;
- the federal civil and criminal false claims laws, including the civil False Claims Act, and civil monetary penalties laws, which prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false, fictitious or fraudulent or knowingly making, using or causing to made or used a false record or statement to avoid, decrease or conceal an obligation to pay money to the federal government;
- the FCPA, which prohibits companies and their intermediaries from making, or offering or promising to make, improper payments to non-U.S. officials for the purpose of obtaining or retaining business or otherwise seeking favorable treatment; and
- the federal transparency requirements known as the federal Physician Payments Sunshine Act, which requires certain manufacturers of drugs, devices, biologics and medical supplies to report annually to CMS, within HHS, information related to payments and other transfers of value made by that entity to physicians and teaching hospitals, and other healthcare providers, as well as ownership and investment interests held by physicians, other healthcare providers and their immediate family members.

Further, some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring manufacturers to report information related to payments to physicians and other health care providers or marketing expenditures. Additionally, some state and local laws require the registration of pharmaceutical sales representatives in the jurisdiction. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA thus complicating compliance efforts.

Pharmaceutical Insurance Coverage and Healthcare Reform

In the United States and markets in other countries, patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payors to reimburse all or part of

the associated health care costs. Significant uncertainty exists as to the coverage and reimbursement status of products approved by the FDA and other government authorities. Thus, even if a product candidate is approved, sales of the product will depend, in part, on the extent to which third-party payors, including government health programs in the United States such as Medicare and Medicaid, commercial health insurers and managed care organizations, provide coverage and establish adequate reimbursement levels for, the product. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors are increasingly challenging the prices charged, examining the medical necessity and reviewing the cost-effectiveness of medical products and services and imposing controls to manage costs. Third-party payors may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the approved products for a particular indication.

In order to secure coverage and reimbursement for any product that might be approved for sale, a company may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the product, in addition to the costs required to obtain FDA or other comparable marketing approvals. Nonetheless, product candidates may not be considered medically necessary or cost effective. A decision by a third-party payor not to cover a product could reduce physician utilization once the product is approved and have a material adverse effect on sales, results of operations and financial condition. Additionally, a payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a product does not assure that other payors will also provide coverage and reimbursement for the product, and the level of coverage and reimbursement can differ significantly from payor to payor.

The containment of health care costs also has become a priority of federal, state and foreign governments and the prices of products have been a focus in this effort. Governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit a company's revenue generated from the sale of any approved products. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which a company or its collaborators receive marketing approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

There have been a number of federal and state proposals during the last few years regarding the pricing of pharmaceutical and biopharmaceutical products, limiting coverage and reimbursement for drugs and biologics and other medical products, government control and other changes to the health care system in the United States. In March 2010, President Obama signed into law the ACA. In addition, other legislative changes have been proposed and adopted since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. These changes included aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which went into effect in April 2013 and will remain in effect through 2031 under the CARES Act. The American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices Syros may obtain for any of its product candidates for which it may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used.

Since enactment of the PPACA, there have been, and continue to be, numerous legal challenges and Congressional actions to repeal and replace provisions of the law. For example, with enactment of the Tax Act, which was signed by former President Trump on December 22, 2017, Congress repealed the "individual

mandate." The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, became effective in 2019. On December 14, 2018, a U.S. District Court judge in the Northern District of Texas ruled that the individual mandate portion of the PPACA is an essential and inseverable feature of the PPACA, and therefore because the mandate was repealed as part of the Tax Act, the remaining provisions of the PPACA are invalid as well. The U.S. Supreme Court heard this case on November 10, 2020, and on June 17, 2021, dismissed this action after finding that the plaintiffs do not have standing to challenge the constitutionality of the ACA. Litigation and legislation over the PPACA are likely to continue, with unpredictable and uncertain results.

The Trump Administration also took executive actions to undermine or delay implementation of the ACA, including directing federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. On January 28, 2021, however, President Biden issued a new Executive Order which directs federal agencies to reconsider rules and other policies that limit Americans' access to health care and consider actions that will protect and strengthen that access. Under this Order, federal agencies are directed to re-examine: policies that undermine protections for people with pre-existing conditions, including complications related to COVID-19; demonstrations and waivers under Medicaid and the ACA that may reduce coverage or undermine the programs, including work requirements; policies that undermine the Health Insurance Marketplace or other markets for health insurance; policies that make it more difficult to enroll in Medicaid and the ACA; and policies that reduce affordability of coverage or financial assistance, including for dependents.

The prices of prescription pharmaceuticals have also been the subject of considerable discussion in the United States. There have been several recent U.S. congressional inquiries, as well as proposed and enacted state and federal legislation designed to, among other things, bring more transparency to pharmaceutical pricing, review the relationship between pricing and manufacturer patient programs, and reduce the costs of pharmaceuticals under Medicare and Medicaid. In 2020, President Trump issued several executive orders intended to lower the costs of prescription products and certain provisions in these orders have been incorporated into regulations. These regulations include an interim final rule implementing a most favored nation model for prices that would tie Medicare Part B payments for certain physician-administered pharmaceuticals to the lowest price paid in other economically advanced countries, effective January 1, 2021. That rule, however, has been subject to a nationwide preliminary injunction and, on December 29, 2021, CMS issued a final rule to rescind it. With issuance of this rule, CMS stated that it will explore all options to incorporate value into payments for Medicare Part B pharmaceuticals and improve beneficiaries' access to evidence-based care.

In addition, in October 2020, HHS and the FDA published a final rule allowing states and other entities to develop a SIP to import certain prescription drugs from Canada into the United States. The final rule is currently the subject of ongoing litigation, but at least six states (Vermont, Colorado, Florida, Maine, New Mexico, and New Hampshire) have passed laws allowing for the importation of drugs from Canada with the intent of developing SIPs for review and approval by the FDA. Further, on November 20, 2020, HHS finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The implementation of the rule has been delayed by the Biden administration from January 1, 2022 to January 1, 2023 in response to ongoing litigation. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a new safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers, the implementation of which have also been delayed by the Biden administration until January 1, 2023.

At the state level, legislatures are increasingly passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional

health care authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other health care programs. These measures could reduce the ultimate demand for Syros' products, once approved, or put pressure on its product pricing. Syros expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for Syros' product candidates or additional pricing pressures.

Regulations and Procedures Governing Approval of Medicinal Products in the European Union

In order to market any product outside of the United States, a company must also comply with numerous and varying regulatory requirements of other countries and jurisdictions regarding quality, safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of products. Whether or not it obtains FDA approval for a product, a sponsor will need to obtain the necessary approvals by the comparable non-U.S. regulatory authorities before it can commence clinical trials or marketing of the product in those countries or jurisdictions. Specifically, the process governing approval of medicinal products in the EU, generally follows the same lines as in the United States. It entails satisfactory completion of preclinical studies and adequate and well-controlled clinical trials to establish the safety and efficacy of the product for each proposed indication. It also requires the submission to the relevant competent authorities of a MAA and granting of a marketing authorization by these authorities before the product can be marketed and sold in the EU.

Clinical Trial Approval

On January 31, 2022, the new Clinical Trials Regulation (EU) No 536/2014 became effective in the European Union and replaced the prior Clinical Trials Directive 2001/20/EC. The new regulation aims at simplifying and streamlining the authorization, conduct and transparency of clinical trials in the European Union. Under the new coordinated procedure for the approval of clinical trials, the sponsor of a clinical trial to be conducted in more than one Member State of the European Union, or EU Member State, will only be required to submit a single application for approval. The submission will be made through the Clinical Trials Information System, a new clinical trials portal overseen by the EMA and available to clinical trial sponsors, competent authorities of the EU Member States and the public.

The new regulation did not change the preexisting requirement that a sponsor must obtain prior approval from the competent national authority of the EU Member State in which the clinical trial is to be conducted. If the clinical trial is conducted in different EU Member States, the competent authorities in each of these EU Member States must provide their approval for the conduct of the clinical trial. Furthermore, the sponsor may only start a clinical trial at a specific study site after the applicable ethics committee has issued a favorable opinion.

Parties conducting certain clinical trials must, as in the United States, post clinical trial information in the EU at the EudraCT website: https://eudract.ema.europa.eu.

PRIME Designation in the EU

In March 2016, EMA launched an initiative to facilitate development of product candidates in indications, often rare, for which few or no therapies currently exist. The PRIority MEdicines, or PRIME, scheme is intended to encourage drug development in areas of unmet medical need and provides accelerated assessment of products representing substantial innovation reviewed under the centralized procedure. Products from small- and medium-sized enterprises may qualify for earlier entry into the PRIME scheme than larger companies. Many benefits accrue to sponsors of product candidates with PRIME designation, including but not limited to, early and proactive regulatory dialogue with the EMA, frequent discussions on clinical trial designs and other development program elements, and accelerated marketing authorization application assessment once a dossier has been submitted.

Marketing Authorization

To obtain a marketing authorization for a product under EU regulatory systems, a sponsor must submit an MAA either under a centralized procedure administered by the EMA, or one of the procedures administered by competent authorities in the EU Member States (decentralized procedure, national procedure or mutual recognition procedure). A marketing authorization may be granted only to a sponsor established in the EU. Regulation (EC) No 1901/2006 provides that prior to obtaining a marketing authorization in the EU, sponsors must demonstrate compliance with all measures included in an EMA-approved Paediatric Investigation Plan, or PIP, covering all subsets of the pediatric population, unless the EMA has granted (i) a product-specific waiver, (ii) a class waiver or (iii) a deferral for one or more of the measures included in the PIP.

The centralized procedure provides for the grant of a single marketing authorization by the European Commission that is valid across the EEA (i.e., the EU as well as Iceland, Liechtenstein and Norway). Pursuant to Regulation (EC) No 726/2004, the centralized procedure is compulsory for specific products, including for medicines produced by certain biotechnological processes, products designated as orphan medicinal products, advanced therapy medicinal products, and products with a new active substance indicated for the treatment of certain diseases, including products for the treatment of cancer. For products with a new active substance indicated for the treatment of other diseases and products that are highly innovative or for which a centralized process is in the interest of patients, the centralized procedure may be optional. The centralized procedure may at the request of the sponsor also be used in certain other cases. Syros anticipates that the centralized procedure will be mandatory for the product candidates Syros is developing.

Under the centralized procedure, the CHMP is also responsible for several post-authorization and maintenance activities, such as the assessment of modifications or extensions to an existing marketing authorization. Under the centralized procedure in the EU, the maximum timeframe for the evaluation of an MAA is 210 days, excluding clock stops, when additional information or written or oral explanation is to be provided by the sponsor in response to questions of the CHMP. Accelerated evaluation might be granted by the CHMP in exceptional cases, when a medicinal product is of major interest from the point of view of public health and in particular from the viewpoint of therapeutic innovation. If the CHMP accepts such request, the time limit of 210 days will be reduced to 150 days, but it is possible that the CHMP can revert to the standard time limit for the centralized procedure if it considers that it is no longer appropriate to conduct an accelerated assessment. At the end of this period, the CHMP provides a scientific opinion on whether a marketing authorization should be granted in relation to a medicinal product. Within 15 calendar days of receipt of a final opinion from the CHMP, the European Commission must prepare a draft decision concerning an application for marketing authorization. This draft decision must take the opinion and any relevant provisions of EU law into account. Before arriving at a final decision on an application for centralized authorization of a medicinal product the European Commission must consult the Standing Committee on Medicinal Products for Human Use. The Standing Committee is composed of representatives of the EU Member States and chaired by a non-voting European Commission representative. The European Parliament also has a related "droit de regard." The European Parliament's role is to ensure that the European Commission has not exceeded its powers in deciding to grant or refuse to grant a marketing authorization.

The European Commission may grant a so-called "marketing authorization under exceptional circumstances." Such authorization is intended for products for which the sponsor can demonstrate that it is unable to provide comprehensive data on the efficacy and safety under normal conditions of use, because the indications for which the product in question is intended are encountered so rarely that the sponsor cannot reasonably be expected to provide comprehensive evidence, or in the present state of scientific knowledge, comprehensive information cannot be provided, or it would be contrary to generally accepted principles of medical ethics to collect such information. Consequently, marketing authorization under exceptional circumstances may be granted subject to certain specific obligations, which may include the following:

- the sponsor must complete an identified program of studies within a time period specified by the competent authority, the results of which form the basis of a reassessment of the benefit/risk profile

- the medicinal product in question may be supplied on medical prescription only and may in certain cases be administered only under strict medical supervision, possibly in a hospital and in the case of a radiopharmaceutical, by an authorized person; and
- the package leaflet and any medical information must draw the attention of the medical practitioner to the fact that the particulars available concerning the medicinal product in question are as yet inadequate in certain specified respects.

Regulatory Data Protection in the EU

In the EU, innovative medicinal products approved on the basis of a complete independent data package qualify for eight years of data exclusivity upon marketing authorization and an additional two years of market exclusivity pursuant to Directive 2001/83/EC. Regulation (EC) No 726/2004 repeats this entitlement for medicinal products authorized in accordance the centralized authorization procedure. Data exclusivity prevents sponsors for authorization of generics of these innovative products from referencing the innovator's data to assess a generic (abridged) application for a period of eight years. During an additional two-year period of market exclusivity, a generic marketing authorization application can be submitted and authorized, and the innovator's data may be referenced, but no generic medicinal product can be placed on the EU market until the expiration of the market exclusivity.

Periods of Authorization and Renewals

A marketing authorization has an initial validity for five years in principle. The marketing authorization may be renewed after five years on the basis of a re-evaluation of the risk-benefit balance by the EMA or by the competent authority of the EU Member State. The European Commission or the competent authorities of the EU Member States may decide on justified grounds relating to pharmacovigilance, to proceed with one further five-year period of marketing authorization. Once subsequently definitively renewed, the marketing authorization shall be valid for an unlimited period. Any authorization which is not followed by the actual placing of the medicinal product on the EU market (in case of centralized procedure) or on the market of the authorizing EU Member State within three years after authorization ceases to be valid.

Orphan Drug Designation and Exclusivity

Regulation (EC) No. 141/2000, as implemented by Regulation (EC) No. 847/2000 provides that a drug can be designated as an orphan drug by the European Commission if its sponsor can establish: that the product is intended for the diagnosis, prevention or treatment of (i) a life-threatening or chronically debilitating condition affecting not more than five in ten thousand persons in the EU when the application is made, or (ii) a life-threatening, seriously debilitating or serious and chronic condition in the EU and that without incentives it is unlikely that the marketing of the drug in the EU would generate sufficient return to justify the necessary investment. For either of these conditions, the sponsor must demonstrate that there exists no satisfactory method of diagnosis, prevention or treatment of the condition in question that has been authorized in the EU or, if such method exists, the drug will be of significant benefit to those affected by that condition.

Once authorized, orphan medicinal products are entitled to ten years of market exclusivity in all EU Member States and a range of other benefits during the development and regulatory review process including scientific assistance for study protocols, authorization through the centralized marketing authorization procedure covering all member countries and a reduction or elimination of registration and marketing authorization fees. However, marketing authorization may be granted to a similar medicinal product with the same orphan indication during the ten-year period with the consent of the marketing authorization holder for the original orphan medicinal product or if the manufacturer of the original orphan medicinal product is unable to supply sufficient quantities. Marketing authorization may also be granted to a similar medicinal product with the same orphan indication if this product is safer, more effective or otherwise clinically superior to the original orphan medicinal product. The

period of market exclusivity may, in addition, be reduced to six years if it can be demonstrated based on available evidence that the original orphan medicinal product is sufficiently profitable not to justify maintenance of market exclusivity.

Regulatory Requirements after a Marketing Authorization has been Obtained

In case an authorization for a medicinal product in the EU is obtained, the holder of the marketing authorization is required to comply with a range of requirements applicable to the manufacturing, marketing, promotion and sale of medicinal products. These include compliance with the EU's stringent pharmacovigilance or safety reporting rules must be ensured, and the manufacturing of authorized medicinal products, for which a separate manufacturer's license is mandatory, must also be conducted in strict compliance with the applicable EU laws, regulations and guidance. These requirements include compliance with EU cGMP standards when manufacturing medicinal products and active pharmaceutical ingredients, including the manufacture of active pharmaceutical ingredients outside of the EU with the intention to import the active pharmaceutical ingredients into the EU, and the marketing and promotion of authorized drugs, including industry-sponsored continuing medical education and advertising directed toward the prescribers of drugs and/or the general public, which are strictly regulated in the EU notably under Directive 2001/83EC, as amended, and EU Member State laws. Direct-to-consumer advertising of prescription medicines is prohibited across the EU.

Pricing Decisions for Approved Products

In the EU, pricing and reimbursement schemes vary widely from country to country. Some countries provide that products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost-effectiveness of a particular product candidate to currently available therapies or so-called health technology assessments, in order to obtain reimbursement or pricing approval. For example, the EU provides options for its Member States to restrict the range of products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. Member States may approve a specific price for a product, or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the product on the market. Other Member States allow companies to fix their own prices for products but monitor and control prescription volumes and issue guidance to physicians to limit prescriptions. Recently, many countries in the EU have increased the amount of discounts required on pharmaceuticals and these efforts could continue as countries attempt to manage health care expenditures, especially in light of the severe fiscal and debt crises experienced by many countries in the EU. The downward pressure on health care costs in general, particularly prescription products, has become intense. As a result, increasingly high barriers are being erected to the entry of new products. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various Member States, and parallel trade, i.e., arbitrage between low-priced and high-priced Member States, can further reduce prices. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any products, if approved in those countries.

Approval of Companion Diagnostic Devices

In the European Union, medical devices such as companion diagnostics must comply with the General Safety and Performance Requirements, or SPRs, detailed in Annex I of the EU Medical Devices Regulation (Regulation (EU) 2017/745), or MDR which came into force on May 26, 2021 and replaced the previously applicable EU Medical Devices Directive (Council Directive 93/42/EEC). Compliance with SPRs and additional requirements applicable to companion medical devices are prerequisites to be able to affix the CE Mark of Conformity to medical devices, without which they cannot be marketed or sold. To demonstrate compliance with the SPRs, a manufacturer must undergo a conformity assessment procedure, which varies according to the type of medical device and its classification. The MDR is meant to establish a uniform, transparent, predictable, and sustainable regulatory framework across the EU for medical devices.

Separately, the regulatory authorities in the EU also adopted a new In Vitro Diagnostic Regulation, or IVDR, (EU) 2017/746, which will become effective in May 2022. The new regulation will replace the In Vitro Diagnostics Directive (IVDD) 98/79/EC. Manufacturers wishing to apply to a notified body for a conformity assessment of their in vitro diagnostic medical device have until May 2022 to update their Technical Documentation to meet the requirements and comply with the new, more stringent Regulation. Once applicable, the regulation will, among other things: strengthen the rules on placing devices on the market and reinforce surveillance once they are available; establish explicit provisions on manufacturers' responsibilities for the follow-up of the quality, performance, and safety of devices placed on the market; improve the traceability of medical devices throughout the supply chain to the end-user or patient through a unique identification number; set up a central database to provide patients, healthcare professionals and the public with comprehensive information on products available in the European Union; and strengthen rules for the assessment of certain high-risk devices, such as implants, which may have to undergo an additional check by experts before they are placed on the market.

General Data Protection Regulation

There are significant privacy and data security laws that apply in Europe and other countries. The collection, use, disclosure, transfer, or other processing of personal data, including personal health data, regarding individuals who are located in the EEA and the processing of personal data that takes place in the EEA, is subject to the GDPR, which became effective on May 25, 2018. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, and it imposes heightened requirements on companies that process health and other sensitive data, such as requiring in many situations that a company obtain the consent of the individuals to whom the sensitive personal data relate before processing such data. Examples of obligations imposed by the GDPR on companies processing personal data that fall within the scope of the GDPR include providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, appointing a data protection officer, providing notification of data breaches, and taking certain measures when engaging third-party processors. The GDPR also imposes strict rules on the transfer of personal data to countries outside the EEA, including the U.S., and permits data protection authorities to impose large penalties for violations of the GDPR, including potential fines of up to €20 million or 4% of annual global revenues, whichever is greater. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. Compliance with the GDPR is a rigorous and time-intensive process that may increase the cost of doing business or require companies to change their business practices to ensure full compliance.

There are ongoing concerns about the ability of companies to transfer personal data from the EU to other countries. In July 2020, the Court of Justice of the European Union, or the CJEU, invalidated the EU-U.S. Privacy Shield framework, or Privacy Shield, one of the mechanisms used to legitimize the transfer of personal data from the EEA to the U.S. The CJEU decision also drew into question the long-term viability of an alternative means of data transfer, the standard contractual clauses, for transfers of personal data from the EEA to the U.S. While Syros is not self-certified under the Privacy Shield, this CJEU decision may lead to increased scrutiny on data transfers from the EU to the U.S. generally and increase Syros' costs of compliance with data privacy legislation as well as its costs of negotiating appropriate privacy and security agreements with Syros' vendors and business partners.

On June 23, 2016, the electorate in the U.K. voted in favor of leaving the EU, commonly referred to as Brexit. As with other issues related to Brexit, there are open questions about how personal data will be protected in the U.K. and whether personal information can transfer from the EU to the U.K. Following the withdrawal of the U.K. from the EU, the U.K. Data Protection Act 2018 applies to the processing of personal data that takes place in the U.K. and includes parallel obligations to those set forth by the GDPR. While the Data Protection Act of 2018 in the U.K. that "implements" and complements the GDPR has achieved Royal Assent on May 23, 2018 and is now effective in the U.K., it is unclear whether transfer of data from the EEA to the U.K. will remain lawful under the

GDPR. The U.K. government has already determined that it considers all European Union 27 and EEA member states to be adequate for the purposes of data protection, ensuring that data flows from the U.K. to the EU/EEA remain unaffected. In addition, a recent decision from the European Commission appears to deem the U.K. as being "essentially adequate" for purposes of data transfer from the EU to the U.K., although this decision may be re-evaluated in the future.

Beyond the GDPR, there are privacy and data security laws in a growing number of countries around the world. While many loosely follow the GDPR as a model, other laws contain different or conflicting provisions. These laws will impact Syros' ability to conduct its business activities, including both its clinical trials and any eventual sale and distribution of commercial products.

Sales and Marketing

Syros holds North American, European, Central and South American, Australian, Israeli and Russian commercialization rights to tamibarotene for all cancer indications, and worldwide rights to SY-2101 and SY-5609 and all of its other preclinical programs, other than Syros' sickle cell disease program in which it is collaborating with GBT, for all potential indications. With respect to Syros' sickle cell disease program, GBT has the option to obtain exclusive commercialization rights to products containing compounds arising out of the collaboration for all uses. If GBT exercises its option, Syros has a co-promotion right in the United States with respect to the first such product.

Subject to receiving marketing approval, Syros intends to build a focused sales and marketing organization in the United States and potentially in Europe to sell its products. Syros believes that such an organization will be able to address the community of physicians who are key specialists in treating the patient populations for which its product candidates are being developed. Syros also plans to build a marketing and sales management organization to create and implement marketing strategies for any products that it markets through its own sales organization and to oversee and support Syros' sales force. The responsibilities of the marketing organization would include developing educational initiatives with respect to approved products and establishing relationships with researchers and practitioners in relevant fields of medicine.

Where appropriate, Syros may elect in the future to utilize strategic partners, distributors or contract sales forces to assist in the commercialization of Syros' products. In certain instances, Syros may consider building its own commercial infrastructure.

Manufacturing

Syros does not currently own or operate manufacturing facilities for the production of clinical or commercial quantities of its product candidates. Although Syros intends to rely on third-party contract manufacturers to produce its product candidates and any products it may develop in the future, Syros has recruited personnel with experience to manage these third-party contract manufacturers.

Employees

As of June 30, 2022, Syros had 128 full-time employees, including 58 employees with M.D., Ph.D. or Pharm.D. degrees. Of these full-time employees, 102 employees are engaged in research and development activities and 26 employees are engaged in general and administrative activities. During the year ended December 31, 2021, Syros hired 52 new employees, of whom 40 are engaged in research and development activities and 12 are engaged in general and administrative activities. None of Syros' employees is represented by a labor union or covered by a collective bargaining agreement. Syros conducts an employee engagement survey every year and, during the year ended December 31, 2021, Syros also conducted several additional surveys to assess employee well-being and productivity in light of the COVID-19 pandemic. Based on the results of these surveys, Syros considers its relationship with its employees to be good. Syros focuses on employee recruiting and attrition rates and its progress against equity, diversity, and inclusion goals as key human capital measures in managing its business.

Corporate Information

Syros was incorporated under the laws of the State of Delaware on November 9, 2011 under the name LS22, Inc. Syros changed its name to Syros Pharmaceuticals, Inc. on August 15, 2012.

Information Available on the Internet

Syros' Internet website address is *www.syros.com*. The information contained on, or that can be accessed through, its website is not a part of or incorporated by reference in this joint proxy statement/prospectus. Syros has included its website address in this in this joint proxy statement/prospectus solely as an inactive textual reference. Syros makes available free of charge through Syros' website its Annual Report, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and amendments to those reports filed or furnished pursuant to Sections 13(a) and 15(d) of the Exchange Act. Syros makes these reports available through the "SEC Filings" section of its website as soon as reasonably practicable after it electronically files such reports with, or furnish such reports to, the SEC. Syros also makes available, free of charge on its website, the reports filed with the SEC by its executive officers, directors and 10% stockholders pursuant to Section 16 under the Exchange Act as soon as reasonably practicable after copies of those filings are provided to Syros by those persons. You can review Syros' electronically filed reports and other information that Syros files with the SEC on the SEC's website at *http://www.sec.gov*.

Properties

Syros currently occupies approximately 52,859 rentable square feet of office and laboratory space in Cambridge, Massachusetts under a lease that expires in February 2030 with an option to extend the lease term for 10 additional years. Syros believes that its office and laboratory space is sufficient to meet its current needs and that suitable additional space will be available as and when needed.

Executive Summary of Our Business

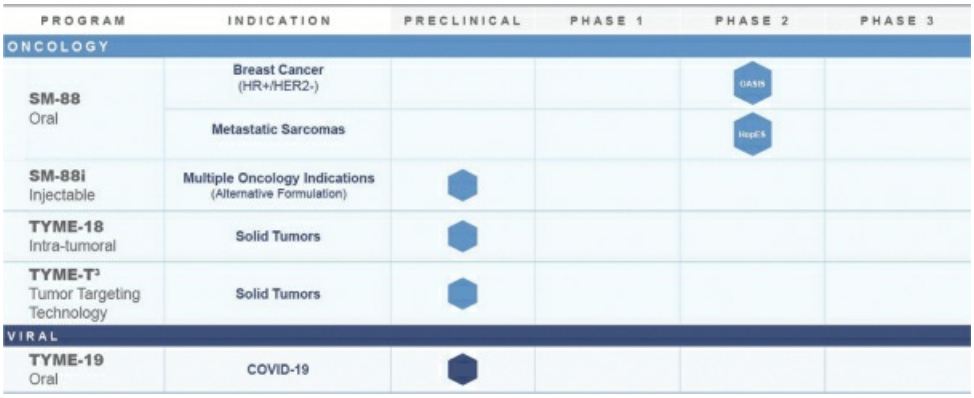
Tyme is an emerging biotechnology company developing cancer metabolism-based therapies, or CMBTs, that are intended to be effective across a broad range of solid tumors and hematologic cancers, while also maintaining patients' quality of life through relatively low toxicity profiles. Unlike targeted therapies that attempt to regulate specific mutations within cancer, Tyme's therapeutic approach is designed to take advantage of a cancer cell's innate metabolic requirements to cause cancer cell death.

Tyme has been focused on developing its novel compound,SM-88, as well as further evaluating its preclinical pipeline of novel CMBT™ programs, and TYME-19 as a potential therapeutic for SARSCoV-2 diseases. Tyme believes that early clinical results demonstrated bySM-88 in multiple advanced cancers, including breast, sarcomas, pancreatic, and prostate, reinforce the potential of its emerging CMBT™ pipeline.

Exploration of Strategic Options and Diversification

On March 29, 2022, Tyme announced that Tyme's board of directors had decided to explore potential strategic options to and engaged outside financial and legal advisors to assist with that process. The Strategic Planning Committee of Tyme's board of directors, which is led by Tyme's Board Member Timothy C. Tyson, who possesses over 35 years of biotechnology and pharmaceutical industry experience, including multiple M&A transactions, is acting as Transaction Committee in connection with this process. On July 3, 2022, Tyme entered into the Merger Agreement with Syros and Merger Sub. Upon the terms and subject to the conditions set forth in the Merger Agreement, Merger Sub will merge with and into Tyme, with Tyme continuing as the surviving entity and a wholly owned subsidiary of Syros. At the effective time of the merger, or the effective time, each share of common stock of Tyme, par value $0.0001 per share, or the Tyme Common Stock, issued and outstanding immediately prior to the effective time will be converted into the right to receive a number of shares of fully paid and non-assessable shares of common stock of Syros, par value $0.001 per share, or the Syros Common Stock, equal to the Exchange Ratio (as defined in the Merger Agreement). The completion of the Merger is subject to the satisfaction or waiver of certain closing conditions, including the adoption of the Merger Agreement by holders of a majority of the outstanding shares of Tyme Common Stock and by holders of a majority of the outstanding shares of Syros Common Stock. If the Merger does not close and Tyme remains an independent company, it may choose to change its strategy, including without limitation to close down its trials and cease operations.

Tyme's Pipeline



Ongoing Studies

OASIS (Metastatic HR+/HER2- Breast Cancer After CDK4/6 Inhibitors)

In June 2021, Tyme announced an agreement with Georgetown University to support a Phase II trial for SM-88 in patients with metastatic breast cancer who have HR+/HER2-. This represents approximately 68% of the annual breast cancer diagnoses in the US each year. According to estimates from Data Monitor and Syneos Health based on data published in 2020, there are approximately 150,000 metastatic breast cancer diagnoses in the US each year. According to Data Monitor, company reported sales figures, and Syneos Health analyses, the total 2019 U.S. market revenues for drug treatment for metastatic breast cancer were $7.7 billion.

The OASIS trial is an investigator-initiated prospective open-label Phase II trial evaluating the efficacy and safety of SM-88 with MPS for the treatment of metastatic hormone-receptor positive, HER2- breast cancer after treatment with a CDK4/6 inhibitor. This trial is designed as a two-stage trial, enrolling up to 50 patients who have failed or progressed after receiving two hormonal agents and a CDK4/6 inhibitor to receive SM-88 with MPS without additional cancer therapies. The primary endpoint of this trial is ORR, with secondary endpoints including duration of response, or DOR, Clinical Benefit Rate, or CBR, at >24 weeks, progression free survival, or PFS, and safety. The trial is being conducted at Georgetown University at a total of five sites within the Georgetown/MEDSTAR system located in Washington DC, Maryland, and New Jersey. Patient enrollment began in 2021 with the first patient dosed in September. Tyme plans to provide an update on the OASIS breast cancer study during the first half of calendar year 2023.

This trial is being conducted as a follow up to the encouraging anti-tumor efficacy observed from the initial trials of SM-88 in this specific patient sub-group. In the first-in-human, or FIH, study and Compassionate Use Program (each discussed below under “Completed Studies”), several heavily pretreated metastatic HR+/HER2- breast cancer patients displayed tumor responses to SM-88, including several complete responses. This trial is aimed to further explore this signal and will also collect cell-free DNA from patients from different time-points with a goal of better understanding potential biomarkers of response and other aspects of SM-88’s mechanism of action. Tyme has also established an academic collaboration with an investigator at Georgetown University to explore the mechanism of SM-88 and MPS, including models of CDK 4/6 resistance.

HoPES Phase II Trial in sarcoma

In early 2020, the open-label Phase 2 investigator sponsored trial of SM-88 therapy in sarcoma, HoPES, opened. This trial has two cohorts each expecting to enroll 12 patients. The first is SM-88 with MPS as salvage treatment in patients with mixed rare sarcomas, and the other is SM-88 with MPS as maintenance treatment for patients with metastatic Ewing’s sarcoma that had not progressed on prior therapy. The primary objectives are to measure objective response rate, or ORR, and PFS. Secondary objectives include DOR, OS, CBR using Response Evaluation Criteria In Solid Tumors, or RECIST, and incidence of treatment-emergent AEs. The Joseph Ahmed Foundation is sponsoring this trial, which is being conducted by Principal Investigator Dr. Chawla at the Sarcoma Oncology Center in Santa Monica, CA. Tyme anticipates that the trial enrollment will continue through the end of calendar year 2022.

The trial was initiated after anti-tumor efficacy and other clinical benefits were observed in several patients with Ewing’s Sarcoma and other heavily pre-treated sarcomas in the FIH study and Compassionate Use Program (each discussed below under “Completed Studies”). This included objective tumor responses in two Ewing’s sarcoma patients. Upon review of the data, Dr. Chawla approached Tyme with an interest in examining SM-88 in a clinical trial.

Ewing’s Sarcoma is an ultra-rare cancer that can affect adolescents and younger adults, with approximately 200 cases diagnosed in the US per year. Broadly there are over 50 types of sarcomas, totaling about 13,500 new cases diagnosed in the US each year. While there have been some recent developments for certain sarcomas, there remains a high need for additional effective therapies, especially for patients with metastatic disease.

Preclinical Pipeline Programs

SM-88 Mechanism of Action and Biomarker Research

Tyme has begun a comprehensive translational preclinical program. Tyme has engaged Evotec, a leading global research and development company, to aid in the execution of these activities, and Tyme is also incorporating several complementary academic collaborations into this multi-faceted program. The overall goal of these activities is to potentially identify actionable biomarkers of sensitivity and activity to SM-88 in various cancers, complementary combination drugs strategies for SM-88, and other cancer metabolism targets that could benefit from treatment. Additionally, Tyme intends to incorporate liquid and tumor biopsies to future clinical trials to contribute to the biomarker identification. Tyme anticipates this engagement will have several stages, and that it is likely to last through this fiscal year and into future periods.

Georgetown Collaboration—Breast Cancer

In May 2021, Tyme initiated a research collaboration with a research investigator at Georgetown University, to examine the effects of SM-88 in breast cancer. This collaboration is examining the effects of SM-88 and MPS in various breast cancer models in culture and animal models. The project is exploring metabolomics, gene expression analysis, and protein array analysis following SM-88 exposure to characterized cancer cell lines, including cell lines with acquired resistance to CDK4/6 inhibitors.

Mayo Collaboration—Pancreatic Cancer

In March 2021, Tyme expanded its pancreatic cancer research collaboration with Mayo Clinic to performin-depth analysis of pancreatic cancer cell gene expression, epigenetic, and metabolism changes from SM-88 treatment. In addition, the collaborator at Mayo has created and characterized multiple pancreatic cancer organoids that could help in the identification of biomarkers and examine the possible impact SM-88 has on the tumor microenvironment.

SM-88 Injectable

Tyme has been developing an injectable form of SM-88 as an additional potential administration for the therapy. This formulation is a distinct drug substance to oral SM-88, however the active product is ultimately the same as the oral formulation. Tyme is working with Evotec to conduct detailed pharmacokinetics and pharmacodynamics of this agent, as well as comprehensive in vivo xenograft studies in animals to determine the optimal dosing and composition of the product. These studies will also include detailed computational analysis of transcriptional, biological, and immune related markers from these studies in order to identify potential biomarkers that may aid in the direction of eventual clinical development. Tyme anticipates much of this work to be complete in the calendar year 2022. Tyme, working with various contractors, has also begun a manufacturing campaign of Good Manufacturing Packages, or GMP, grade drug product for potential clinical use. Tyme has completed the initial formulation stages of the program and anticipates it would be able to complete this campaign during the first half of calendar year 2023.

TYME-18 and TYME-19

TYME-18 is a CMBT™ compound that is delivered intratumorally. TYME-18 leverages a member of the bile acid family to create a potential treatment for inoperable tumors. Preliminary observations of the local administration of TYME-18, a combination of a proprietary surfactant system and natural sulfonic acid, suggested its potential as an important regulator of energy metabolism that may impede the ability of tumors to increase in size, which, in addition to its lytic functionality, could prove useful in difficult-to-treat cancers Tyme is assessing development priorities to determine if additional advancement of this program is warranted at this time.

TYME-19 is an oral synthetic member of the bile acid family. Tyme also uses bile acids in its anti-cancer drug candidate,TYME-18. Because of its expertise in bile acids and their effects, Tyme was able to identify TYME-19 as a well-characterized bile acid with potential antiviral properties. Bile acids have primarily been used for liver disease; however, like all steroids, they are messenger molecules that modulate a number of diverse critical cellular processes. Bile acids can modulate lipid and glucose metabolism and can remediate dysregulated protein folding, with potentially therapeutic effects on cardiovascular, neurologic, immune, and other metabolic systems. Some agents in this class have also previously shown antiviral properties.

Tyme retained virology experts at Evotec to assess the mechanisms ofTYME-19. Evotec is a global drug development company that has the capability to access the multiple existing and emerging variants of the COVID-19 virus. Tyme and Evotec have tested the ability ofTYME-19 to interrupt the cellular pathways commonly used by viruses to produce viral proteins as well as cellular responses to viral infection that cause local inflammation. Prolonged inflammation from SARS-CoV-2 can lead to some of the severe outcomes experienced by infected patients. Tyme aimed for the work by Evotec to provide Tyme with information that could allowing it to assess the potential path forward for the program. However, with the changes in the demand for COVID-19 therapeutic landscape, and potential capital required to advance the program, Tyme management decided to currently pause additional development of this program.

Tumor Targeting Technology

Tyme has developed a technology, or Tumor Targeting Technology, by which the tyrosine isomer L metyrosine(L-α-methylparatyrosine) can be fused with a second therapeutic agent in a manner that creates a fusion compound that may allow targeted accumulation of the treatment by the cancer cells in a novel manner. Tyme is assessing potential development paths for this technology.

Completed Studies

First in Human Study

The FIH study was the initial clinical trial withSM-88, which began in 2012 and was conducted in 30 actively progressing metastatic cancer patients who had failed or refused all available treatments options. The Phase I study was designed to assess the safety of monotherapy SM-88, although the trial was extended beyond the initial six-week period based on reported treatment efficacy, with several patients remaining on treatment for over 12 months. Patients were given SM-88 with conditioning agents melanin, melanotan II, phenytoin, and sirolimus (these conditioning agents will hereafter be referred to as "M2PS").

The results of the FIH study were published in the journal,*Investigational New Drugs,* in March 2019, including data from the trial's initiation in January 2012 through September 2017. Patients were treated with monotherapy SM-88 and achieved median overall survival, or mOS, of 29.8 months, median PFS of 13 months, and a 33% ORR. The ORR consisted of four CRs and six PRs, based on RECIST. In addition, 57% of patients (17/30) achieved RECIST stable disease, or SD, with a median SD duration of 11 months. Five FIH study patients with metastatic cancer survived for over five years after commencing SM-88 treatment. All FIH study patients improved or maintained Eastern Cooperative Oncology Group Performance Status, or ECOG PS, a measure of quality of life, after initiating SM-88 therapy, and overall survival, or OS, was comparable for patients who entered the trial with ECOG PS ranging from 0 (asymptomatic) to 2 (unable to perform any work-related activities).

Tyme believes that traditional RECIST response criteria, a commonly used clinical endpoint based primarily on computerized tomography images, may not fully reflect the therapeutic benefit from SM-88. This is based in part on the observation in the FIH study where a total of 17 of the 30 patients achieved SD with mOS of 29.0 months. Because Tyme believes many patients on SM-88 experience therapeutic benefit without necessarily achieving a complete response, or CR, or partial response, or PR, under RECIST criteria, Tyme commonly refers to "Clinical Benefit," which includes CR, PR and SD designations.

SM-88 used with M2PS demonstrated a favorable safety profile and was well tolerated. All related AEs forSM-88 were classified as mild or moderate. The most common treatment AEs experienced included hyperpigmentation by 100% of patients (30/30), fatigue by 56.7% of patients (17/30) and pain by 10% of patients (3/30). No dose limiting toxicities were observed.

Compassionate Use Program

In parallel with and following the FIH study, Tyme also allowed advanced cancer patients' access toSM-88 through a compassionate use program under Institutional Review Board, or IRB, supervision (the "Compassionate Use Patients"). In early 2018, Tyme performed a retrospective analysis on 53 Compassionate Use Patients who had available data and received at least six weeks of treatment. These patients had their scans reviewed by independent radiologists to determine response under RECIST, and 75% of these patients (40 of 53) were deemed to have experienced Clinical Benefit, consisting of 8 CRs, 16 PRs and 16 SD designations.

Through these two programs, patients being treated withSM-88 have achieved confirmed responses across 15 different cancer types, including some of the most common and difficult to treat cancers, such as pancreatic, prostate, breast, lung, glioma, ovarian, sarcoma and colon cancer. Based on preliminary data from the FIH study and the Compassionate Use Patients suggesting SM-88 may have broad potential applicability and acceptable toxicity, Tyme believes that SM-88 may ultimately be utilized as a treatment for a wide range of cancers prior to theend-stage setting.

Phase II Prostate Trial

In 2019 Tyme completed our Phase II clinical data forbio-marker recurrent prostate cancer and the final results were published in the peer-reviewed journal, *Investigational New Drugs*, on September 13, 2020.

The Phase II trial of SM-88 in patients with non-metastatic, biochemical-recurrent prostate cancer enrolled 23 patients with rising prostate-specific antigen levels, detectable circulating tumor cells, or CTCs, and no radiographically detectable metastases. The study duration was six months, per the study protocol, although some patients were granted a waiver to remain on treatment for longer periods. Seventy-four percent (74%) of patients (17/23) had previously received androgen deprivation therapy as treatment for prostate cancer. All enrolled patients were given daily oral SM-88 with MPS for the duration of treatment.

Based on data as of September 2019, 100% of patients (23/23) on trial remained free of metastatic progression and 87% of patients (20/23) maintained radiographic progression-free survival, or rPFS, with a median duration of 6.5 months from the initial diagnoses of prostate specific antigen, or PSA, rise. All patients who maintained rPFS also exhibited meaningful reductions in CTCs.

All patients with available CTC results for at least 3 cycles (n=19) achieved a decrease from baseline, with a median decrease of 65.3% at the end of 3 cycles. The median baseline PSA for patients with radiographic progression was 13.4 compared to 5.6 for patients with no radiographic progression (p=0.02). 13% of patients experienced a PSA progression after commencing therapy and 52% of patients (12/23) experienced an improvement in median PSA doubling time, a positive prognostic indicator.

The SM-88 therapy was well tolerated in all patients in the trial. There were no treatment-related severe adverse events, or SAEs. No adverse events resulted in dose delay, discontinuation, or reduction. The majority of Grade 1 adverse events that were deemed possibly or probably related to the SM-88 investigational therapy were gastrointestinal in nature.

TYME-88 Pancreatic Trial Reported Results

In April 2022 Tyme reported on the final results of itsTYME-88-Panc trial, a multicenter, prospective open-label phase II/III randomized clinical trial of oral SM-88 plus MPS in patients with metastatic pancreatic ductal

adenocarcinomam, or mPDAC, who had failed at least one prior line of therapy. (TYME-88-Panc Part 1) Study subjects received either 460 or 920 mg PO daily of SM-88 plus oral MPS. Patients in both arms of the study received the same dose of oral MPS. The primary endpoint of the trial was objective response rate (RECIST 1.1).

On March 12, 2019, the last trial subject was enrolled and as of September 1, 2021, 49 subjects had been randomized to either the 460 (n = 26) or 920 mg (n = 23) dose of SM-88, with 37 subjects deemed evaluable after completing at least one28-day cycle of treatment and having a minimum of 23 days on treatment. Of the evaluable patients, five had failed one prior line of therapy, 18 patients had failed two prior lines and 14 patients had failed three or more prior lines. Twenty of these patients (54.0%) had received FOLFIRINOX in the first line.

The disease control rate, or DCR, OS, and PFS did not differ significantly between the two dose levels. Stable disease was achieved in nine of 37 patients (DCR, 24.3%), and there were no complete or partial responses. In the intent to treat population of 49 patients, the mOS was 3.4 months (95% CI: 2.7- 4.9 months). Those treated in the second line had a mOS of 8.1 months and a median PFS of 3.8 months. Survival was higher for patients with stable disease than those with progressive disease (any line; median OS: 10.6 months compared to 3.9 months; p = 0.01).

Quality of life, as measured by QOL scores as reflected in completed Eastern Cooperative Oncology Group Performance Status, or EORTC, quality of life questionnaires (the EORTC QLQ-C30 questionnaire) was maintained or improved in 24 of 37 evaluable patients (65%) and trended in favor of the 920 mg SM-88 dose (p=ns). The SM-88 with oral MPS was well tolerated; only a single patient (1/49) experienced related grade 3 and 4 SAEs on treatment, which consisted of Grade 3 abdominal pain and Grade 4 hypotension, each of which eventually resolved.

Although Tyme completed and reports the results of Part 1 of this trial, as discussed below under *"—Discontinuing Programs—TYME-88-PANC (Part 2) (third-line Metastatic Pancreatic Cancer)",* Tyme decided to stop enrollment in this trial and has begun the process of closing down the remaining Part 2 of this trial.

Discontinuing Programs

Precision Promise Trial- SM-88 with MPS as 2nd line therapy in metastatic pancreatic cancer

In October 2018 Tyme partnered with PanCAN to studySM-88 in an adaptive randomized Phase II/III trial with registration intent known as Precision Promise[SM]. The objective of Precision Promise is to expedite the study and approval of promising therapies for pancreatic cancer by bringing multiple stakeholders together, including academic, industry and regulatory entities. The trial, began in early 2020, SM-88 (with the conditioning agents MPS) was being studied as monotherapy in a treatment arm for patients who have failed one prior line of chemotherapy.

On January 26, 2022, Tyme announced the discontinuation ofSM-88 with MPS in the Precision Promise trial in mPDAC upon learning from PanCAN, the trial sponsor, that it terminated the arm due to futility compared to the control of standard of care chemotherapy in second-line mPDAC. Based on the information provided by PanCAN, the OS for SM-88 with MPS in monotherapy was lower compared to standard of care chemotherapies with either Gemcitabine and Abraxane or modified FOLFIRINOX. As of March 31, 2022, remaining estimated costs to close out the trial have been expensed.

TYME-88-PANC (Part 2) (third-line Metastatic Pancreatic Cancer)

In fiscal year 2020, Tyme launched its pivotal study forSM-88 in the third-line treatment of pancreatic cancer through an amendment to our ongoing TYME-88-Panc trial (Part 2), with the first patient dosed in the third quarter of the fiscal year. As described previously, theCOVID-19 pandemic significantly impacted enrollment of

this trial, such that it appeared it was likely to complete enrollment in a similar timeline to the second-line Precision Promise pancreatic cancer trial. There was also a higher than expected dropout of patients randomized to the chemotherapy control arm, which could have potentially impacted the interpretative and regulatory utility of the data.

Following the strategic review discussed above, considering, in part, the timeline and regulatory utility for this trial compared to the parallel Precision Promise trial and concentration of investment in this specific cancer, management concluded that it would be best to focus on the second-line Precision Promise trial that offers treatment options to patients earlier in their disease and includes tumor biopsy and biomarker analyses that align with Tyme's overall strategic focus on identifying targeted therapies.

Therefore, Tyme decided to stop enrollment and begin the process of closing down the trial. Patients currently on therapy are allowed to continue treatment until progression or unacceptable toxicity. The closing of this trial is expected to require several months to complete. During the year ended March 31, 2022, Tyme expensed $723,000 of estimated closeout costs. The trial's remaining ongoing expense to Tyme was approximately $400,000 as of March 31, 2022, and such expense is expected to be incurred over the five months following March 31, 2022.

SM-88 Mechanism of Action

SM-88 is an orally administered CMBT that is chemically altered to benon-functional for fundamental tumor cell processes, including protein synthesis. Scientific literature has highlighted that cancer cells can have a significantly higher consumption of certain amino acids compared to healthy cells, and these amino acids are required for cancer cell growth and function. Tyme believes that SM-88, our proprietary modified dysfunctional tyrosine is selectively consumed by cancer cells, and interrupts various cell functions, including protein synthesis, autophagy, and other cellular defenses, that ultimately leads to an oxidative stress-related apoptosis or cell death. Tyme also believes this selective cancer uptake of non-essential amino acids is supported by the current safety profile for SM-88, that has shown minimal observed drug-related SAEs.

SM-88 is currently administered with the conditioning agents MPS. The conditioning agents are administered at doses between 5% and 25% of their FDA, approved doses in non-cancer indications. Tyme believes, based on scientific literature of their respective biologic functions, the physiologic, but sub-therapeutic doses of these agents may augment either the uptake of SM-88 or destabilize cancer cells to increase their susceptibility to SM-88's effects.

As a result of its strategic review, Tyme intends to significantly increase its investment on exploringSM-88's mechanism of action and the current dosing regimen. Tyme has engaged with the global research and development firm, Evotec, to aid in the execution of these activities. Tyme has also expanded its academic pre-clinical research collaborations, including with the Mayo Clinic and Georgetown University. In addition, in Tyme's recently announced OASIS breast cancer trial, the investigators will be collecting cell-free DNA from patients throughout their treatment. Working with a leading diagnostics company, Tyme aims to leverage these samples to better understand response dynamics for SM-88 and to begin to identify potential biomarkers forSM-88 response and sensitivity.

The overall goals of these efforts are to potentially identify patient subsets or disease biomarkers that could be applied to patient selection in future, clinical trials, as well as identify potential optimal combinations with other anti-cancer mechanisms that could aid future clinical development.

Portfolio Development Strategy and Key Product Properties

In the first half of calendar year 2021, Tyme undertook a comprehensive strategic review with the goal of aligning Tyme's development plans with core strategic goals. Key elements of our strategy to achieve this goal were to:

- **Successfully advance the development of SM-88 across a broad range of cancers**.
- **Work towards identifying actionable biomarkers for patient selection or treatment response to SM-88.**
- **Continue to invest in our technology platform and expand the breadth and depth of Tyme's IP portfolio**
- **Build a balanced portfolio of proprietary and partnered programs**.

By leveraging our confidence in SM-88's ability to disrupt key aspects of cancer's unique metabolism, Tyme's intention is to create an innovative therapeutic program with SM-88 that is:

- **Broadly effective across different cancer types**—Because a vast majority of cancers use the same metabolic process, known as the Warburg Effect, Tyme believes that they could likely also have the same susceptibilities to SM-88 treatment, regardless of physiologic origin;
- **Highly specific to cancer**—As supported by the current safety data reported for approximately 180 patients, together with recent advances in radiographic imaging that use tyrosine-based agents to selectively image cancer cells, cancer appears to have a high affinity for tyrosine uptake compared to normal healthy cells;
- **Well-tolerated/ broad therapeutic margin**—Safety findings are available for approximately 180 patients, and only two patients (1%) have reported any drug-related serious adverse events;
- **Suitable for monotherapy or combination therapy**—Although most of Tyme's clinical and compassionate use experience has been in monotherapy, SM-88's differentiated mechanism of action and safety profile may also allow it to be effective in combination with other cancer therapeutics; and
- **Potentially effective treatment for patients who have failed other therapeutic options**—Current cancer therapies are often intended to inhibit or change a particular aspect of cancer's cellular function, known as selective pressure. However, cancers typically develop resistance mechanisms that can make them less responsive to subsequent selective pressure treatments, while at the same time patients also accumulate treatment-related toxicities that can make them ineligible for subsequent therapies. SM-88 is designed to avoid selective pressure and this fundamental limitation of traditional therapies by utilizing cancer's innate metabolic weaknesses to compromise its defenses, leading to cell death through oxidative stress and exposure to the body's natural immune system. We believe this novel mechanism of action may allow SM-88 to be used in traditional treatment-resistant patients and also limit development of resistance.

Some outcomes aimed to be achieved in this pipeline review process were to: 1) assure the current clinical programs were optimally aligned with both the current data for SM-88 and were in areas that were clinically and strategically relevant to the company, 2) identify any key gaps in preclinical or mechanism information that would optimally guide the clinical development of SM-88, and 3) assess the appropriate capital commitment to each of these areas in order to improve the potential to achieve the long-term development and strategic goals of the company. Tyme's recent strategy, including ongoing studies, the Preclinical Pipeline Program and diversification efforts, was developed based on the key takeaways from the strategic review, as well as on subsequent developments.

Intellectual Property

Tyme will strive to protect and enhance its proprietary technology, inventions and improvements that are commercially important to the development of its business, including through seeking, maintaining and

defending patent rights (when required), whether developed internally or licensed from third parties. Tyme also intends to rely on trade secrets related to its proprietary technology platform and its know-how, continuing technological innovation and in-licensing opportunities to develop, strengthen and maintain its proprietary position in the fields of cancer and viral infection treatment, which may be important for the development of Tyme's business. Tyme additionally may rely on regulatory protection afforded through data exclusivity, market exclusivity and patent term extensions, where available.

Tyme's commercial success may depend, in part, on its ability to obtain and maintain patent and other proprietary protection for commercially important technology, inventions and know-how related to its business, defend and enforce our patents, preserve the confidentiality of its trade secrets and operate without infringing the valid enforceable patents and proprietary rights of third parties. Tyme's ability to stop third parties from making, using, selling, offering to sell or importing our products may depend on the extent to which it has rights under valid and enforceable licenses, patents or trade secrets that cover these activities. With respect to both Tyme's owned and licensed IP, it cannot be sure that patents will be granted with respect to any of its pending patent applications or with respect to any patent applications filed by Tyme in the future, nor can it be sure that any of its existing patents or any patents that may be granted to Tyme in the future will be commercially useful in protecting its commercial products and methods of manufacturing such products, as well as being held valid if challenged.

Tyme maintains a broad IP portfolio of 270 patent applications granted or pending worldwide as of May 6, 2022. The patents encompass SM-88 as well as inventions that fight cancer and aid in the creation of novel mechanisms to further that effort, and also a new potential treatment of COVID-19. Tyme's policy is to file patent applications to protect technology, inventions and improvements to inventions that are commercially important to the development of our business. Tyme has and will continue to seek U.S. and international patent protection for a variety of technologies, including: pharmaceutical compositions, methods for treating diseases of interest, methods for manufacturing the pharmaceutical compositions and research tools and methods. Tyme also intends to seek patent protection or rely upon trade secret rights to protect other technologies that may be used to discover and validate targets and that may be used to identify and develop novel products. Tyme will also seek protection, in part, through confidentiality and proprietary information agreements.

Tyme believes it has no need to license any technologies for SM-88 to be commercially viable. Tyme believes its Company owns all the IP necessary for SM-88 to perform as intended and to be commercially marketed, once all applicable regulatory requirements have been obtained. Additionally, Tyme believes the drug substances utilized in SM-88 are not covered by any patents that would impede our use of such drug substances.

Tyme also relies on trademark laws to protect our proprietary rights. Tyme's trademark portfolio currently consists of one domestic trademark: CMBT (cancer metabolism-based therapies).

Competition

Tyme's business strategy is intended to effectively position SM-88 and its pipeline for competition with products manufactured by other companies in the highly fragmented and competitive cancer treatment market. Tyme's competition comes from other commercial and research enterprises working in the field of cancer research. This includes pharmaceutical and biotechnology companies, academic institutions, patient advocacy groups and hospitals and government private research institutes around the globe.

Important competitive factors include patient safety, effectiveness,quality-of-life and ease of use of products; price and demonstrated cost-effectiveness; marketing effectiveness; payor access and research and development of new products and processes. Most new products Tyme intends to market, assuming regulatory approval, will and must compete with other products already on the market as well as products that are later developed by existing or new competitors. If competitors introduce new products or delivery systems with therapeutic or cost advantages, Tyme's products would be subject to progressive price reductions, decreased volume of sales or

both. Increasingly, to obtain favorable reimbursement and formulary positioning with government payers, managed care organizations and pharmacy benefits managers, Tyme would be required to demonstrate that its products offer not only medical benefits, but also more value as compared with other treatment regimens.

The pharmaceutical and biotechnology industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. While Tyme believes that its technology, development and regulatory plans in addition to proprietary scientific knowledge provide it with certain competitive advantages, Tyme currently has limited financial resources and no revenue source and face potential competition from many different sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions and governmental agencies and public and private research institutions, each of which has significantly greater financial resources than Tyme. Any drugs that Tyme successfully develops and commercializes will compete with existing therapies and new potential therapies that may become available in the future.

Tyme's products, if approved for sale, would eventually be subject to competition from generic drug manufacturers. Manufacturers of generic biopharmaceuticals generally invest far less in R&D and marketing than R&D companies such as Tyme. Tyme anticipates that any manufacturer of a generic version of its drugs will invest far less than Tyme has in the past and intends to do in the future. They, therefore, have the advantage in that they can price their drugs much lower than the brand-name drugs for which Tyme obtains approval. Additionally, in many countries outside the United States, IP protection is weak or nonexistent and Tyme would be forced to compete with generic or counterfeit versions of its products in such countries whether or not we hold legal exclusivity.

The most common methods of treating patients with cancer are surgery, radiation and drug therapy, including chemotherapy, hormone therapy and targeted drug therapy. Tyme's products once approved, would compete not only with other drugs, but also with such other types of therapies and treatments.

There are a variety of available drug therapies marketed for cancer. In many cases, these drugs are administered in combination to enhance efficacy. Some of the currently approved drug therapies are branded and subject to patent protection and others are available on a generic basis. Many of these approved drugs are well-established therapies and widely accepted by physicians, patients and third-party payers. In general, although there has been considerable progress over the past few decades in the treatment of cancer with currently marketed therapies providing benefits to many patients, these therapies often are limited to some extent by a lack of efficacy and/or the significance or frequency of AEs.

In addition to currently marketed therapies, there are also a number of medicines in late-stage clinical development to treat cancer. These medicines in development may provide efficacy, safety, convenience and other benefits that are not provided by currently marketed therapies. As a result, they may provide significant, additional competition for SM-88 and Tyme's pipeline.

FDA Approval Process

SM-88 is subject to regulation in the U.S. by the FDA as a drug product. The FDA subjects drug products to extensivepre- and post-market regulation. The Public Health Service Act, the FDCA and other federal and state statutes and regulations govern, among other things, the research, development, testing, manufacture, storage, recordkeeping, approval, labeling, promotion and marketing, distribution, post-approval monitoring and reporting, sampling and the import and export of drugs. Failure to comply with applicable U.S. requirements may subject a company to a variety of administrative or judicial sanctions, such as FDA refusal to approve pending NDAs, withdrawal of approvals, clinical holds, warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions and/or fines or civil or criminal penalties.

The drug development process required by the FDA before a new drug may be marketed in the U.S. is long, expensive and inherently uncertain. Drug development in the U.S. typically involves preclinical laboratory and

animal testing, the submission to the FDA of an IND, which must become effective before clinical testing may commence, and adequate and well-controlled clinical trials to establish the safety and effectiveness of the drug for each indication for which FDA approval is sought. Developing the data to satisfy FDA pre-market approval requirements typically takes many years and the actual time required may vary substantially based upon the type, complexity and novelty of the product or disease.

Preclinical tests include laboratory evaluation of product chemistry, formulation and toxicity, as well as animal trials to assess the characteristics and potential safety and efficacy of the product. The conducting of the preclinical tests must comply with federal regulations and requirements, including Good Laboratory Practices. The results of preclinical testing are submitted to the FDA as part of an Investigational New Drug, or IND, along with other information, including information about product chemistry, manufacturing and controls, or CMC, and a proposed clinical trial protocol. Long-term preclinical tests, such as animal tests of reproductive toxicity and carcinogenicity, may continue after the IND is submitted.

An IND must become effective before U.S. clinical trials may begin. A30-day waiting period after the submission of each IND is required prior to the commencement of clinical testing in humans. If the FDA has neither commented on nor questioned the IND submission within this 30-day period, the clinical trial proposed in the IND may begin. Clinical trials involve the administration of the investigational new drug to healthy volunteers or subjects with the condition under investigation, all under the supervision of a qualified investigator. Clinical trials must be conducted: (i) in compliance with federal regulations; (ii) in compliance with good clinical practices, or GCP, an international standard meant to protect the rights and health of patients and to define the roles of clinical trial sponsors, administrators and monitors; and (iii) under protocols detailing the objectives of the trial, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. Each protocol involving testing on U.S. patients and subsequent protocol amendments must be submitted to the FDA as part of the ongoing IND file.

The FDA may order the temporary or permanent discontinuation of a clinical trial at any time or impose other sanctions if it believes that the clinical trial is not being conducted in accordance with FDA requirements or presents an unacceptable risk to clinical trial subjects. The study protocol and informed consent information for subjects in clinical trials must be submitted to an IRB for review and approval. An IRB may also require the clinical trial at a clinical site to be halted, either temporarily or permanently, for failure to comply with the IRB's requirements or may impose other conditions to assure subject safety. The study sponsor may also suspend a clinical trial at any time on various grounds, including a determination that the subjects are being exposed to an unacceptable health risk.

Clinical trials to support NDAs for marketing approval are typically conducted in three sequential phases, but the phases may overlap or be combined. In Phase I, the drug is initially introduced into healthy human subjects and is tested to assess pharmacokinetics, pharmacological actions, AEs associated with increasing doses and, if possible, early evidence of effectiveness. In the case of some products targeted for severe or life-threatening diseases, such as cancer treatments, initial human testing may be conducted in the intended patient population. Phase II usually involves trials in a limited patient population to determine the effectiveness of the drug for a particular indication, dosage tolerance and optimum dosage, as well as identification of common AEs and safety risks. If a compound demonstrates evidence of effectiveness and an acceptable safety profile in Phase II, Phase III trials are initiated to obtain additional information about clinical efficacy and safety in a larger number of subjects, typically at geographically dispersed clinical trial sites. Phase III clinical trials are intended to establish data sufficient to demonstrate substantial evidence of the efficacy and safety of the product to permit the FDA to evaluate the overall benefit-risk relationship of the drug and to provide adequate information for the labeling of the drug. Trials conducted outside of the U.S. under similar, GCP-compliant conditions in accordance with local applicable laws may also be acceptable to the FDA in support of product licensing.

Sponsors of clinical trials for investigational drugs must publicly disclose certain clinical trial information, including detailed trial design and trial results, in FDA public databases. These requirements are subject to specific timelines and apply to most controlled clinical trials of FDA-regulated products.

After completion of the required clinical testing, an NDA is prepared and submitted to the FDA. The FDA review and approval of the NDA is required before marketing of the product may begin in the U.S. The NDA must include the results of all preclinical, clinical and other testing and a compilation of data relating to the product's pharmacology and CMC and must demonstrate the safety and efficacy of the product based on these results. The NDA must also contain extensive manufacturing information. The cost of preparing and submitting an NDA is substantial and is in addition to the costs of conducting clinical trials. Under federal law, the submission of most NDAs is additionally subject to a substantial application user fee, as well as annual product and establishment user fees, which may total several million dollars and are typically increased annually.

The FDA has 60 days from its receipt of an NDA to determine whether the application will be accepted for filing based on the agency's threshold determination that the NDA is sufficiently complete to permit substantive review. Once the submission is accepted for filing, the FDA begins an in-depth review. The FDA has agreed to certain performance goals in the review of NDAs. Most applications for standard review drugs are reviewed within 10 months from the date the application is accepted for filing. Although the FDA often meets its user fee performance goals, it can extend these timelines if necessary and its review may not occur on a timely basis at all. The FDA usually refers applications for novel drugs, which present complex questions of safety or efficacy, to an advisory committee—typically a panel that includes clinicians and other experts – for review, evaluation and a recommendation as to whether the application should be approved. The FDA is not bound by the recommendation of an advisory committee, but it generally follows such recommendations. Before approving an NDA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP. Additionally, the FDA will inspect the facility or the facilities at which the drug is manufactured. The FDA will not approve the drug product unless it verifies that compliance with cGMP standards is satisfactory and the NDA contains data that provide substantial evidence that the drug is safe and effective in the indication(s) being studied.

After the FDA evaluates the NDA and the manufacturing facilities, it issues either an approval letter or a complete response letter. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional nonclinical or clinical testing or supplemental information for the FDA to reconsider the application. If or when those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the NDA, the FDA will issue an approval letter. The FDA has committed to reviewing such resubmissions in two to six months depending on the type of information that was included. FDA approval is never guaranteed, and the FDA may refuse to approve an NDA if the applicable regulatory criteria are not satisfied.

An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. The approval for a drug may be significantly more limited than requested in the application, including limitations on the specific diseases and dosages or the indications for use, which could restrict the commercial value of the product. The FDA may also require that certain contraindications, warnings or precautions be included in the product labeling. In addition, as a condition of NDA approval, the FDA may require a REMS to further ensure that the benefits of the drug outweigh the potential risks. REMS can include medication guides, communication plans for healthcare professionals and elements to assure safe use, or ETASU. ETASU can include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring and the use of patient registries. The requirement for a REMS or use of a companion diagnostic with a drug can materially affect the potential market and profitability of the drug. Moreover, product approval may require, as a condition of approval, substantial post-approval testing and surveillance to monitor the drug's safety or efficacy. Once granted, product approvals may be withdrawn if compliance with regulatory standards is not maintained or problems are identified following initial marketing. Additionally, as with an existing number of previously approved oncology products, the FDA will likely require us to educate health care providers and patients about the proper use and administration of our drug candidates and obtain FDA approval to market.

As of March 31, 2022, Tyme has two active INDs with the FDA, both of which are associated with SM-88. The two INDs are active with the relevant FDA divisions within the Office of Oncologic Diseases that oversee

Tyme's trials, the Division of Oncology 1 and the Division of Oncology 2. In addition, clinical investigators have previously and may in the future request their own INDs in order to use SM-88 or other products in Investigator Initiated Trials, or IITs. For example, the HoPES trial for sarcoma is an IIT where the IND for SM-88 use is held directly by the clinical trial site.

Priority Review/Standard Review (U.S.) and Related Requirements

The FDA may grant an NDA a priority review designation upon the request of an applicant and based on the results of the Phase III clinical trial(s) submitted in the NDA. This designation sets the target date at six months for FDA action on the application. Priority review is granted where preliminary trial results indicate that a product, if approved, has the potential to provide a safe and effective therapy for a situation where no satisfactory alternative therapy exists or where the product is possibly a significant improvement over the existing marketed products. If these criteria are not met for priority review, the NDA is subject to the standard FDA review period of ten months. However, priority review designation does not change the scientific/medical standard for regulatory approval or the quality of evidence necessary to support approval. There can be no assurance that Tyme would be able to satisfy the eligibility criteria for priority review or to receive regulatory approval under either standard review.

Breakthrough Therapy Approvals

The Food and Drug Administration Safety and Innovation Act provides another designation for an expedited FDA review process called Breakthrough Therapy Designation. A breakthrough therapy is a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition and where preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. If an investigational drug is designated as a breakthrough therapy, the drug will be eligible for all fast track designation features, including expedited development and review of such drug for trial and market approval. Interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens. All requests for Breakthrough Therapy Designation are to be reviewed within 60 days of receipt and FDA will either grant or deny the request.

Fast Track Program

The fast track program, a provision of the Food and Drug Administration Modernization Act of 1997, or FDAMA, is designed to facilitate interactions between a sponsor and the FDA before and during submission of an NDA for an investigational agent that, alone or in combination with one or more drugs, that is intended to treat a serious or life-threatening disease or condition and demonstrates the potential to address an unmet medical need for that disease or condition. Under the fast track program, the FDA may consider reviewing portions of a marketing application before the sponsor submits the complete application, if the FDA determines, after a preliminary evaluation of the clinical data, that a fast track drug may be effective. A fast track designation provides the opportunity for more frequent interactions with the FDA and could make the drug eligible for accelerated approval priority review if supported by clinical data at the time of submission of the NDA.

The Hatch-Waxman Act

Under the Hatch-Waxman Act, newly approved drugs and indications may benefit from a statutory period of non-patent marketing exclusivity. The Hatch-Waxman Act provides five-year marketing exclusivity to the first applicant to gain approval of an NDA for an NCE, meaning that the FDA has not previously approved any other new drug containing the same active moiety. The Hatch-Waxman Act prohibits having an effective approval date for an ANDA or a Section 505(b)(2) NDA for another version of such drug during the five-year exclusive period; however, submission of an ANDA or Section 505(b)(2) NDA containing a paragraph IV certification is permitted

after four years, which may trigger a 30-month stay of approval of the ANDA or Section 505(b)(2) NDA. Protection under the Hatch-Waxman Act will not prevent the submission or approval of another "full" NDA; however, the applicant for the "full" NDA would be required to conduct its own preclinical studies and adequate and well-controlled clinical trials to demonstrate safety and effectiveness. The Hatch-Waxman Act also provides three years of marketing exclusivity for the approval of new and supplemental NDAs, including Section 505(b)(2) NDAs, for, among other things, new indications, dosages or strengths of a currently approved drug, if new clinical investigations conducted or sponsored by the applicant are determined by the FDA to be essential to the approval of the new or supplemental NDA.

In addition to non-patent marketing exclusivity, the Hatch-Waxman Act amended the Food, Drug and Cosmetic Act to require each NDA sponsor to submit with its application information on any patent that claims the active pharmaceutical ingredient, drug product (formulation and composition) and method-of-use for which the applicant submitted the NDA and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use or sale of the drug. Generic applicants that wish to rely on the approval of a drug listed in the Orange Book must certify to each listed patent. The Orange Book is a listing of all drug products that have been approved by the FDA and their generic equivalences. Tyme intends to submit for Orange Book listing all relevant patents for SM-88 and to vigorously defend any Orange Book-listed patents for our approved products.

The Hatch-Waxman Act also permits a patent term extension of up to five years as compensation for the patent term lost during product development and the FDA regulatory review process. However, a patent term extension cannot extend the remaining term of a patent beyond a total of 14 years after the FDA approves a marketing application. The patent term extension period is generally equal to the sum of one-half the time between the effective date of an IND and the submission date of an NDA and all the time between the submission date of an NDA and the approval of that application, up to a total of five years. Only one patent applicable to a regulatory review period that represents the first commercial marketing of that drug is eligible for the extension and it must be applied for prior to expiration of the patent. The USPTO, in consultation with the FDA, reviews and approves the application for patent term extension. Tyme will consider applying for a patent term extension for some of our patents, to add patent life beyond the expiration date, depending on our ability to meet certain legal requirements permitting such extension and the expected length of clinical trials and other factors involved in the submission of an NDA. There can be no assurance that such an extension, if applied for, will be granted.

Advertising and Promotion

The FDA prohibits the pre-approved marketing and promotion of drugs and closely regulates the post-approval marketing and promotion of drugs, including through standards and regulations for direct-to-consumer advertising, off-label promotion, industry-sponsored scientific and educational activities and promotional activities involving the internet and social media. Failure to comply with these regulations can result in significant penalties, including the issuance of untitled and warning letters directing a company to correct deviations from FDA standards, a requirement that future advertising and promotional materials are pre-cleared by the FDA and federal and state civil and criminal investigations and prosecutions.

Drugs may be marketed only after initial approval and only for the approved indications and in accordance with the provisions of the approved labeling. Changes to some of the conditions established in an approved application, including changes to indications, labeling or manufacturing processes or facilities, may require a submission and FDA approval of a new NDA or NDA supplement before the change can be implemented. An NDA supplement for a new indication typically requires clinical data similar to that in the original application and the FDA uses the same procedures and actions in reviewing NDA supplements as it does in reviewing original and resubmitted NDAs.

Adverse Event Reporting and cGMP Compliance

Adverse event reporting and submission of periodic reports are required following FDA approval of an NDA. The FDA also may require post-marketing testing, known as Phase IV testing, REMS and surveillance to monitor the effects of an approved product or the FDA may place conditions on an approval that could restrict the distribution or use of the product. In addition, manufacturing, packaging, labeling, storage and distribution procedures must continue to conform to cGMPs after approval. Drug manufacturers and certain manufacturing subcontractors are required to register their establishments with the FDA and certain state agencies. Registration with the FDA subjects' entities to periodic unannounced inspections by the FDA, during which the agency inspects manufacturing facilities to assess compliance with cGMPs. Accordingly, manufacturers must continue to expend time, money and effort in the areas of production and quality control to maintain compliance with cGMPs. Regulatory authorities may withdraw product approvals, request product recalls or impose marketing restrictions through labeling changes or product removals if a company fails to comply with regulatory standards, if the product encounters problems following initial marketing or if previously unrecognized problems are subsequently discovered.

Orphan Drug Designation

Under the Orphan Drug Act, the FDA may grant orphan drug designation to drugs intended to treat a rare disease or condition; generally, a disease or condition that affects fewer than 200,000 individuals in the U.S. annually. Orphan drug designation must be requested before submitting an NDA. After the FDA grants orphan drug designation, the generic identity of the drug and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not necessarily convey any advantage in or shorten the duration of the regulatory review and approval process. The first NDA applicant to receive FDA approval for a product to treat a particular disease with FDA orphan drug designation is entitled to a seven-year exclusive marketing period in the U.S. for the product for treatment of the specified indication. During the seven-year exclusivity period, the FDA may not approve any other applications to market the same drug for the same disease, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity. Orphan drug exclusivity does not prevent the FDA from approving a different drug for the same disease or condition or the same drug for a different disease or condition. Among the other benefits of orphan drug designation are tax credits for certain research and a waiver of the NDA application user fee. Orphan drug exclusivity may be lost in the United States if the FDA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition.

In July 2020, Tyme received from the FDA orphan drug designation forSM-88, as a potential treatment for patients with pancreatic cancer.

Other Healthcare Laws and Compliance Requirements

In the U.S., Tyme's activities are potentially subject to regulation by federal, state and local authorities in addition to the FDA, including CMS, other divisions of HHS (for example, the Office of Inspector General), the DOJ and individual U.S. Attorney offices within the DOJ and state and local governments.

International Regulation

In order to market any product outside of the United States, Tyme would need to comply with numerous and varying regulatory requirements of other countries regarding safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of our products. Whether or not we obtain FDA approval for a product, Tyme would need to obtain the necessary approvals by the comparable regulatory authorities of foreign countries before we can commence clinical trials or marketing of the product in those countries. The approval process varies from country to country and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries might differ

from and be longer than that required to obtain FDA approval. Regulatory approval in one country does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country may negatively impact the regulatory process in others.

Manufacturing

Tyme does not own or operate, and currently have no near-term plans to establish, any manufacturing facilities. Tyme currently relies on and expect to continue to rely on, third party contract manufacturers for supplies of SM-88 for preclinical and clinical testing, as well as for the initial commercial manufacture of any products that it may market following regulatory approval.

Tyme currently purchases all its drug substance and drug products from contract manufacturers and intend to continue to do so on an as-needed purchase order basis. Tyme has entered into limited term supply arrangements for certain SM-88 components related to supply for our clinical activities in order to secure favorable pricing terms. Tyme intends to identify and qualify any further necessary contract manufacturers to provide all active pharmaceutical ingredients, or APIs, and finished drug product services during the IND stages and before submission of an NDA to the FDA.

Tyme has started some focused precommercial technical development activities toward commercial manufacturing. These precommercial manufacturing activities are expected to be able to support ongoing clinical manufacturing activities as needed. Tyme's current intention is that, during the ongoing development of SM-88, other than its limited and focused precommercial activities, Tyme will transition the needed manufacturing, CMC and GMP programs towards commercial third-party manufacturing when appropriate. The overall manufacturing program includes, but is not limited to, the development of product and process specifications, producing and validating standards and the development of suitable analytical methods for test and release, as well as stability testing. Before and during the use of contract manufacturers, Tyme (or qualified designee) will conduct audits to ensure compliance with the mutually agreed process descriptions and cGMP regulations. Tyme's manufacturers themselves must comply with their in-house quality assurance programs and be available for inspections by regulatory agencies, including the FDA and European drug regulatory agencies. During the development of Tyme's drug candidates, Tyme anticipates scaling the manufacturing process to a suitable size. Increasing scale involves several steps and may involve modification of the process, in which case modifications to Tyme's CMC sections will occur, with continuous submissions to the FDA and European regulatory authorities.

As Tyme progresses through the regulatory approval process, there is a possibility that its intended manufacturing process will undergo modifications, primarily based on initial manufacturing results and data generated during the manufacture of the drug substance and product to be used in Tyme's clinical trials. Modifications could cause delays in obtaining regulatory approval of SM-88, if at all, as well increase Tyme's research and development and manufacturing costs and potentially make such product costs prohibitive to its intended end users and their medical insurance providers.

SM-88 is currently administered with the conditioning agents MPS. MPS each previously received regulatory approval in areas other than cancer treatment. SM-88 and the three agents within MPS are organic compounds of low molecular weight, generally called small molecules. They can be manufactured in reliable and reproducible synthetic processes from readily available starting materials. The chemistry is amenable to scale-up and Tyme does not believe unusual equipment would be required in the manufacturing process.

Tyme's tyrosine-based component is a derivative product that has been modified by a proprietary process to modify its functionality. This drug substance is being manufactured on an exclusive basis by a leading, FDA-audited contract manufacturer that has previously manufactured tyrosine-based products on a commercial scale. This manufacturer currently is our sole supplier of this drug substance. To Tyme's knowledge, the current manufacturer of this drug substance is the only FDA registered and inspected manufacturer of this drug. Tyme believes this contract manufacturer has sufficient capacity to meet its projected needs into the near future and

Tyme maintains inventory on hand to meet its immediate clinical needs. In the event of a catastrophic event or if this contract manufacturer is unable to meet Tyme's needs, it will need to find an alternative source. This will likely result in delays for the clinical development program or future commercial programs. It is not impossible to find a substitute for this supplier in the event that it becomes necessary, but it may be costly, including in terms of development time. Tyme does not currently have arrangements in place for a redundant supply of the drug substance.

To date, Tyme has, through an FDA-audited contract manufacturer, produced cGMP drug substance for use in our planned clinical trials. In addition, Tyme has produced cGMP clinical trial materials utilizing such drug substance, through an FDA-audited contract manufacturer. Such newly produced drug substance and clinical trial materials are currently undergoing long term regulatory testing. Tyme believes it has produced enough drug substance to create an inventory to meet its immediate needs regarding our planned clinical trials.

For future work involving the drug product, it is anticipated that manufacture process development work will continue, focusing on manufacturing improvements, and increasing scale. It is anticipated that future manufacturing of clinical trial materials may be required to fill clinical trial needs. Additional tyrosine derivative drug product variations have also been developed for research purposes and some are being validated and tested for clinical purposes.

The three APIs for MPS are available from several contract manufacturers, each holding Drug Master Files at the FDA for their respective APIs. Tyme believes that the loss of or the inability of any single source to provide its required ingredients would not have any substantive delaying effect on its research program, clinical trials or future commercial sale of SM-88, as Tyme believes other sources are readily available.

Tyme had started a development program focused on a new potential treatment of COVID-19, TYME-19, and would need to assess manufacturing and clinical and service options for the TYME-19 if the development program was to progress further.

Employees and Human Capital

As of March 31, 2022, Tyme had a total of 13 employees, all full-time and all located in the United States. Of this total workforce, 6 full time equivalent, or FTE, employees were engaged in or directly supported Tyme's research and development activities and 7 FTE employees perform general and administrative functions. The roles of certain employees include both R&D activities and general administrative functions, and, as such, for purposes of the immediately preceding sentence they are categorized in more than one role based on time spent on each function. None of Tyme's employees are represented by a labor union or covered by a collective bargaining agreement. Tyme has not experienced any work stoppages, and it considers its relations with its employees to be good. In order to enable Tyme to further develop and potentially commercialize SM-88 and other pipeline candidates Tyme will need to maintain and continue to hire additional experienced personnel as well as to rely on third-party consultants for certain activities.

Tyme is committed to a work environment that is welcoming, inclusive and encouraging, and believes that it can be at its best when it brings together diverse teams with different perspectives, experiences and ideas. In furtherance of its commitment to diversity and inclusion, and diverse perspectives on Tyme's board of directors and among its employees, Tyme's Corporate Governance Guidelines provide that, when evaluating candidates for nominations as new directors, the pool of candidates from which the nominating and governance committee of Tyme's board of directors recommends nominees will include qualified persons who reflect diverse backgrounds, including both underrepresented people of color and different genders, and if any third party search firm is used, it will be specifically instructed to include such candidates.

The success of Tyme's business is fundamentally connected to the well-being of its employees. Tyme provides competitive compensation and benefits programs to help meet the needs of its employees. In addition to salaries,

these programs include potential annual discretionary bonuses, equity awards, healthcare and insurance benefits, health savings and flexible spending accounts, paid time off, family leave, and flexible work schedules, among others. Tyme has also historically offered its employees the ability to work remotely as well as in our office and expect to continue to do so in the future. These benefits provide Tyme's employees choices where possible so they can customize their benefits to meet their needs and the needs of their families, as well as access to tools and resources to help them improve or maintain their health status and encourage engagement in healthy behaviors to improve their physical and mental health.

Throughout the COVID-19 pandemic, many of Tyme's employees have worked remotely. In June 2021, Tyme's employees returned to its officein-person from time to time while also continuing to work remotely and being permitted to fully "work-from-home" if preferred, and Tyme has relaxed its travel restrictions. For in-office work, Tyme implemented a number of significant safety measures based on current guidelines recommended by the Centers for Disease Control.

Consultants

Where necessary, Tyme has entered into consulting contracts to provide it with subject matter expertise. Tyme believes there is a sufficient number of available contractors with appropriate subject matter expertise for its current and near-term needs. Tyme retains each consultant according to the terms of a consulting agreement. Under such agreements, Tyme generally pays them a consulting fee and reimburses them for out-of-pocket expenses incurred in performing their services for it. In addition, Tyme has in the past and may again in the future grant options to purchase our common stock to consultants, subject to the vesting requirements contained in their consulting agreements. Tyme's consultants may be employed by other entities and therefore may have commitments to their employer, or may have other consulting or advisory agreements that may limit their availability to it.

Collaboration with Eagle Pharmaceuticals

On January 7, 2020, Tyme and Eagle entered into a Securities Purchase Agreement, or the Eagle SPA, pursuant to which Tyme issued and sold to Eagle 10,000,000 shares of common stock, at a price of $2.00 per share. The Eagle SPA provides that Eagle will, subject to certain conditions, make an additional payment of $20 million upon the occurrence of a milestone event, which is defined as the earlier of (i) achievement of the primary endpoint of overall survival in the TYME-88-Panc pivotal trial; or (ii) achievement of the primary endpoint of overall survival in the PanCAN Precision Promise SM-88 registration arm; or (iii) FDA approval of SM-88 in any cancer indication. This payment would be split into a $10 million milestone cash payment and a $10 million investment in Tyme at a 15% premium to the then prevailing market price, or the Milestone Payment. Eagle's shares will be restricted from sale until the earlier of three months following the milestone event or the three-year anniversary of the agreement. In the event that Tyme enters into a "Corporate Transaction" (as such term is defined in the Eagle SPA), which would include the Merger, Eagle would be released from any obligation to make the Milestone Payment.

Also, on January 7, 2020, Tyme entered intoa Co-Promotion Agreement with Eagle, or the Co-Promote, whereby Eagle agreed to provide sales representatives to cover 25% of Tyme's sales force requirements and will receive 15% of the net sales of all SM-88 products in the U.S. during the term of the Co-Promote. Tyme will also be responsible for clinical development, regulatory approval, commercial strategy, marketing, reimbursement and manufacturing of SM-88. Tyme retains the remaining 85% of net U.S. revenues and reserves the right to repurchase Eagle's rights under theCo-Promote for $200 million.

Corporate Information

Tyme was reincorporated on September 18, 2014 under the laws of the State of Delaware, after being incorporated in Florida as Global Group Enterprises Corp. on November 22, 2011, as discussed further below

under Corporate History; Significant Organizational Events. Tyme's principal executive office is located at One Pluckemin Way, Bedminster, NJ 07921. Tyme's telephone number is 212-461-2315. Tyme's website address is www.tymeinc.com. The contents of Tyme's website are not incorporated by reference into this joint proxy statement/prospectus or any other document Tyme files with the SEC, and any reference to its website is intended to be an inactive textual reference only.

Corporate History; Significant Organizational Events

Tyme was originally incorporated in Florida as Global Group Enterprises Corp. on November 22, 2011. Effective as of September 18, 2014, Tyme reincorporated in the State of Delaware and later engaged in a merger and certain other transactions. As a result of these events and related transactions, among other things, Tyme (i) changed its jurisdiction of incorporation from Florida to Delaware; (ii) changed its name from Global Group Enterprises Corp. to Tyme Technologies, Inc., and (iii) acquired its current clinical-stage pharmaceutical business.

At-the-Market Sales of Common Stock

On October 18, 2019, Tyme entered into an Open Market Sale Agreement℠, or the Sale Agreement, with Jefferies LLC, or Jefferies, as sales agent, pursuant to which Tyme may, from time to time, sell shares of Common Stock through Jefferies having an aggregate offering price of up to $30.0 million, or the Jefferies ATM. Under the Sale Agreement the minimum share sales price, or Floor Price, shall not be less than $1.00 without Jefferies prior written consent. Since its initiation, Tyme raised approximately $7.3 million in net proceeds after commissions and other transaction expenses and sold 5,815,254 shares of Common Stock. Tyme has not sold any securities pursuant to the Jefferies ATM during fiscal year 2022 or into fiscal year 2023.

Registered Direct Offering

On February 8, 2021, Tyme closed its registered direct offering of 40,000,000 shares of its Common Stock at a purchase price of $2.50 per share. The gross proceeds of the offering were $100 million, prior to deducting placement agent's fees and other offering expenses payable by Tyme. The net proceeds to Tyme, after deducting placement agent fees and other offering expenses payable by Tyme, were approximately $93.8 million.

Exchange Agreements

On May 20, 2020, Tyme entered into exchange agreements with holders, or the Holders, of the April 2019 Warrants. The April 2019 Warrants were offered and issued pursuant to Tyme's previous shelf registration statement on Form S-3 (Registration No. 333-211489).

Pursuant to exchange agreements, or the Share Exchange Agreements, with Holders of April 2019 Warrants to purchase 5,833,333 shares of Common Stock in the aggregate, Tyme issued an aggregate of 2,406,250 shares of common stock, or the Exchange Shares, in exchange for such April 2019 Warrants. Concurrently therewith, each such Holder executed and delivered to Tyme a leak-out agreement, or a Share Leak-Out Agreement, that contains trading restrictions with respect to the Exchange Shares, which (i) for the first 90 days, prohibit any sales of Exchange Shares, (ii) for the subsequent 90 days, limit sales of Exchange Shares on any day to 2.5% of that day's trading volume of Common Stock, and (iii) prohibit new short positions or short sales on Common Stock for the combined 180 day period.

Tyme also entered into an exchange agreement, or the Warrant Exchange Agreement, with another Holder of April 2019 Warrants to purchase 2,166,667 shares of Common Stock in the aggregate. Pursuant to the Warrant Exchange Agreement, Tyme issued such Holder a new warrant, or the "May 2020 Warrant, to purchase the same number of shares of Common Stock. The May 2020 Warrant has the same expiration date, April 2, 2024, as the April 2019 Warrants, but has an exercise price of $1.80 and does not include the price protection, anti-dilution

provisions or other restrictions on Company action from the April 2019 Warrants. Concurrently therewith, such Holder executed and delivered to Tyme a leak-out agreement that contained trading restrictions on sales of Common Stock issued upon exercise of the May 2020 Warrant that are substantially similar to the restrictions on Exchange Shares in the Share Leak-Out Agreement, provided that the leak-out restrictions will only apply to the first 893,750 shares of Common Stock issued pursuant to the May 2020 Warrant.

Available Information

Tyme's Annual Report on Form 10-K, as amended, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, and other filings with the SEC and all amendments to these filings, are available, free of charge, on its website at www.tymeinc.com as soon as reasonably practicable following its filing of any of these reports with the SEC. You can also obtain copies free of charge by contacting our Investor Relations department at Tyme's office address listed above. The SEC also maintains a website that contains all the materials Tyme files with, or furnish to, the SEC. Its website is www.sec.gov.

The contents of Tyme's website are not incorporated by reference into this joint proxy statement/prospectus or any other document it files with the SEC, and any reference to its website is intended to be an inactive textual reference only.

Properties

Tyme's principal executive offices are located at 1 Pluckemin Way—Suite 103, Bedminster, NJ 07921 where it leases and occupies approximately 1,962 square feet of office space. Tyme estimates its annual costs for this office at approximately $43,200 per year plus utilities and other expenses.

Tyme believes that its existing office space is adequate for its current and near-term growth of its administrative operations. Tyme will rely on clinical research centers, hospitals, contract research organizations and other parties for suitable space and facilities to conduct its clinical trials. Tyme will explore, in the future, establishing a dedicated technical facility, when its believes the need for such a facility has arisen. No assurance can be given that such a facility can be located without difficulty or at a cost favorable to Tyme.

SYROS MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

The following discussion and analysis of Syros' financial condition and results of operations should be read in conjunction with Syros' financial statements and related notes thereto appearing elsewhere in this joint proxy statement/prospectus. Syros' actual results and timing of certain events may differ materially from the results discussed, projected, anticipated, or indicated in any forward-looking statements. Syros cautions you that forward-looking statements are not guarantees of future performance and that its actual results of operations, financial condition and liquidity, and the development of the industry in which Syros operates, may differ materially from the forward-looking statements contained in this joint proxy statement/prospectus. In addition, even if Syros' results of operations, financial condition and liquidity, and the development of the industry in which it operates are consistent with the forward-looking statements contained in this joint proxy statement/prospectus, they may not be predictive of results or developments in future periods.

The following information and any forward-looking statements should also be considered in light of risks identified under the caption "Risk Factors" in this joint proxy statement/prospectus. Syros cautions you not to place undue reliance on any forward-looking statements made by it, which speak only as of the date they are made. Syros disclaims any obligation, except as specifically required by law and the rules of the SEC, to publicly update or revise any such statements to reflect any change in its expectations or in events, conditions or circumstances on which any such statements may be based, or that may affect the likelihood that actual results will differ from those set forth in the forward-looking statements.

Overview

Syros is a biopharmaceutical company seeking to redefine the power of small molecules to control the expression of genes. Based on Syros' unique ability to elucidate regulatory regions of the genome, Syros aims to develop medicines that provide a profound benefit for patients with diseases that have eluded other genomics-based approaches. Syros is currently focused on developing treatments for cancer and diseases resulting from mutations of a single gene, also known as monogenic diseases, and building a clinical stage pipeline of gene control medicines.

Syros' clinical-stage product candidates are:

- tamibarotene, a selective retinoic acid receptor alpha, or RARα, agonist for which Syros is conducting SELECT-MDS-1, a Phase 3 clinical trial evaluating tamibarotene in combination with azacitidine in a genomically defined subset of patients with HR-MDS and for which Syros is conducting SELECT-AML-1, a randomized Phase 2 clinical trial evaluating tamibarotene in combination with venetoclax and azacitidine in a genomically defined subset of newly diagnosed patients with AML who are not suitable candidates for standard intensive chemotherapy;
- SY-2101, a novel oral form of ATO which Syros is evaluating in a dose confirmation study to enable the conduct of a Phase 3 clinical trial, in patients with newly diagnosed low-risk APL; and
- SY-5609, a highly selective and potent oral inhibitor of CDK7 that Syros is evaluating in combination with chemotherapy in pancreatic cancer patients in an expansion cohort of its existing Phase 1 clinical trial, and which is being evaluated in combination with atezolizumab, a PD-L1 inhibitor, in BRAF-mutant colorectal cancer in an arm of a Phase 1/1b clinical trial sponsored by Roche which is now open for enrollment.

Syros also has multiple preclinical and discovery programs in oncology, including programs targeting the inhibition of CDK12, CDK11, and WRN. Syros expects that its next development candidate will be nominated from its CDK12 program in the third quarter of 2022. Syros is seeking partnerships for its oncology discovery programs, including CDK12.

In December 2019, Syros entered into a collaboration with GBT to discover, develop and commercialize novel therapies for sickle cell disease and beta thalassemia. Syros also uses its gene control platform in collaboration with third parties to identify and validate targets in diseases beyond Syros' current areas of focus. To this end, Syros entered into a target discovery, research collaboration and option agreement with Incyte in January 2018, under which Syros is using Syros' platform to identify novel therapeutic targets with a focus on myeloproliferative neoplasms.

Tamibarotene

At the 62nd American Society of Hematology Annual Meeting and Exposition held in December 2020, or ASH 2020, Syros presented data from its fully enrolled Phase 2 clinical trial evaluating the safety and efficacy of tamibarotene in combination with azacitidine in newly diagnosed AML patients who are not suitable candidates for standard chemotherapy, as well as in relapsed or refractory, or R/R, AML patients who have been prospectively selected using Syros' proprietary RARA, the gene that codes for RARα, biomarker. As of an October 1, 2020 data cut-off, 51 newly diagnosed unfit AML patients, including both RARA-positive and RARA-negative patients, were eligible for a safety analysis. Among these patients, tamibarotene in combination with azacitidine was generally well-tolerated, with no evidence of increased toxicity relative to either as a single agent, including rates of myelosuppression that were comparable to single-agent azacitidine. As of the data cut-off, of the 18 RARA-positive patients that were evaluable for clinical response, the overall response rate, or ORR, was 67%, with a composite complete response rate of 61%, with 50% of patients achieving complete response, or CR, and 11% achieving a complete response with incomplete blood count recovery, or CRi. The median time to initial response was 1.2 months, the median duration of response was 10.8 months, and the median overall survival, or OS, among patients who achieved a CR or CRi was 18 months. As of the data cut-off, of the 28 RARA-negative patients that were evaluable for clinical response, the ORR was 43%, with a composite complete response rate of 32%, with 25% of patients achieving CR and 7% achieving CRi. The median time to initial response was 3.0 months, and the median duration of response was 10.3 months. Syros also presented translational data demonstrating that most RARA-positive newly diagnosed unfit AML patients enrolled in Syros' Phase 2 study had a monocytic disease phenotype that is associated with resistance to venetoclax. These data suggest that the RARA biomarker not only selects for patients who are more likely to respond to treatment with tamibarotene but also for patients who may be less likely to benefit from treatment with venetoclax. Approximately 25,000 patients are diagnosed with unfit AML in the United States and Europe annually and Syros expects the overall total addressable market opportunity for all AML patients to grow to approximately $6.6 billion by 2025.

Based on these data and Syros' assessment of ongoing areas of high unmet need, Syros advanced tamibarotene in combination with azacitidine into a registration-enabling Phase 3 clinical trial in RARA-positive newly diagnosed HR-MDS patients, which Syros refers to as SELECT-MDS-1. HR-MDS is a hematologic malignancy that is closely related to AML, and Syros believes that approximately 50% of HR-MDS patients are RARA-positive. Syros believes that approximately 21,000 patients are diagnosed with HR-MDS in the United States and Europe annually and Syros expects the total addressable market opportunity for MDS patients of all risk groups to grow to approximately $3.3 billion by 2026. Syros plans to enroll approximately 190 RARA-positive newly diagnosed HR-MDS patients in the double-blind placebo-controlled trial, randomized 2:1 to receive tamibarotene in combination with azacitidine or placebo with azacitidine, respectively. The primary endpoint of the trial will be the CR rate. The trial is designed with 90% power and a one-sided alpha of 0.025 to detect a difference in CR rates between the experimental and control arms. Syros is currently dosing patients in SELECT-MDS-1, and Syros expects to report data from the SELECT-MDS-1 trial in the fourth quarter of 2023 or first quarter of 2024, with a potential submission to the FDA of an NDA expected in 2024. In addition, Syros is advancing tamibarotene in combination with venetoclax and azacitidine in RARA-positive newly diagnosed unfit AML patients. The trial, which Syros refers to as SELECT-AML-1, is designed with a single-arm safety lead-in of approximately 15 patients to confirm the dosing regimen of the triplet to be used in the randomized portion of the Phase 2 clinical trial, which will evaluate the safety and efficacy of tamibarotene in combination with venetoclax and azacitidine compared to venetoclax and azacitidine in approximately 80 patients randomized 1:1. The primary endpoint of the trial will be

the composite CR rate. The trial will also evaluate the triplet as a salvage strategy for patients in the control arm who do not respond to venetoclax and azacitidine. Syros has begun dosing patients in the SELECT-AML-1 trial, and Syros expects to report clinical activity data from the safetylead-in portion of the trial in the second half of 2022. Syros also plans to initiate the randomized portion of the trial, with data expected in 2023 or 2024.

In March 2022, Syros entered into an agreement with Qiagen under which Qiagen agreed to develop and commercialize an assay as a companion diagnostic test to determine the expression level of Syros' proprietary RARA biomarker for use with tamibarotene in newly diagnosed HR- MDS patients. Qiagen will also be responsible for obtaining and maintaining regulatory approvals for the commercial diagnostic test.

SY-2101

In December 2020, Syros acquired from Orsenix a novel oral form of ATO, which Syros refers toas SY-2101. SY-2101 is in development for the treatment of APL, a subtype of AML defined by a fusion of the RARA and promyelocytic leukemia, or PML, genes. APL represents approximately 10% of all AML cases, and approximately 2,000 patients are diagnosed with APL in the United States and Europe annually. An intravenously administered, or IV, formulation of ATO is approved for use in combination with All-Trans-Retinoic-Acid, or ATRA, in patients with newly diagnosed low-risk APL and, while curative in more than 80% of patients, its administration requires up to 140 two- to four-hour infusions over the typical course of induction and consolidation treatment. If SY-2101 demonstrates comparable efficacy to IV ATO in Syros' clinical studies, Syros believes it has the potential to become the standard-of-care frontline therapy for APL by providing a substantially more convenient option that reduces the treatment burden on patients, improving access, and lowering costs to the healthcare system. In a Phase 1 clinical trial, SY-2101 demonstrated bioavailability, pharmacokinetic, or PK, exposures similar to IV ATO, and a generally well-tolerated safety profile. Syros has begun dosing patients in a dose confirmation study of SY-2101. The ongoing dose confirmation study is evaluating the PK, food effect, safety and tolerability of SY-2101 and is expected to enroll between six and 24 adult APL patients undergoing consolidation with IV ATO plus ATRA. Participants receive a single dose of 15 mg of SY-2101 in both the fasted and in the fed state, and a single dose of IV ATO for PK assessments, with flexibility to allow for other SY-2101 doses to be evaluated. Daily administration ofSY-2101 is also being evaluated in a multiple-dose treatment module substituting for IV ATO during consolidation to assess steady state SY-2101 PK and safety. Syros anticipates reporting PK and safety data from this study in mid-2022. The feedback from a Type C meeting to review Syros' Phase 3 study design with the FDA in November 2021 continues to support molecular complete response rate as the primary endpoint for accelerated approval and event free survival as the primary endpoint for full approval, in each case compared to historic IV ATO data. In addition, FDA feedback supports the inclusion of patients randomized to IV ATO for comparative safety assessments. Based on this feedback and following confirmation of a dose that demonstrates comparable PK exposures to IV ATO, Syros intends to initiate a registration-enabling Phase 3 clinical trial in approximately 215 patients with newly diagnosed low-risk APL, randomized 2:1 to receive SY-2101 or IV ATO, in the second half of 2023.

SY-5609

At the European Society for Medical Oncology Congress held in September 2021, or ESMO 2021, Syros presented data from the dose-escalation portion of the Phase 1 multi-center, open-label study of SY-5609 evaluating patients with advanced breast, colorectal, lung, ovarian and pancreatic cancers, as well as patients with solid tumors of any histology harboring Rb pathway alterations. Patients were treated in cohorts exploring continuous daily dosing as well as intermittent dosing regimens, including seven days on treatment and seven days off, or 7d on/7d off, and five days on treatment and two days off, or 5d on/2d off. As of a July 6, 2021 data cut-off, 54 patients treated with single-agentSY-5609 in the study were eligible for a safety analysis and 45 patients were evaluable for clinical response. The median age of patients enrolled in the study was 65.5. Patients had been heavily pre-treated with as many as eight prior therapies and a median of four prior therapies. Across all doses and schedules, the majority of adverse events, or AEs, were low-grade and reversible, and there was a low

rate of discontinuations due to AEs. The most common treatment-emergent AEs were gastrointestinal (nausea, diarrhea, decreased appetite, abdominal pain, vomiting), fatigue, thrombocytopenia, and anemia. Tolerability was optimized with the 7d on/7d off schedule, which had the lowest rates of treatment-emergent AEs relative to other regimens, while demonstrating comparable rates of stable disease, or SD, as seen with more dose-intense regimens, supporting the selection of this schedule for further development of SY-5609. The maximum tolerated dose of the 7d on/7d off schedule has not yet been reached as of the data cut-off date. Changes in POLR2A mRNA expression, a pharmacodynamic marker for CDK7 inhibition, were associated with anti-tumor activity and were sustained for at least three days following drug cessation, supporting intermittent dosing. As of the data cut-off date, thirteen response-evaluable patients (29%) had achieved SD, with tumor regressions of up to 20% in six of those patients, across multiple tumor types. The most substantial clinical activity was observed in heavily pre-treated patients with advanced pancreatic cancer, for which five of 13 (39%) evaluable patients achieved SD, with tumor reductions in two of those SD patients. Further, reductions in the CA 19-9 tumor marker, which is used in clinical practice to monitor tumor progression, were observed in three of four pancreatic cancer patients with serial CA 19-9 data, with these reductions ranging from 32% to 72%. Notably, one metastatic pancreatic cancer patient who had failed two prior lines of therapy and relapsed after a third line of treatment experienced prolonged SD of up to ten months. The analysis of clinical activity by tumor type and mutational status supported the mechanistic rationale for SY-5609 in Rb-altered and KRAS-mutant cancers.

Syros also presented preclinical data at ESMO 2021 evaluating the anti-tumor and PD activity of intermittent dosing regimens for SY-5609, as well as preclinical data evaluating SY-5609 as a single agent and in combination with chemotherapy in pancreatic cancer models.

Based on these data, Syros has initiated an expansion cohort that includes two arms evaluating SY-5609 in combination with chemotherapy for the treatment of pancreatic cancer. Following completion of safety lead-ins, Syros expects to enroll approximately 50 patients with metastatic pancreatic cancer, with one arm evaluating SY-5609 in combination with gemcitabine in patients in first or second relapse who have progressed following treatment with the chemotherapy regimen known as FOLFIRINOX, and another arm exploring SY-5609 in combination with gemcitabine and nab-paclitaxel in patients following first relapse after FOLFIRINOX. SY-5609 will be administered 7d on/7d off at a starting dose of 4 mg. in the gemcitabine combination arm, and the combination agents will be administered at the approved doses. The study will evaluate safety and tolerability, as well as efficacy measures such as disease control rate and progression free survival. Syros expects to report clinical activity data of SY-5609 in combination with chemotherapy from the safety lead-in portion of the trial in the second half of 2022. Based on the safety lead-in data, Syros will determine the best course for further development of SY-5609.

In August 2021, Syros announced entry into a clinical supply agreement with Roche, pursuant to which Syros agreed to supply SY-5609 for a combination dosing cohort with atezolizumab in Roche's ongoing Phase 1/1b INTRINSIC trial, which is evaluating multiple targeted therapies or immunotherapy, including atezolizumab, as single agents or in rational specified combinations in molecularly defined subsets of colorectal cancer patients. SY-5609 is being evaluated in combination with atezolizumab in patients with BRAF-mutant disease, and this arm of the trial is now open for enrollment. Under the terms of the agreement, Roche will sponsor and conduct the Phase 1/1b study to evaluate the safety, tolerability and preliminary efficacy of the combination of SY-5609 and atezolizumab and will assume all costs associated with the study. In exchange for providing SY-5609, Syros will receive access to the data on SY-5609 in combination with atezolizumab. Syros retains all rights to SY-5609.

Merger Agreement and PIPE Financing

On July 3, 2022, Syros, Merger Sub and Tyme entered into the Merger Agreement. More information regarding the merger and the terms of the Merger Agreement are discussed throughout this joint proxy statement/prospectus, particularly in sections entitled "*The Merger*" and "*The Merger Agreement*".

Also on July 3, 2022, immediately prior to the execution and delivery of the Merger Agreement, Syros entered into the Securities Purchase Agreement with certain accredited investors, pursuant to which the investors agreed

to purchase (i) an aggregate of 138.1 million shares of Syros common stock and/or pre-funded warrants to purchase shares of Syros common stock and (ii) accompanying warrants to purchase an aggregate of up to 138.1 million additional shares of Syros common stock (or pre-funded warrants in lieu thereof), at a price per unit of $0.94 (or $0.9399 per unit comprising a pre-funded warrant and accompanying warrant). This private placement transaction is referred to as the PIPE Financing. More information regarding the Securities Purchase Agreement and the PIPE Financing are discussed throughout this joint proxy statement/prospectus, particularly in sections entitled "*Agreements Related to the Merger—Securities Purchase Agreement and Registration Rights Agreements*."

Financial Operations Overview

Revenue

To date, Syros has not generated any revenue from product sales and does not expect to generate any revenue from product sales for the foreseeable future. For the year ended December 31, 2021, Syros recognized $23.5 million of revenue, $19.4 million of which was related to its collaboration with GBT and $4.1 million of which was related to its target discovery collaboration with Incyte. For the year ended December 31, 2020, Syros recognized $15.1 million of revenue, $11.7 million of which was related to its collaboration with GBT and $3.4 million of which was related to its target discovery collaboration with Incyte. For the year ended December 31, 2019, Syros recognized $2.0 million of revenue, all of which was attributable to its collaboration agreement with Incyte.

For the three months ended March 31, 2022 and 2021, Syros recognized $5.5 million and $4.8 million of revenue, of which $5.1 million and $4.0 million was related to its collaboration with GBT and $0.4 million and $0.8 million to Syros' collaboration with Incyte, respectively.

Expenses

Research and Development Expenses

Research and development expenses consist primarily of costs incurred for Syros' research activities, including development of its gene control platform and the development of its product candidates, which include:

- employee-related expenses including salaries and benefits;
- stock-based compensation expense;
- external costs of funding activities performed by third parties that conduct research and development on Syros' behalf and of purchasing supplies used in designing, developing and manufacturing preclinical study and clinical trial materials;
- consulting, licensing and professional fees related to research and development activities; and
- facilities costs, depreciation and amortization and other expenses, which include direct and allocated expenses for rent and maintenance of facilities, insurance and other operating costs.

Research and development costs are expensed as incurred. Nonrefundable advance payments made to vendors for goods or services that will be received in the future for use in research and development activities are deferred and capitalized, even when there is no alternative future use for the research and development, until related goods or services are provided.

Syros typically uses its employee, consultant and infrastructure resources across its research and development programs. Syros tracks outsourced development costs by product candidate or development program, but it does not allocate personnel costs, other internal costs or certain external consultant costs to specific product candidates or development programs.

The following table summarizes Syros' external research and development expenses by program, as well as expenses not allocated to programs, for the years ended December 31, 2021, 2020 and 2019 (in thousands):

	Year Ended December 31,		
	2021	2020	2019
Tamibarotene external costs(1)	$ 30,670	$ 12,175	$ 7,076
SY-5609 and other CDK7 program external costs(1)(2)	11,452	11,229	15,992
SY-2101 program external costs(3)	3,947	12,062	—
Other research and platform program external costs	17,134	10,996	10,580
Employee-related expenses, including stock-based compensation	29,857	23,295	19,034
Facilities and other expenses	6,812	6,308	5,563
Total research and development expenses	$ 99,872	$ 76,065	$ 58,245

(1) The results for the year ended December 31, 2019 include credits of $1.9 million and $1.2 million for Syros' tamibarotene andSY-1365 clinical trials, respectively, due to a change in estimate of costs incurred over the life of these clinical trials through March 31, 2019.

(2) Syros' SY-1365 clinical trial costs are included within this caption as part of its CDK7 programs. In October 2019, Syros announced its decision to discontinue further development of SY-1365, which was completed during the year ended December 31, 2020.

(3) In December 2020, Syros acquired SY-2101, a product candidate in development for the treatment of APL, from Orsenix. In connection with this acquisition, Syros made an up-front payment of $12.0 million to Orsenix, which it recorded as research and development expenses.

The following table summarizes Syros' external research and development expenses by program, as well as expenses not allocated to programs, for the three months ended March 31, 2022 and 2021 (in thousands):

	Three Months Ended March 31,	
	2022	2021
Tamibarotene external costs	$ 6,096	$ 4,512
SY-5609 and other CDK7 program external costs	2,670	3,106
SY-2101 program external costs	1,662	767
Other research and platform program external costs	4,285	3,351
Employee-related expenses, including stock-based compensation	8,681	6,710
Facilities and other expenses	1,777	1,583
Total research and development expenses	$ 25,171	$ 20,029

Syros expects its research and development expenses will increase for the foreseeable future as it seeks to advance its programs. At this time, Syros cannot reasonably estimate or know the nature, timing and estimated costs of the efforts that will be necessary to complete the development of its product candidates. Syros is also unable to predict when, if ever, material net cash inflows will commence from sales of its product candidates. This is due to the numerous risks and uncertainties associated with developing such product candidates, including the uncertainty of:

- successful completion of preclinical studies, including activities related to preparation of investigational new drug applications, or INDs, and minimally efficacious dose studies in animals, where applicable and required, under the requirements of the FDA or another regulatory authority;
- approval of INDs for Syros' product candidates to commence planned or future clinical trials;

- successful enrollment in, and completion of, clinical trials;
- successful data from Syros' clinical programs that support an acceptable benefit-risk profile of its product candidates in the intended populations;
- successful development, and subsequent clearance or approval, of companion diagnostic tests for use in identifying potential patients;
- receipt of regulatory approvals from applicable regulatory authorities;
- establishment of arrangements with third-party manufacturers for clinical supply and commercial manufacturing and, where applicable, commercial manufacturing capabilities;
- establishment and maintenance of patent and trade secret protection or regulatory exclusivity for Syros' product candidates;
- commercial launch of Syros' product candidates, if and when approved, whether alone or in collaboration with others;
- enforcement and defense of IP rights and claims;
- maintenance of a continued acceptable safety profile of the product candidates following approval;
- retention of key research and development personnel; and
- the continuing impact of the COVID-19 pandemic.

Any changes in the outcome of any of these variables with respect to the development of Syros' product candidates in preclinical and clinical development could mean a significant change in the costs and timing associated with the development of these product candidates. For example, if the FDA or another regulatory authority were to delay Syros' planned start of clinical trials or require it to conduct clinical trials or other testing beyond those that Syros currently expects or if it experiences significant delays in enrollment in any of its planned clinical trials, Syros could be required to expend significant additional financial resources and time on the completion of clinical development of Syros' product candidates.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries and other related costs, including stock-based compensation, for personnel in executive, finance and administrative functions. Other significant costs include corporate facility costs not otherwise included in research and development expenses, legal fees related to patent and corporate matters, and fees for accounting and consulting services.

Syros anticipates that its general and administrative expenses will increase in the future as Syros increases its headcount to support its continued research activities and development of its product candidates.

Interest Income

Interest income consists of interest income on Syros' cash, cash equivalents, and investments in marketable securities, including the related amortization of premium and discounts.

Interest Expense

Interest expense consists of interest, amortization of debt discount, and amortization of deferred financing costs associated with Syros' loans payable, and interest on finance lease arrangements.

Change in Fair Value of Warrant Liability

Change in fair value of warrant liability is the result of the remeasurement of the fair value of Syros' warrant liability at each reporting period end.

Critical Accounting Policies and Estimates

Syros' management's discussion and analysis of its financial condition and results of operations are based on its financial statements, which have been prepared in accordance with GAAP. The preparation of these financial statements requires Syros to make judgments and estimates that affect the reported amounts of assets, liabilities, revenues and expenses and the disclosure of contingent assets and liabilities in Syros' financial statements. Syros bases its estimates on historical experience, known trends and events and various other factors that are believed to be reasonable under the circumstances. Actual results may differ from these estimates under different assumptions or conditions. On an ongoing basis, Syros evaluates its judgments and estimates in light of changes in circumstances, facts and experience. The effects of material revisions in estimates, if any, will be reflected in the financial statements prospectively from the date of the change in estimates.

While Syros' significant accounting policies are described in more detail in the notes to Syros' financial statements appearing elsewhere in this joint proxy statement/prospectus, Syros believes the following accounting policies used in the preparation of its financial statements require the most significant judgments and estimates.

Revenue

To date Syros' only revenue has consisted of collaboration and license revenue. Syros has not generated any revenue from product sales and does not expect to generate any revenue from product sales for the foreseeable future. For the year ended December 31, 2021, Syros recognized $23.5 million of revenue, $19.4 million of which was related to its collaboration with GBT and $4.1 million of which was related to Syros' target discovery collaboration with Incyte. For the year ended December 31, 2020, Syros recognized $15.1 million of revenue, $11.7 million of which was related to its collaboration with GBT and $3.4 million of which was related to its target discovery collaboration with Incyte. For the year ended December 31, 2019, Syros recognized $2.0 million of revenue, all of which was attributable to its target discovery collaboration with Incyte.

Syros recognizes revenue in conformity with Accounting Standards Codification, or ASC, *Revenue from Contracts with Customers,* or ASC 606. ASC 606 applies to all contracts with customers, except for contracts that are within the scope of other standards, such as leases, insurance, collaboration arrangements and financial instruments. Under ASC 606, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration the entity expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that an entity determines are within the scope of ASC 606, the entity performs the following five steps:

(i) identify the contract(s) with a customer;

(ii) identify the performance obligations in the contract;

(iii) determine the transaction price;

(iv) allocate the transaction price to the performance obligations in the contract; and

(v) recognize revenue when (or as) the entity satisfies a performance obligation.

Syros only applies the five-step model to contracts when it is probable that Syros will collect the consideration to which it is entitled in exchange for the goods or services Syros transfers to the customer. At contract inception, once the contract is determined to be within the scope of ASC 606, Syros assesses the goods or services promised within each contract and determine those that are performance obligations, and assess whether each promised good or service is distinct. Syros then recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied.

From time to time, Syros may enter into agreements that are within the scope of ASC 606. The terms of these arrangements typically include payment to Syros of one or more of the following: non-refundable, up-front license fees, prepaid research and development services, development, regulatory and commercial milestone

payments; and royalties on net sales of licensed products. Each of these payments would result in license and collaboration revenues, except for revenues from royalties on net sales of licensed products, which will be classified as royalty revenues.

Syros analyzes its collaboration arrangements to assess whether they are within the scope of ASC 808, *Collaborative Arrangements*, or ASC 808, to determine whether such arrangements involve joint operating activities performed by parties that are both active participants in the activities and exposed to significant risks and rewards dependent on the commercial success of such activities. This assessment is performed throughout the life of the arrangement based on changes in the responsibilities of all parties in the arrangement. For collaboration arrangements within the scope of ASC 808 that contain multiple elements, Syros first determines which elements of the collaboration are deemed to be within the scope of ASC 808 and those that are more reflective of a vendor-customer relationship and therefore within the scope of ASC 606. For elements of collaboration arrangements that are accounted for pursuant to ASC 808, an appropriate recognition method is determined and applied consistently, generally by analogy to ASC 606. For those elements of the arrangement that are accounted for pursuant to ASC 606, Syros applies the five-step model described above.

Research and Development Expenses

Expenditures relating to research and development are expensed in the period incurred. Research and development expenses consist of both internal and external costs associated with the development of Syros' gene control platform and product candidates. Research and development costs include salaries and benefits, materials and supplies, external research, preclinical and clinical development expenses, stock-based compensation expense and facilities costs. Facilities costs primarily include the allocation of rent, utilities, depreciation and amortization.

In certain circumstances, Syros is required to make nonrefundable advance payments to vendors for goods or services that will be received in the future for use in research and development activities. In such circumstances, the nonrefundable advance payments are deferred and capitalized, even when there is no alternative future use for the research and development, until related goods or services are provided.

Syros records accruals for estimated ongoing research costs. When evaluating the adequacy of the accrued liabilities, Syros analyzes progress of the work being performed, including the phase or completion of the event, invoices received and costs. Significant judgements and estimates may be made in determining the accrued balances at the end of any reporting period. Actual results could differ from Syros' estimates.

Syros may in-license the rights to develop and commercialize product candidates. For each in-license transaction, Syros evaluates whether it has acquired processes or activities along with inputs that would be sufficient to constitute a "business" as defined under U.S. GAAP. A "business" as defined under U.S. GAAP consists of inputs and processes applied to those inputs that have the ability to create outputs. Although businesses usually have outputs, outputs are not required for an integrated set of activities to qualify as a business. When Syros determines that it has not acquired sufficient processes or activities to constitute a business, any up-front payments, as well as milestone payments, are immediately expensed as acquired research and development in the period in which they are incurred.

Warrants

Syros accounts for its issued warrants as either liability or equity in accordance with ASC 480-10, *Accounting for Certain Financial Instruments with Characteristics of both Liabilities and Equity*, or ASC 480-10, or ASC 815-40, *Accounting for Derivative Financial Instruments Indexed to, and Potentially Settled in, a Company's Own Stock, or* ASC 815-40. Under ASC 480-10, warrants are considered liability if they are mandatorily redeemable and they require settlement in cash or other assets, or a variable number of shares. If warrants do not meet liability classification under ASC 480-10, Syros considers the requirements of ASC 815-40

to determine whether the warrants should be classified as liability or equity. Under ASC 815-40, contracts that may require settlement for cash are liabilities, regardless of the probability of the occurrence of the triggering event. Liability classified warrants are measured at fair value on the issuance date and at the end of each reporting period. Any change in the fair value of the warrants after the issuance date is recorded in the consolidated statements of operations as a gain or loss. If warrants do not require liability classification under ASC 815-40, in order to conclude warrants should be classified as equity, the Company assesses whether the warrants are indexed to its common stock and whether the warrants are classified as equity under ASC 815-40 or other applicable GAAP. Equity classified warrants are accounted for at fair value on the issuance date with no changes in fair value recognized after the issuance date.

On December 8, 2020, through a private placement, Syros issued 10,312,500 shares of Syros common stock and, in lieu of common stockpre-funded warrants to purchase an aggregate of 1,000,000 shares of common stock, and, in each case, accompanying warrants to purchase an aggregate of up to 2,828,125 additional shares of common stock (or pre-funded warrants to purchase common stock in lieu thereof) at a price of $8.00 per share and accompanying warrant (or $7.99 per pre-funded warrant and accompanying warrant). The private placement resulted in aggregate gross proceeds of $90.5 million, before $0.4 million of transaction costs.

In the event of certain fundamental transactions, the holders of warrants may require us to make a payment based on a Black-Scholes valuation, using specified inputs. The holders of the pre-funded warrants issued in the December 2020 private placement do not have similar rights. Therefore, Syros accounted for the warrants as a liability, while the pre-funded warrants met the permanent equity criteria classification. Thepre-funded warrants are classified as a component of permanent equity because they are freestanding financial instruments that are legally detachable and separately exercisable from the shares of common stock with which they were issued, are immediately exercisable, do not embody an obligation for Syros to repurchase those shares, and permit the holders to receive a fixed number of shares of common stock upon exercise. In addition, the Pre-Funded Warrants do not provide any guarantee of value or return. The initial fair value of the warrants at issuance was $19.3 million, determined using Black-Scholes valuation model. Syros remeasured the warrant's fair value at December 31, 2021 and 2020 as $3.0 million and $19.7 million, respectively. The change in fair value of $16.7 million (loss) and $0.4 million (gain) was recorded in Syros' consolidated statement of operations for the years ended December 31, 2021 and 2020, respectively.

Stock-Based Compensation

Syros accounts for its stock-based compensation awards in accordance with ASC 718,*Compensation—Stock Compensation*, or ASC 718. ASC 718 requires all stock-based payments to employees, directors and non-employees, including grants of restricted stock units and stock option awards, to be recognized as expense in the consolidated statements of operations based on their grant date fair values. Syros estimates the fair value of stock options granted using the Black-Scholes option-pricing model. Prior to June 30, 2016, Syros was a private company and, therefore, lack company-specific historical and implied volatility information. As a result, Syros estimates its expected stock volatility based on a combination of Syros' historical volatility and that of a publicly traded set of peer companies. Syros expects to continue to do so until such time as it has adequate historical data regarding the volatility of its own traded stock price. The expected term of Syros' stock options granted to employees has been determined utilizing the "simplified" method for awards that qualify as "plain-vanilla" options. Syros uses the contractual term in determining the expected term of stock option to non-employees. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the time of grant of the award for time periods approximately equal to the expected term of the award. Expected dividend yield is based on the fact that Syros has never paid cash dividends and do not expect to pay any cash dividends in the foreseeable future. Syros uses the value of its common stock to determine the fair value of restricted stock awards.

Syros expenses the fair value of its stock-based awards to employees and non-employees on a straight-line basis over the associated service period, which is generally the vesting period. Syros accounts for forfeitures as they

occur instead of estimating forfeitures at the time of grant. Ultimately, the actual expense recognized over the vesting period will be for only those options that vest.

Compensation expense for discounted purchases under the employee stock purchase plan is measured using the Black-Scholes model to compute the fair value of the lookback provision plus the purchase discount and is recognized as compensation expense over the offering period.

For stock-based awards that contain performance-based milestones, Syros records stock-based compensation expense in accordance with the accelerated attribution model. Management evaluates when the achievement of a performance-based milestone is probable based on the expected satisfaction of the performance conditions as of the reporting date. For certain of Syros' performance-based awards, notwithstanding any vesting in accordance with the achievement of performance-based milestones, such awards vest in full on the sixth anniversary of the vesting commencement date. Compensation expense for such awards is recognized over the six-year vesting period unless management determines that the achievement of any performance-based milestones is probable, in which case expense is accelerated. Compensation expense related to these awards were all recognized as of December 31, 2020 as the performance-based milestones were achieved.

Syros has computed the fair value of stock options at the date of grant using the following weighted-average assumptions:

	Year Ended December 31,		
	2021	2020	2019
Weighted-average risk-free interest rate	0.99%	1.28%	2.42%
Expected dividend yield	— %	— %	— %
Expected option term (in years)	6.03	5.99	6.00
Volatility	81.56%	78.27%	91.35%

Results of Operations

Comparison of Years Ended December 31, 2021 and 2020

The following table summarizes Syros' results of operations for the years ended December 31, 2021 and 2020, together with the changes in those items in dollars (in thousands):

	Year Ended December 31,			
	2021	2020	Dollar Change	% Change
Statements of Operations Data:				
Revenue	$ 23,488	$ 15,093	$ 8,395	56%
Operating expenses:				
Research and development	99,872	76,065	23,807	31%
General and administrative	23,036	21,325	1,711	8%
Total operating expenses	122,908	97,390	25,518	26%
Loss from operations	(99,420)	(82,297)	(17,123)	21%
Interest income	87	426	(339)	(80)%
Interest expense	(3,907)	(1,792)	(2,115)	118%
Change in fair value of warrant liability	16,682	(375)	17,057	(4,549)%
Net loss	$ (86,558)	$(84,038)	$ (2,520)	3%

Revenue

For the year ended December 31, 2021, Syros recognized approximately $23.5 million of revenue, $19.4 million of which was attributable to its collaboration with GBT and $4.1 million of which was attributable to its target

discovery collaboration with Incyte. For the year ended December 31, 2020, Syros recognized $15.1 million of revenue, $11.7 million of which was attributable to its collaboration with GBT and $3.4 million of which was attributable to its target discovery collaboration with Incyte.

Research and Development Expense

Research and development expense increased by approximately $23.8 million, or 31%, from $76.1 million for the year ended December 31, 2020 to $99.9 million for the year ended December 31, 2021. The following table summarizes Syros' research and development expenses for the years ended December 31, 2021 and 2020, together with the changes to those items in dollars (in thousands):

	Year Ended December 31,			
	2021	2020	Dollar Change	% Change
External research and development	$56,809	$42,981	$ 13,828	32%
Employee-related expenses, excluding stock-based compensation	24,151	18,563	5,588	30%
Stock-based compensation	5,706	4,732	974	21%
Consulting, licensing and professional fees	6,394	3,481	2,913	84%
Facilities and other expenses	6,812	6,308	504	8%
Total research and development expenses	$99,872	$76,065	$ 23,807	31%

The change in research and development expense was primarily attributable to research and development activities associated with advancing Syros' lead clinical and preclinical programs and enhancing its internal capabilities, and included the following:

- an increase of approximately $13.8 million, or 32%, in external research and development, primarily attributable to the increases in costs associated with the continued advancement of Syros' existing clinical trials of tamibarotene, SY-2101 and SY-5609 and advancement of its preclinical programs, including its sickle cell disease development activities in collaboration with GBT;
- an increase of approximately $5.6 million, or 30%, for employee-related expenses, including increased salary and benefits primarily due to Syros' increased headcount;
- an increase of approximately $2.9M, or 84%, for consulting, licensing and professional fees, primarily related to the advancement of Syros' clinical and pre-clinical programs;
- an increase of approximately $1.0 million, or 21%, for stock-based compensation, also primarily due to Syros' increased headcount;and
- an increase of approximately $0.5 million, or 8%, in facilities and other expenses primarily due to the rent expense related to the lease for Syros' headquarters.

General and Administrative Expense

General and administrative expense increased by approximately $1.7 million, or 8%, from $21.3 million for the year ended December 31, 2020 to $23.0 million for the year ended December 31, 2021. The change in general and administrative expense was primarily attributable to an increase in employee-related expenses driven by increased headcount, COVID-19 testing expenses incurred by Syros to support the health and safety of its employees, an increase in legal costs including patent prosecution expenses, and an increase in consulting fees.

Interest Income

Interest income was derived from Syros' investments in cash, cash equivalents and marketable securities. The decrease in interest income during the year ended December 31, 2021 as compared to the year ended

December 31, 2020 was due to lower yield on Syros' investments in cash, cash equivalents and marketable securities due to capital market conditions during the year ended December 31, 2021.

Interest Expense

Interest expense was related to Syros' credit facility with Oxford and equipment financing arrangements. The increase in interest expense during the year ended December 31, 2021 as compared to the year ended December 31, 2020 was driven by a higher average outstanding balance of Syros' credit facility with Oxford during the year ended December 31, 2021 compared to the year ended December 31, 2020.

Change in Fair Value of Warrant Liability

The increase in the change in fair value of warrant liability during the year ended December 31, 2021 as compared to the year ended December 31, 2020 was a result of the remeasurement of the fair values of warrants issued in connection with the private placement financing in December 2020.

Comparison of Years Ended December 31, 2020 and 2019

The following table summarizes Syros' results of operations for the years ended December 31, 2020 and 2019, together with the changes in those items in dollars (in thousands):

	Year Ended December 31,			
	2020	2019	Dollar Change	% Change
Statements of Operations Data:				
Revenue	$ 15,093	$ 1,982	$ 13,111	662%
Operating expenses:				
Research and development	76,065	58,245	17,820	31%
General and administrative	21,325	21,478	(153)	(1)%
Total operating expenses	97,390	79,723	17,667	22%
Loss from operations	(82,297)	(77,741)	(4,556)	6%
Interest income	426	2,375	(1,949)	(82)%
Interest expense	(1,792)	(72)	(1,720)	2,389%
Change in fair value of warrant liability	(375)	—	(375)	100%
Net loss	$(84,038)	$(75,438)	$ (8,600)	11%

Revenue

For the year ended December 31, 2020, Syros recognized approximately $15.1 million of revenue, $11.7 million of which was attributable to its collaboration with GBT and $3.4 million of which was attributable to its target discovery collaboration with Incyte. For the year ended December 31, 2019, Syros recognized $2.0 million of revenue, all of which was attributable to its target discovery collaboration with Incyte.

Research and Development Expense

Research and development expense increased by approximately $17.8 million, or 31%, from $58.2 million for the year ended December 31, 2019 to $76.1 million for the year ended December 31, 2020. The following table

summarizes Syros' research and development expenses for the years ended December 31, 2020 and 2019, together with the changes to those items in dollars (in thousands):

	Year Ended December 31,			
	2020	2019	Dollar Change	% Change
External research and development	$42,981	$30,129	$ 12,852	43%
Employee-related expenses, excluding stock-based compensation	18,563	15,561	3,002	19%
Stock-based compensation	4,732	3,472	1,260	36%
Consulting, licensing and professional fees	3,481	3,520	(39)	(1)%
Facilities and other expenses	6,308	5,563	745	13%
Total research and development expenses	$76,065	$58,245	$ 17,820	31%

The change in research and development expense was primarily attributable to research and development activities associated with advancing Syros' lead clinical and preclinical programs and enhancing its internal capabilities, and included the following:

- an increase of approximately $12.9 million, or 43%, in external research and development, primarily attributable to the $12.0 million paid to Orsenix for the acquisition of the SY-2101, and due to the increases in costs associated with the continued advancement of Syros' existing clinical trials of SY-5609 and tamibarotene and advancement of its preclinical programs, including its sickle cell disease development activities in collaboration with GBT;
- an increase of approximately $3.0 million, or 19%, for employee-related expenses, including increased salary and benefits primarily due to Syros' increased headcount;
- an increase of approximately $1.3 million, or 36%, for stock-based compensation, also primarily due to Syros' increased headcount;and
- an increase of approximately $0.7 million, or 13%, in facilities and other expenses primarily due to the rent expense related to the lease for Syros' headquarters, over which it took possession for accounting purposes in May 2019.

General and Administrative Expense

General and administrative expense remained consistent during the year ended December 31, 2020 when compared to the year ended December 31, 2019. A slight decrease in consulting and outside services fees led to a decrease in general and administrative expense of approximately $0.2 million, or 1%, from $21.5 million for the year ended December 31, 2019 to $21.3 million for the year ended December 31, 2020.

Interest Income

Interest income was derived from Syros' investments in cash equivalents and marketable securities. The decrease in interest income during the year ended December 31, 2020 as compared to the year ended December 31, 2019 was due to lower yield on Syros' investments in cash, cash equivalents and marketable securities due to capital market conditions in light of the COVID-19 pandemic during the majority of the year ended December 31, 2020.

Interest Expense

Interest expense was related to Syros' credit facility with Oxford and equipment financing arrangements. The increase in interest expense during the year ended December 31, 2020 as compared to the year ended December 31, 2019 was driven by proceeds of $39.6 million, net of issuance costs, from Syros' credit facility with Oxford, which was drawn in two tranches in February 2020 and December 2020.

Change in Fair Value of Warrant Liability

The increase in the change in fair value of warrant liability during the year ended December 31, 2020 as compared to the year ended December 31, 2019 was a result of the remeasurement of the fair values of warrants issued in connection with the private placement financing in December 2020.

Comparison of three months ended March 31, 2022 and 2021

The following table summarizes Syros' results of operations for the three months ended March 31, 2022 and 2021, together with the changes in those items in dollars (in thousands):

	Three Months Ended March 31,			
	2022	2021	Dollar Change	% Change
Statements of Operations Data:				
Revenue	$ 5,467	$ 4,827	$ 640	13%
Operating expenses:				
Research and development	25,171	20,029	5,142	26%
General and administrative	6,949	5,739	1,210	21%
Total operating expenses	32,120	25,768	6,352	25%
Loss from operations	(26,653)	(20,941)	(5,712)	27%
Interest income	35	10	25	250%
Interest expense	(976)	(967)	(9)	1%
Change in fair value of warrant liability	2,448	7,670	(5,222)	(68)%
Net loss	$(25,146)	$(14,228)	$ (10,918)	77%

Revenue

For the three months ended March 31, 2022, revenue was $5.5 million, of which $5.1 million was attributable to Syros' collaboration with GBT and $0.4 million was attributable to Syros' collaboration with Incyte. For the three months ended March 31, 2021, revenue was $4.8 million, of which $4.0 million was attributable to Syros' collaboration with GBT and $0.8 million was attributable to Syros' collaboration with Incyte.

Research and Development Expense

Research and development expense increased by approximately $5.1 million, or 26%, from $20.0 million for the three months ended March 31, 2021 to $25.2 million for the three months ended March 31, 2022. The following table summarizes Syros' research and development expenses for the three months ended March 31, 2022 and 2021, together with the changes to those items in dollars (in thousands):

	Three Months Ended March 31,			
	2022	2021	Dollar Change	% Change
External research and development	$13,099	$10,806	$ 2,293	21%
Employee-related expenses, excluding stock-based compensation	7,286	5,386	1,900	35%
Stock-based compensation	1,395	1,324	71	5%
Consulting, licensing and professional fees	1,614	931	683	73%
Facilities and other expenses	1,777	1,582	195	12%
Total research and development expenses	$25,171	$20,029	$ 5,142	26%

The change in research and development expense was primarily attributable to activities associated with advancing Syros' clinical and preclinical programs as well as enhancing its internal capabilities, including the following:

- an increase of approximately $2.3 million, or 21%, for external research and development costs, primarily due to increases in costs associated with the continued advancement of Syros' existing clinical trials of tamibarotene, SY-2101 and SY-5609, and advancement of Syros' preclinical programs, including its sickle cell disease development activities in collaboration with GBT;
- an increase of approximately $1.9 million, or 35%, for employee-related expenses, including increased salary and benefits, primarily due to Syros' increased headcount;
- an increase of approximately $0.7 million, or 74%, for consulting, licensing and professional fees, primarily related to the advancement of Syros' clinical and pre-clinical programs; and
- an increase of approximately $0.2 million, or 12%, for facilities and other expenses, primarily due to Syros' increased headcount.

General and Administrative Expense

General and administrative expense increased by approximately $1.2 million, or 21%, from $5.7 million for the three months ended March 31, 2021 to $6.9 million for the three months ended March 31, 2022. The change in general and administrative expense was primarily attributable to an increase in employee-related expenses driven by increased headcount, an increase in legal costs including patent prosecution expenses, and an increase in consulting fees.

Interest Income

Interest income was derived generally from Syros' investments in cash, cash equivalents, and marketable securities. The increase in interest income during the three months ended March 31, 2022 as compared to the three months ended March 31, 2021 was due to an increase in Syros' investments in these securities during the period ended March 31, 2022.

Interest Expense

Interest expense was related to Syros' credit facility with Oxford and equipment financing arrangements. Interest expense increased slightly from the three months ended March 31, 2021 to the three months ended March 31, 2022. The increase in interest expense during the three months ended March 31, 2022 as compared to the three months ended March 31, 2021 was driven by a higher average outstanding credit facility balance during the three months ended March 31, 2022.

Change in Fair Value of Warrant Liability

The change in fair value of warrant liability during the three months ended March 31, 2022 as compared to the three months ended March 31, 2021 was a result of the remeasurement of the fair value of warrants issued in connection with the December 2020 private placement.

Liquidity and Capital Resources

Sources of Liquidity

Syros funded its operations from inception through March 31, 2022, primarily through the sale of equity securities, through license and collaboration agreements, including those with Incyte and GBT, and through the credit facility with Oxford.

On February 12, 2020, Syros entered into the Loan Agreement with Oxford. Pursuant to the Loan Agreement, a term loan of up to an aggregate principal amount of $60.0 million is available to Syros. A $20.0 million term loan was funded on February 12, 2020, and another $20.0 million term loan was funded on December 23, 2020. As of March 31, 2022, $20.0 million remains available under the Loan Agreement at the sole discretion of Oxford.

On June 12, 2020, Syros filed a universal shelf registration statement on FormS-3 with the SEC to register for sale from time to time up to $300.0 million of common stock, preferred stock, debt securities, warrants and/or units in one or more registered offerings. The registration statement was declared effective on June 22, 2020. Further, in June 2020, Syros entered into an at-the-market sales agreement, or the sales agreement, with Cowen & Co., or Cowen, pursuant to which Syros may offer and sell shares of Syros common stock having an aggregate offering price of up to $75.0 million through Cowen pursuant to the registration statement. In January 2021, Syros issued shares of its common stock in an underwritten public offering resulting in gross proceeds of $75.6 million, before deducting underwriting discounts and commissions and other transaction expenses of approximately $5.1 million, pursuant to the Form S-3 that was filed with the SEC on June 12, 2020.

As of March 31, 2022, $75.0 million in common stock remained available for future issuance under the sales agreement.

As of March 31, 2022, $224.4 million of securities remained available for future issuance under the shelf registration statement.

As of March 31, 2022, Syros had cash, cash equivalents, and marketable securities of approximately $112.9 million.

Cash Flows

Years Ended December 2021, 2020 and 2019

The following table provides information regarding Syros' cash flows for the years ended December 31, 2021, 2020 and 2019 (in thousands):

	Year Ended December 31,		
	2021	2020	2019
Net cash (used in) provided by:			
Operating activities	$(99,540)	$ (57,364)	$(60,253)
Investing activities	(52,653)	46,664	(11,734)
Financing activities	70,511	142,953	65,990
Net (decrease) increase in cash, cash equivalents and restricted cash	$(81,682)	$132,253	$ (5,997)

Net Cash Used in Operating Activities

The use of cash in all periods presented resulted primarily from Syros' net losses adjusted fornon-cash charges and changes in components of working capital.

Net cash used in operating activities was $99.5 million during the year ended December 31, 2021, compared to $57.4 million during the year ended December 31, 2020. The increase in cash used in operating activities was primarily due to a $17.1 million increase in loss from operations during the year ended December 31, 2021 and a $20.0 million collection of the advanced payment pursuant to Syros' collaboration agreement with GBT during the year ended December 31, 2020, which did not recur during the year ended December 31, 2021.

Net cash used in operating activities was $57.4 million during the year ended December 31, 2020, compared to $60.3 million during the year ended December 31, 2019. The decrease in cash used in operating activities was primarily due to a $20.0 million collection of the advanced payment pursuant to Syros' collaboration agreement with GBT, offset by higher operating expenses associated with Syros' ongoing preclinical and clinical development activities and the asset acquisition of SY-2101 during the year ended December 31, 2020.

Net Cash (Used in) Provided by Investing Activities

Net cash used in investing activities was $52.7 million during the year ended December 31, 2021, compared to net cash provided by investing activities of $46.7 million during the year ended December 31, 2020. The net cash used in investing activities during the year ended December 31, 2021 was primarily due to Syros' reinvestment of $51.4 million of its funds from cash equivalents into marketable securities and the purchase of $1.2 million of property and equipment. Net cash provided by investing activities during the year ended December 31, 2020 was primarily due to Syros' reinvestment of $50.0 million of its funds from marketable securities upon their maturities into cash equivalents, partially offset by its $3.3 million purchase of property and equipment.

Net cash provided by investing activities was $46.7 million during the year ended December 31, 2020, compared to net cash used in investing activities of $11.7 million during the year ended December 31, 2019. The change in net cash provided by investing activities was primarily due to Syros' reinvestment of $50.0 million of our funds from marketable securities upon their maturities into cash equivalents during the year ended December 31, 2020, and its purchase of $12.6 million of property and equipment for the buildout of its corporate headquarters during the year ended December 31, 2019.

Net Cash Provided by Financing Activities

Net cash provided by financing activities was $70.5 million during the year ended December 31, 2021, compared to net cash provided by financing activities of $143.0 million during the year ended December 31, 2020. Cash provided by financing activities for the year ended December 31, 2021 was the result of net proceeds of $70.3 million from an underwritten public offering of shares of Syros common stock, $0.2 million from the issuance of shares of Syros common stock through its 2016 Stock Incentive Plan and $0.3 million from the issuance of Syros common stock through its employee stock purchase plan, offset by payments of $0.3 million under its capital lease obligations. Cash provided by financing activities for year ended December 31, 2020 of $143.0 million was the result of net proceeds of $39.6 million drawn from Syros' credit facility with Oxford, $90.4 million from the issuance of securities in the December 2020 private placement, $11.9 million from the issuance of shares of Syros common stock pursuant to the 2017 sales agreement, $1.1 million from the issuance of shares of Syros common stock through its 2015 Stock Incentive Plan and $0.4 million from issuance of common stock through its employee stock purchase plan, offset by payments of $0.2 million under its capital lease obligations and payments of $0.2 million of offering costs.

Net cash provided by financing activities was $143.0 million during the year ended December 31, 2020, compared to net cash provided by financing activities of $66.0 million during the year ended December 31, 2019. Cash provided by financing activities for the year ended December 31, 2020 was the result of net proceeds of $39.6 million drawn from Syros' credit facility with Oxford, $90.4 million from the issuance of securities in the December 2020 private placement, $11.9 million from the issuance of shares of Syros common stock pursuant to the 2017 sales agreement, $1.1 million from the issuance of shares of Syros common stock through its 2016 Stock Incentive Plan and $0.4 million from issuance of common stock through its employee stock purchase plan, offset by payments of $0.2 million under Syros' capital lease obligations and payments of $0.2 million of offering costs. Cash provided by financing activities for year ended December 31, 2019 of $66.0 million was primarily due to $65.0 million in net proceeds raised through two concurrent public offerings of equity securities that closed in April 2019.

Material Cash Requirements from Known Contractual Obligations

Syros' material cash requirements from known contractual obligations as of December 31, 2021 consisted of:

- Principal and interest payments under our loan and security agreement with Oxford. For additional information regarding the terms of the debt and interest payable, see Note 7 to the consolidated financial statements in Item 8 of Syros' Annual Report on Form 10-K for the year ended December 31, 2021.
- Operating lease liabilities with respect to Syros' lease of approximately 52,859 square feet of space in Cambridge, Massachusetts for a lease term ending in February 2030. For additional information regarding the terms of this operating lease, see Note 10 to the consolidated financial statements in Item 8 of Syros' Annual Report on Form 10-K for the year ended December 31, 2021.
- Contingent milestone obligations that may become payable pursuant to the asset purchase agreement with Orsenix. For additional information regarding these contingent milestone obligations, see Note 10 to the consolidated financial statements in Item 8 of Syros' Annual Report on Form 10-K for the year ended December 31, 2021.
- Obligations pursuant to our license agreement and supply management agreement with TMRC. For additional information regarding these obligations, see Note 10 to the consolidated financial statements in Item 8 of Syros' Annual Report on Form 10-K for the year ended December 31, 2021.

Three Months Ended March 31, 2022 and 2021

The following table provides information regarding Syros' cash flows for the three months ended March 31, 2022 and 2021 (in thousands):

	Three Months Ended March 31,	
	2022	2021
Net cash (used in) provided by:		
Operating activities	$(30,017)	$(21,990)
Investing activities	7,383	(262)
Financing activities	(93)	70,410
Net (decrease) increase in cash, cash equivalents and restricted cash	$(22,727)	$ 48,158

Net Cash Used in Operating Activities

Net cash used in operating activities for the three months ended March 31, 2022 and 2021 resulted primarily from Syros' net losses adjusted for non-cash charges and changes in components of working capital.

Net cash used in operating activities was $30.0 million during the three months ended March 31, 2022 compared to $22.0 million for the three months ended March 31, 2021. The increase in net cash used in operating activities during the three months ended March 31, 2022 was primarily due to $5.9 million increase in loss from operations and $2.1 million increase in net operating assets during the three months ended March 31, 2022.

Net Cash Provided by (Used in) Investing Activities

Net cash provided by investing activities was $7.4 million during the three months ended March 31, 2022 compared to net cash used in investing activities of $0.3 million during the three months ended March 31, 2021. The increase in net cash provided by investing activities was primarily due to maturities of marketable securities of $7.5 million, offset by the purchase of $0.1 million of property and equipment during the three months ended March 31, 2022, as compared to the decrease in net cash used in investing activities due to the $0.3 million purchase of property and equipment during the three months ended March 31, 2021.

Net Cash (Used in) Provided by Financing Activities

Net cash used in financing activities was $0.1 million during the three months ended March 31, 2022 compared to net cash provided by financing activities of $70.4 million for the three months ended March 31, 2021. Cash used in financing activities for the three months ended March 31, 2022 was primarily due to $0.1 million of payments made under Syros' financing lease. In comparison, the cash provided by financing activities for the three months ended March 31, 2021 was primarily due to net proceeds of $70.4 million from a public offering of shares of Syros common stock, and $0.2 million of proceeds from the exercise of stock options, offset by $0.1 million of payments made under Syros' financing lease.

Funding Requirements and Going Concern

Syros expects its expenses to increase in connection with its ongoing activities, particularly as Syros continues to advance its clinical trials of tamibarotene, SY-2101 and SY-5609, seek to develop companion diagnostic tests for use with its product candidates, initiate new research and preclinical development projects and seek marketing approval for any product candidates that Syros successfully develops. In addition, if Syros obtains marketing approval for any of its product candidates, Syros expects to incur significant commercialization expenses related to establishing sales, marketing, distribution and other commercial infrastructure to commercialize such products. Syros will need to obtain substantial additional funding in connection with its continuing operations. If Syros is unable to raise capital when needed or on favorable terms, Syros would be forced to delay, reduce, eliminate, or out-license its research and development programs or future commercialization rights to its product candidates.

Syros future funding requirements, both short-term and long-term, will depend on many factors, including:

- the scope, progress, timing, costs and results of clinical trials of tamibarotene,SY-2101 and SY-5609 and any associated companion diagnostic tests;
- research and preclinical development efforts for any future product candidates that Syros may develop;
- the number of future product candidates that Syros pursues and their development requirements;
- Syros' ability to enter into, and the terms and timing of, any collaborations, licensing agreements or other arrangements;
- whether a drug candidate will be nominated to enter investigational new drug application-enabling studies under Syros' sickle cell disease collaboration with GBT, whether GBT will exercise its option to exclusively license IP arising from the collaboration, whether and when any option exercise fees, milestone payments or royalties under the collaboration agreement with GBT will ever be paid, and whether Syros exercises its U.S. co-promotion option under the GBT agreement;
- whether Syros' target discovery collaboration with Incyte will yield any validated targets, whether Incyte will exercise any of its options to exclusively license IP directed to such targets, and whether and when any of the target validation fees, option exercise fees, milestone payments or royalties under the collaboration agreement with Incyte will ever be paid;
- the outcome, timing and costs of seeking regulatory approvals;
- the costs of commercialization activities for any of Syros' product candidates that receive marketing approval to the extent such costs are not the responsibility of any future collaborators, including the costs and timing of establishing product sales, marketing, distribution and manufacturing capabilities;
- the costs of acquiring potential new product candidates or technology;
- the costs of any physician education programs relating to selecting and treating genomically defined patient populations;
- the timing and amount of milestone and other payments due to licensors for patent and technology rights used in Syros' gene control platform or to TMRC associated with the development, manufacture and commercialization of tamibarotene;

- the timing and amount of milestone payments due to Orsenix associated with the development and commercialization ofSY-2101;
- revenue received from commercial sales, if any, of Syros' current and future product candidates;
- Syros' headcount growth and associated costs as Syros advances its research and development programs and establish a commercial infrastructure;
- the costs of preparing, filing and prosecuting patent applications, maintaining and protecting Syros' IP rights and defending against IP related claims; and
- the continuing impact of the COVID-19 pandemic.

Identifying potential product candidates and conducting preclinical studies and clinical trials is a time-consuming, expensive and uncertain process that takes many years to complete, and Syros may never generate the necessary data or results required to obtain marketing approval and achieve product sales. In addition, Syros' product candidates, if approved, may not achieve commercial success. Accordingly, Syros will need to continue to rely on additional financing to achieve its business objectives. Adequate additional financing may not be available to Syros on acceptable terms, or at all.

Until such time, if ever, as Syros can generate substantial product revenues, Syros expects to finance its cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances and licensing arrangements. To the extent that Syros raises additional capital through the sale of equity or convertible debt securities, the ownership interests of Syros common stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of Syros' common stockholders. Debt financing, if available, may involve agreements that include covenants limiting or restricting Syros' ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends.

If Syros raises funds through additional collaborations, strategic alliances or licensing arrangements with third parties, Syros may have to relinquish valuable rights to its technologies, future revenue streams, research programs or product candidates or to grant licenses on terms that may not be favorable to it. If Syros is unable to raise additional funds through equity or debt financings when needed, Syros may be required to delay, limit, reduce or terminate its product development or future commercialization efforts or grant rights to develop and market product candidates that Syros would otherwise prefer to develop and market itself.

Syros has incurred significant net operating losses in every year since its inception. Syros expects to continue to incur significant and increasing net operating losses for at least the next several years. Syros' net losses were $86.6 million, $84.0 million and $75.4 million for the years ended December 31, 2021, 2020 and 2019, respectively. As of March 31, 2022, Syros had an accumulated deficit of $488.7 million. Syros has not generated any revenues from product sales, has not completed the development of any product candidate and may never have a product candidate approved for commercialization. Syros has financed its operations to date primarily through a credit facility, the sale of equity securities and through license and collaboration agreements. Syros has devoted substantially all of its financial resources and efforts to research and development and general and administrative expense to support such research and development. Syros' net losses may fluctuate significantly from quarter to quarter and year to year. Net losses and negative cash flows have had, and will continue to have, an adverse effect on Syros' stockholders' equity and working capital.

As discussed in Note 1 of the Notes to the Condensed Consolidated Financial Statements in Syros' Quarterly Report on Form10-Q for the period ended March 31, 2022, under ASC Topic 205-40, *Presentation of Financial Statements—Going Concern*, management is required at each reporting period to evaluate whether there are conditions and events, considered in the aggregate, that raise substantial doubt about an entity's ability to continue as a going concern within one year after the date that the financial statements are issued. This evaluation initially does not take into consideration the potential mitigating effect of management's plans that have not been fully implemented as of the date the financial statements are issued.

Based on Syros' current operating plan, it anticipates that its cash, cash equivalents and marketable securities of $112.9 million as of March 31, 2022 will allow Syros to meet its liquidity requirements into the second quarter of 2023. Syros' history of significant losses, its negative cash flows from operations, its limited liquidity resources currently on hand, and its dependence on its ability to obtain additional financing to fund its operations after the current resources are exhausted, about which there can be no certainty, have resulted in Syros' assessment that there is substantial doubt about its ability to continue as a going concern for a period of at least twelve months from the issuance date of this joint proxy statement/prospectus. Syros has plans in place to mitigate this risk, which primarily consist of raising additional capital through a combination of equity or debt financings and potential new collaborations and reducing cash expenditures. Following the closing of the merger, PIPE Financing and Loan Amendment, the total cash balance of the combined company is expected to be approximately $240 million (after transaction expenses), which Syros believes will be sufficient to fund its planned operating expenses and capital expenditure requirements into 2025, allowing it to advance its late-stage clinical programs toward commercialization, including tamibarotene, currently being studied in the SELECT-MDS-1 trial and the randomized portion of the SELECT-AML-1 trial, and SY-2101, which it plans to advance into a Phase 3 trial for the treatment of APL in the second half of 2023. There is no guarantee that these transactions will close as planned or that Syros will be successful in any other capital raising efforts, in which case, Syros may not be able to continue its research and development programs as planned.

QUALITATIVE AND QUANTITATIVE DISCLOSURE ABOUT THE MARKET RISK OF SYROS

Syros is exposed to market risk related to changes in interest rates. Its primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates, particularly because its investments, including cash equivalents, are in the form of money market funds and marketable securities and are invested in U.S. treasury or government obligations. However, because of the short-term nature of the duration of Syros' portfolio and the low-risk profile of its investments, Syros believes an immediate 10% change in market interest rates would not be expected to have a material impact on the fair market value of its investments portfolio or on its financial condition or results of operations.

Syros is also exposed to market risk related to changes in foreign currency exchange rates. Syros contracts with vendors that are located in Asia and Europe and certain invoices are denominated in foreign currencies. Syros is subject to fluctuations in foreign currency rates in connection with these arrangements. Syros does not currently hedge its foreign currency exchange rate risk. As of December 31, 2021, Syros had no significant liabilities denominated in foreign currencies.

Inflation generally affects Syros by increasing its cost of labor and clinical trial costs. Syros does not believe that inflation had a material effect on its business, financial condition or results of operations during the year ended December 31, 2021.

You should read the following discussion and analysis of Tyme's financial condition and results of operations together with our financial statements and related notes appearing in this joint proxy statement/prospectus. Some of the information contained in this discussion and analysis or set forth elsewhere in this joint proxy statement/prospectus, including information with respect to our plans and strategy for our business, includes forward-looking statements that involve risks and uncertainties. As a result of many factors, including those factors set forth in the "Risk Factors" section of this joint proxy statement/prospectus, our actual results could differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

Overview

Tyme is an emerging biotechnology company developing CMBTs that are intended to be effective across a broad range of solid tumors and hematologic cancers, while also maintaining patients' quality of life through relatively low toxicity profiles. Unlike targeted therapies that attempt to regulate specific mutations within cancer, Tyme'stherapeutic approach is designed to take advantage of a cancer cell's innate metabolic requirements to cause cancer cell death through oxidative stress and exposure to the body's natural immune system.

Tyme has been focused on developing its novel compound,SM-88, as well as further evaluating its preclinical pipeline of novel CMBT™ programs, and TYME 19 as a potential therapeutic for SARS Co V-2 diseases. Tyme is also exploring options to further diversify its product candidate pipeline. The Company believes that early clinical results demonstrated by SM-88 in multiple advanced cancers, including breast, sarcomas, pancreatic, and prostate, reinforce the potential of our emerging CMBT™ pipeline.

The Merger Agreement provides that the combined company will continue to explore and consider in good faith the viability of continuing to develop SM-88 assets after the consummation of the merger in parallel with Syros' other drug candidates, or the sale or out-license of SM-88, in each case with a view toward maximizing stockholder value. However, Tyme is permitted, with the prior written consent by Syros (which consent shall not be unreasonably withheld, conditioned or delayed) and subject to any required Tyme stockholder approval, to sell, assign, license, or otherwise dispose of, in one or more transactions, some or all of Tyme's clinical pipeline candidates, including but not limited to, SM-88 in all formulations, TYME-18 and TYME-19. Tyme has no current plans or agreements for any such sale.

Exploration of Strategic Options and Diversification

On March 29, 2022, Tyme announced that Tyme's board of directors had decided to explore potential strategic options to enhance stockholder value and engaged outside financial and legal advisors to assist with that process. The Strategic Planning Committee of Tyme's board of dreictors, which is led by Tyme's Board Member Timothy C. Tyson, who possesses over 35 years of biotechnology and pharmaceutical industry experience, including multiple M&A transactions, is acting as Transaction Committee in connection with this process. On July 3, 2022, Tyme entered into an Agreement and Plan of Merger, or the Merger Agreement, with Syros Pharmaceuticals, Inc., or Syros, and Merger Sub. Upon the terms and subject to the conditions set forth in the Merger Agreement, Merger Sub will merge with and into Tyme with Tyme continuing as the surviving entity and a wholly owned subsidiary of Syros. At the effective time of the merger, or the effective time, each share of common stock of Tyme, par value $0.0001 per share, or the Tyme Common Stock, issued and outstanding immediately prior to the Effective Time will be converted into the right to receive a number of shares of fully paid and non-assessable shares of common stock of Syros, par value $0.001 per share, or the Syros Common Stock, equal to the Exchange Ratio (as defined in the Merger Agreement). The completion of the merger is subject to the satisfaction or waiver of certain closing conditions, including the adoption of the Merger Agreement by holders of a majority of the outstanding shares of Tyme Common Stock. If the

merger does not close and Tyme remains an independent company, it may choose to change its strategy, including without limitation to close down its trials and cease operations.

Strategic Review

In the first half of calendar year 2021, Tyme undertook a comprehensive strategic review with the goal of aligning Tyme's development plans with core strategic goals.

The strategic review was extensive and involved internal and external assessments by industry experts, KOLs and advisors with considerable experience in the various areas we sought to probe and explore.

The strategic review process resulted in several key takeaways including, but not limited to:

- broad activity across 15 cancer types as seen in the First in Human study and Compassionate Use program and confirmation of strong IP portfolio provides us extra development opportunities, for which focus is critical;
- the second-line Precision Promise trial was the priority in pancreatic cancer;
- breast cancer is a priority indication for development as part of pipeline diversification beyond pancreatic cancer;
- there is a need to refine our understanding of the MOA and identify biomarkers to enhance targeting of patient populations; and
- the rapidly changing COVID-19 landscape requires a reevaluation of the market potential and development pathway forTYME-19.

Tyme's recent strategy, including ongoing studies, the Preclinical Pipeline Programs and diversification efforts, was developed based on the takeaways from the strategic review, as well as on subsequent developments. Key elements of Tyme's strategy include to (i) successfully advance the development of SM-88 across a broad range of cancers, (ii) work towards identifying actionable biomarkers for patient selection or treatment response toSM-88, (iii) continue to invest in our technology platform and expand the breadth and depth of our IP portfolio, and (iv) build a balanced portfolio of proprietary and partnered programs. For more information about our strategy, see "*Tyme Business—Portfolio Development Strategy and Key Product Properties.*"

Ongoing Studies

OASIS (Metastatic HR+/HER2- Breast Cancer After CDK4/6 Inhibitors)

Tyme is collaborating with Georgetown University to support a Phase II trial, OASIS, forSM-88 in patients with metastatic breast cancer who have HR+ and HER2- disease, orHR+/HER2-. This represents approximately 68% of the annual breast cancer diagnosis in the US each year. The OASIS trial is an investigator-initiated prospective open-label Phase II trial evaluating the efficacy and safety of SM-88 with MPS for the treatment of metastatic HR+/HER2- breast cancer after treatment with a CDK4/6 inhibitor. This trial is designed as a two-stage trial, enrolling up to 50 patients who have failed or progressed after receiving two hormonal agents and a CDK4/6 inhibitor to receive SM-88 with MPS without additional cancer therapies. The primary endpoint of this trial is ORR, with secondary endpoints including DOR, CBR at >24 weeks, PFS, and safety. The trial is being conducted at Georgetown University at a total of five sites within the Georgetown/MEDSTAR system located in Washington DC, Maryland, and New Jersey. Patient enrollment began in 2021 with the first patient dosed in September. Tyme plans to provide an update on the OASIS breast cancer study during the first half of calendar year 2023.

HoPES Phase II Trial in sarcoma

In early 2020, the open-label Phase 2 investigator sponsored trial ofSM-88 therapy in sarcoma, HoPES, opened. This trial has two cohorts, each expecting to enroll 12 patients. The first is SM-88 with MPS as salvage treatment

in patients with mixed rare sarcomas, the other is SM-88 with MPS as maintenance treatment for patients with metastatic Ewing's sarcoma that had not progressed on prior therapy. The primary objectives are to measure ORR and PFS. Secondary objectives include DOR, OS, CBR using RECIST, and incidence of treatment-emergent AEs. The Joseph Ahmed Foundation is sponsoring this trial, which is being conducted by Principal Investigator Dr. Chawla at the Sarcoma Oncology Center in Santa Monica, CA. Tyme anticipates that the trial enrollment will continue through the end of calendar year 2022.

Preclinical Pipeline Programs

SM-88 MOA and Biomarker Research

In fiscal year 2022, Tyme began a comprehensive translational preclinical program. Tyme engaged Evotec, a leading global research and development company to aid in the execution of these activities, and Tyme is also incorporating several complementary academic collaborations into this multi-faceted program. The overall goal of these activities is to potentially identify actionable biomarkers of sensitivity and activity to SM-88 in various cancers, complementary combination drugs strategies for SM-88, and other cancer metabolism targets that could benefit from treatment. Additionally, the Company intends to incorporate liquid and tumor biopsies to future clinical trials to contribute to the biomarker identification. Tyme anticipates this engagement will have several stages, and that it is likely to last through this fiscal year and potentially into future periods.

TYME-18 and TYME-19

TYME-18 is a CMBT™ compound that is delivered intratumorally. TYME-18 leverages a member of the bile acid family to create a potential treatment for inoperable tumors. Preliminary observations of the local administration of TYME-18, a combination of a proprietary surfactant system and natural sulfonic acid, suggested its potential as an important regulator of energy metabolism that may impede the ability of tumors to increase in size, which, in addition to its lytic functionality, could prove useful in difficult-to-treat cancers. Tyme is assessing development priorities to determine if additional advancement of this program is warranted at this time.

TYME-19 is an oral synthetic member of the bile acid family. Tyme also uses bile acids in its anti-cancer drug candidate, TYME18. Because of its expertise in bile acids and their effects, Tyme was able to identify TYME-19 as a well-characterized bile acid with potential antiviral properties. Bile acids have primarily been used for liver disease; however, like all steroids, they are messenger molecules that modulate a number of diverse critical cellular processes. Bile acids can modulate lipid and glucose metabolism and can remediate dysregulated protein folding, with potentially therapeutic effects on cardiovascular, neurologic, immune, and other metabolic systems. Some agents in this class have also previously shown antiviral properties. In in vitro preclinical testing, TYME-19 prevented COVID-19 viral replication at doses without meaningful cytotoxicity to the treated cells. Previous independent preclinical research has also shown select bile acids may have had broad antiviral activity.

Tyme retained virology experts at Evotec to assess the mechanisms ofTYME-19. Evotec is a global drug development company that has the capability to access the multiple existing and emerging variants of the COVID-19 virus. Tyme and Evotec tested the ability ofTYME-19 to interrupt the cellular pathways commonly used by viruses to produce viral proteins as well as cellular responses to viral infection that cause local inflammation. Prolonged inflammation from SARS-CoV-2 can lead to some of the severe outcomes experienced by infected patients. Tyme aimed for the work by Evotec to provide Tyme with information that could allow Tyme to assess the potential path forward for the program. However, with the changes in demand for COVID-19 therapeutic landscape, and potential capital required to advance the program, Tyme management decided to currently pause additional development of this program.

Tumor Targeting Technology

Tyme has developed a technology ("Tumor Targeting Technology") by which the tyrosine isomer L metyrosine(L-α-methylparatyrosine) can be fused with a second therapeutic agent in a manner that creates a fusion

compound that may allow targeted accumulation of the treatment by the cancer cells in a novel manner. Tyme is assessing potential development paths for this technology.

Discontinuing Programs

Precision Promise Trial- SM-88 with MPS as 2nd line therapy in metastatic pancreatic cancer

In October 2018 Tyme partnered with PanCAN to study SM-88 in an adaptive randomized Phase II/III trial with registration intent known as Precision Promise[SM]. The objective of Precision Promise is to expedite the study and approval of promising therapies for pancreatic cancer by bringing multiple stakeholders together, including academic, industry and regulatory entities. The trial, began in early 2020, SM-88 (with the conditioning agents MPS) is being studied as monotherapy in a treatment arm for patients who have failed one prior line of chemotherapy.

On January 26, 2022, Tyme announced the discontinuation of SM-88 with MPS in the Precision Promise trial in mPDAC upon learning from PanCAN, the trial sponsor, that it terminated the arm due to futility compared to the control of standard of care chemotherapy in second-line mPDAC. Based on the information provided by PanCAN, the OS for SM-88 with MPS in monotherapy was lower compared to standard of care chemotherapies with either Gemcitabine and Abraxane or modified FOLFIRINOX. As of March 31, 2022, remaining estimated costs to close out the trial have been expensed.

TYME-88-PANC (Part 2) (third-line Metastatic Pancreatic Cancer)

In fiscal year 2020, Tyme launched its pivotal study for SM-88 in the third-line treatment of pancreatic cancer through an amendment to its ongoing TYME-88-Panc trial (Part 2), with the first patient dosed in the third quarter of the fiscal year. As described previously, the COVID-19 pandemic significantly impacted enrollment of this trial such that it appeared likely to complete enrollment in a similar timeline to the second-line Precision Promise pancreatic cancer trial. There has also been a higher than expected dropout of patients randomized to the chemotherapy control arm, which could potentially impact the interpretative and regulatory utility of the data.

Following the strategic review discussed above, considering, in part, the timeline and regulatory utility for this trial compared to the parallel Precision Promise trial and concentration of investment in this specific cancer, management concluded that it would be best to focus on the second-line Precision Promise trial which offers treatment options to patients earlier in their disease and includes tumor biopsy and biomarker analyses that aligns with Tyme's overall strategic focus on targeted identifying therapies.

Therefore, Tyme decided to stop enrollment and begin the process of closing down the trial. Patients currently on therapy are allowed to continue treatment until progression or unacceptable toxicity. The closing of this trial may require several months to complete. During the year ended March 31, 2022, Tyme expensed $723,000 of estimated closeout costs. The trial's remaining ongoing expense to Tyme is approximately $400,000 as of March 31, 2022, and is expected to be incurred over the five months following March 31, 2022.

COVID-19 Update

In March 2020, the World Health Organization categorized COVID-19 as a pandemic and the President of the United States declared the COVID-19 outbreak a national emergency. The COVID-19 pandemic, and actions taken by governments and others to reduce its spread, including travel restrictions, shutdowns of businesses deemed non-essential, and stay-at-home or similar orders, has negatively impacted the global economy, financial markets, and our industry and has disrupted day-to-day life and business operations. Tyme continues to closely monitor the impact of COVID-19 on all aspects of its business, its clinical trials, and the safety of patients as the situation continues to evolve. Tyme will continue to work closely with its clinical trial sites during the pandemic and are committed to working with them to assure appropriate access for patients who are seeking clinical trial options for these advanced cancers for which the patients have limited or no other treatment options.

Tyme has also taken important steps to protect the health and welfare of our employees, consultants and board members, by continuing to provide a fully "work-from-home" option. Although Tyme has operated in the COVID-19 environment for approximately two years, there remains substantial uncertainty about the extent to which COVID-19 will impact our product candidates and business, including patients' willingness to participate and remain in clinical trials, the timing of meeting enrollment expectations, the ability of its third-party partners to remain operational and its access to capital markets and financing sources and depends on numerous evolving factors that are highly uncertain and cannot be accurately predicted, including those identified under "*Risk Factors—Risks Related to Tyme's Business and the Development, Regulatory Approval and Commercialization of Tyme's Product Candidates*." in this joint proxy statement/prospectus, many of which are beyond Tyme's control. Management continues to monitor the situation closely and intends to continue to adapt and implement process adjustments as needed.

Recent Developments

Nasdaq Notice

On December 22, 2021, Tyme received notice from The Nasdaq Stock Market that the closing bid price for our common stock had been below $1.00 per share for the previous 30 consecutive business days, and that Tyme is therefore not in compliance with the minimum bid price requirement for continued inclusion on The Nasdaq Capital Market under Nasdaq Listing Rule 5550(a)(2). On June 21, 2022, Tyme received notice from Nasdaq that it had granted the Company a 180-day extension to regain compliance with The Nasdaq Stock Market continued listing standards. The Nasdaq Stock Market informed Tyme that it granted the extension, in part, due to Tyme's intention to cure the deficiency during the extension period by effecting a reverse split, if necessary. The extension runs through December 19, 2022. The Nasdaq Stock Market's notices have no immediate effect on the listing or trading of our common stock. Tyme can regain compliance with the $1.00 minimum bid listing requirement if the closing bid price of our common stock is at least $1.00 per share for a minimum of ten (10) consecutive business days. Tyme has asked its stockholders to approve an amendment to Tyme's Certificate of Incorporation to implement a reverse stock split in an effort to regain compliance with the $1.00 minimum bid listing requirement and avoid delisting.

Critical Accounting Policies and Estimates and Recent Accounting Pronouncements

Critical accounting estimates are those made in accordance with GAAP that involve a significant level of estimation and have had or are reasonably likely to have a material impact on Tyme's financial condition or results of operations. In preparing these financial statements, management has used available information in forming its estimates, assumptions and judgments. Actual performance may differ from estimates and Tyme's estimates may differ from those of other companies. While Tyme's significant accounting policies are more fully described in Note 2 to the Tyme Consolidated Financial Statements appearing elsewhere in this joint proxy statement/prospectus, we believe the following accounting policies and estimates are critical to the preparation of our financial statements. The financial information presented in this section is in conformity with GAAP.

Research and Development Expenses

Research and development costs are expensed as incurred and are primarily comprised of, but not limited to, external research and development expenses incurred under arrangements with third parties, such as CROs, CMOs and consultants that conduct clinical and preclinical studies, costs associated with preclinical and development activities, costs associated with regulatory operations, depreciation expense for assets used in research and development activities and employee related expenses, including salaries and benefits for research and development personnel. Costs for certain development activities, such as clinical studies, are accrued, over the service period specified in the contract and recognized based on an evaluation of the progress to completion of specific tasks using data such as patient enrollment, clinical site activations or information provided to us by Tyme's vendors on their actual costs incurred. Payments for these activities are based on the terms of the individual arrangements, which may differ from the patterns of costs incurred, and are reflected in the consolidated financial statements as prepaid or accrued expense.

Income Taxes

Tyme's income tax expense, deferred tax assets and liabilities, and liabilities for unrecognized tax benefits reflect management's best estimate of current and future taxes to be paid. Tyme issubject to federal income taxes in the United States, as well as in various U.S. state jurisdictions. Significant judgments and estimates are required in the determination of the income tax expense.

Deferred income taxes arise from temporary differences between the tax basis of assets and liabilities and their reported amounts in the financial statements, which will result in taxable or deductible amounts in the future. Deferred tax assets and liabilities are measured using enacted tax rates expected to apply to taxable income in the years in which those temporary differences are expected to be recovered or settled. The effect on deferred tax assets and liabilities of a change in tax rates is recognized in income in the period that includes the enactment date. The assumptions about future taxable income require the use of significant judgment and are consistent with the plans and estimates Tyme isusing to manage the underlying businesses. In evaluating the objective evidence that historical results provide, Tyms considers three years of cumulative operating income (loss).

A valuation allowance is provided when, after consideration of available positive and negative evidence, that it is not more likely than not that the benefit from deferred tax assets will be realizable. In recognition of this risk, Tyme has provided a full valuation allowance against the net deferred tax assets.

The calculation of Tyme's tax liabilities involves dealing with uncertainties in the application of complex tax laws and regulations in various jurisdictions. ASC 740 "Income Taxes" states that a tax benefit from an uncertain tax position may be recognized when it is more likely than not that the position will be sustained upon examination, including resolutions of any related appeals or litigation processes, on the basis of the technical merits.

As of March 31, 2022, Tyme had gross U.S. federal net operating loss carryforwards of approximately $119.1 million, which may be available to offset future income tax liabilities and will begin to expire at various dates starting in 2033. As of March 31, 2022, Tyme had gross federal research and development tax credit carryforwards of $5.9 million available to reduce future tax liabilities, which will begin to expire at various dates starting in 2030. As of March 31, 2022, none of Tyme's state net operating losses have value due to the apportionment rule in the states where state income tax returns are currently filed. Tyme had unrecognized tax benefits of $890,000 and $559,000 at March 31, 2022 and 2021, respectively. Increases or decreases would not have an effect on the effective tax rate.

Tyme files federal income tax returns in the United States, and various state jurisdictions. The federal and state income tax returns are generally subject to tax examinations for the period January 1, 2017 through March 31, 2022. To the extent Tyme has tax attribute carryforwards, the tax years in which the attribute was generated may still be adjusted upon examination by the Internal Revenue Service or state tax authorities to the extent utilized in a future period. In addition, Tyme had no income tax related penalties or interest for periods presented in these consolidated financial statements. When and if we were to recognize interest and penalties related to unrecognized tax benefits, they would be reported in tax expense.

Stock-Based Compensation

Tyme follows the authoritative guidance for accounting for stock-based compensation in ASC 718, "Compensation-Stock Compensation." The guidance requires that stock-based payment transactions be recognized in the financial statements based on their fair value at the grant date and recognized as compensation expense over the vesting period as services are being provided.

The fair value of each stock option grant is estimated on the date of grant using the Black-Scholes option-pricing model. The use of the Black-Scholes option pricing model requires management to make assumptions with

respect to the expected term of the option, the expected volatility of the common stock consistent with the expected term of the option, using a blend of Tyme's expected volatility and those of similar companies, risk-free interest rates, the value of the common stock and expected dividend yield of the common stock. For awards subject to time-based vesting conditions, we recognize stock-based compensation expense equal to the grant date fair value of stock options on a straight-line basis over the requisite service period, which is generally the vesting term. Tyme accounts for forfeitures as they occur, rather than estimating forfeitures as of an award's grant date.

Tyme adopted ASU 2018-07 and, as such, the fair value of options granted tonon-employees is estimated at the date of grant only, and the expected term is determined using the simplified method for options granted to non-employees and consultants.

Derivative Warrant Liability

Certain freestanding common stock warrants that are related to the issuance of common stock are classified as liabilities and recorded at fair value due to characteristics that require liability accounting, primarily the obligation to issue registered shares of common stock upon notification of exercise and certain price protection provisions. Warrants of this type are subject to re-measurement at each balance sheet date and any change in fair value is recognized as a component of other income (expense) in the consolidated statement of operations.

As noted in Note 8 to the Tyme Consolidated Financial Statements, Stockholders' Equity, Tyme classifies a warrant to purchase shares of its Common Stock as a liability on its consolidated balance sheet if the warrant is a free-standing financial instrument that contains certain price protection features that cause the warrants to be treated as derivatives or requires the issuance of registered common shares upon exercise. Each warrant of this type is initially recorded at fair value on date of grant using the Monte Carlo simulation model or the Black Scholes model and is subsequently re-measured to fair value at each subsequent balance sheet date. Changes in fair value of the warrant are recognized as a component of other income (expense) in the consolidated statement of operations. Tyme will continue to adjust the liability for changes in fair value until the earlier of the exercise or expiration of the warrant. Tyme utilizes Level 3 fair value criteria to measure the fair value of the warrants.

Refer to Note 2 to the Tyme Consolidated Financial Statements for a discussion of Recent Accounting Pronouncements.

Results of Operations

Year ended March 31, 2022 Compared to Year Ended March 31, 2021

Net loss for the year ended March 31, 2022 was $23,626,000 or $0.14 per share compared to $28,979,000 or $0.22 per share for the year ended March 31, 2021. The decrease in the net loss compared to the prior year was due to the non-cash favorable variance of $5,722,000 in the change in fair value of the warrant liability and decreased operating costs, offset by $2,229,000 prior years gain on the warrant exchange. The decrease in operating costs for the current year of $1,703,000 related to decreased research and development costs of $3,264,000 and decreased general and administrative costs of $554,000, partially offset by $2,115,000 increased severance expenses, explained below under "*Operating Expenses.*"

Cash used in operating activities for the year ended March 31, 2022 was $21,243,000 compared to $23,564,000 for the year ended March 31, 2021. See "*Cash Flows*" section below for further details.

Adjusted net loss, which excludes the change in fair value of warrant liability, amortization of employees, directors and consultants stock options and gain on warrant exchange, was $22,981,000 or $0.13 per share for the year ended March 31, 2022 compared to $23,836,000 or $0.18 per share for the year ended March 31, 2021. Adjusted net loss and adjusted net loss per share are non-GAAP measures. See "*Use of Non-GAAP Measures*" below for a reconciliation to the comparable GAAP measures.

Revenue

During the years ended March 31, 2022 and March 31, 2021, Tyme did not realize any revenues from operations. Tyme does not anticipate recognizing any revenues until such time as one of its products has been approved for marketing by appropriate regulatory authorities or Tyme enters into collaboration or licensing arrangements, none of which is anticipated to occur in the near future.

Operating Expenses

For the year ended March 31, 2022, operating costs and expenses totaled $25,514,000, compared to $27,217,000 for the year ended March 31, 2021, representing a decrease of $1,703,000. Operating costs and expenses by function were comprised of the following:

- Research and development expenses were $13,445,000 for the year ended March 31, 2022, compared to $16,709,000 for the year ended March 31, 2021, representing a decrease of $3,264,000. The majority of research and development expenditures have been incurred in respect of our lead drug candidate SM-88 and its technology platform. Research and development expenditures also included costs for pre-clinical studies on SM-88 MOA, biomarker identification and TYME-19. Research and development activities primarily consist of the following:
  - Study and consulting expenses were $11,022,000 for the year ended March 31, 2022, compared to $12,637,000 for the year ended March 31, 2021 representing a decrease of $1,615,000 between the comparable periods. The decrease is mainly attributable to lower ongoing trial costs due to the discontinued TYME-88-Panc Part 2 third-line Metastatic Pancreatic Cancer and Precision Promise trials, partially offset by costs incurred related to the OASIS clinical trial as well as mechanism of action and biomarker preclinical studies.
  - Salary and salary related expenses for research and development personnel were $1,846,000 for the year ended March 31, 2022, compared to $2,693,000 for the year ended March 31, 2021, representing a decrease of $847,000 between comparable periods, primarily due to lower headcount for roles currently outsourced to consultants.
  - Included in research and development expense for the year ended March 31, 2022 is $577,000 of stock based compensation related to stock options granted to research and development personnel compared to $1,379,000 for the year ended March 31, 2021, representing a decrease of $802,000 between the comparable periods, primarily attributable to fully vested grants and cancellation/forfeiture of options.
- General and administrative expenses were $9,632,000 for the year ended March 31, 2022, compared to $10,186,000 for the year ended March 31, 2021, representing a decrease of $554,000. The general and administrative expenses include:
  - Stock based compensation related to stock options granted was $1,875,000 for the year ended March 31, 2022, compared to $2,078,000 for the year ended March 31, 2021, representing a decrease of $203,000, primarily attributable to fully vested grants and cancellation/forfeiture of options.
  - Legal, professional services, accounting and auditing expenses for the year ended March 31, 2022, were $2,668,000, compared to $3,150,000 for the year ended March 31, 2021, representing a decrease of $482,000.
  - Salary and salary related expenses for non-research and development personnel were $3,301,000 for the year ended March 31, 2022, compared to $3,235,000 for the year ended March 31, 2021, representing an increase of $66,000 between the comparable periods.
  - Other general and administrative expenses for the year ended March 31, 2022 were $1,788,000, compared to $1,723,000 for the year ended March 31, 2021, an increase of $65,000.

- Severance expense was $2,437,000 for the year ended March 31, 2022, compared to $322,000 for the year ended March 31, 2021, representing an increase of $2,115,000 which primarily represents severance expense attributable to the Release Agreement, dated March 24, 2022, pursuant to which the Chief Science Officer resigned and received a lump sum severance payment of $2.1 million that would have been payable under his employment agreement. Severance expense for the year ended March 31 2021 included amounts related to the Separation and General Release Agreement entered into with its Chief Medical Officer for separation of employment as of March 31, 2021, classified in salary and salary related expenses for research and development personnel in prior year.

Other Income/Expenses

For the year ended March 31, 2022, Tyme had $1,807,000non-cash income relating to the change in fair value of the warrant liability during the period compared to $3,915,000 of non-cash expense for the year ended March 31, 2021, resulting in a $5,722,000 variance between the periods. See Note 7 to the Tyme Consolidated Financial Statements for details regarding changes in the fair value of the warrant liability.

For the year ended March 31, 2021, Tyme had anon-cash gain on warrant exchanges of $2,229,000 pursuant to the Share Exchange Agreements and the Warrant Exchange Agreement (See Historical Financings – Exchange Agreements below.)

For the year ended March 31, 2022, Tyme incurred $70,000 of interest expense as compared to $97,000 in the year ended March 31, 2021 primarily related to the amortization of severance payable discount.

Investment and interest income for the year ended March 31, 2022 was $151,000 as compared to $22,000 in the year ended March 31, 2021, due to the establishment of our investment portfolio.

Income Tax

Tyme's effective income tax rate for the years ended March 31, 2022 and 2021 was zero percent.

Use of Non-GAAP Measures

Adjusted net loss and adjusted net loss per share as presented in this joint proxy statement/prospectus arenon-GAAP measures. The adjustments relate to the change in fair value of warrant liability, amortization of employees, directors and consultants stock options and gain on warrant exchange. These financial measures are presented on a basis other than in accordance with U.S. generally accepted accounting principles, or Non-GAAP Measures. In the reconciliation tables that follow, Tyme presents adjusted net loss and adjusted net loss per share, reconciled to their comparable GAAP measures, net loss and net loss per share. These items are adjusted because they are not operational or because they are significant noncash charges and management believes these adjustments are meaningful to understanding Tyme's performance during the periods presented. These Non-GAAP Measures should be considered a supplement to, not a substitute for, or superior to, the corresponding financial measures calculated in accordance with GAAP. Our definitions of adjusted net loss and adjusted loss per share may not be comparable to similar measures reported by other companies.

Reconciliation of Net Loss to Adjusted Net Loss

	For the Year Ended March 31,	
	2022	2021
Net loss (GAAP)	$ (23,626,000)	$ (28,979,000)
Adjustments:		
Change in fair value of warrant liability	(1,807,000)	3,915,000
Gain on warrant exchange	—	(2,229,000)
Amortization of employees, directors and consultants stock options	2,452,000	3,457,000
Adjusted net loss (non-GAAP)	$ (22,981,000)	$ (23,836,000)

Reconciliation of Net Loss Per Share to Adjusted Basic and Diluted Net Loss Per Share

	For the Year Ended March 31,	
	2022	2021
Net loss per share (GAAP)	$(0.14)	$(0.22)
Adjustments:		
Change in fair value of warrant liability	(0.01)	0.03
Gain on warrant exchange	—	(0.02)
Amortization of employees, directors and consultants stock options	0.02	0.03
Adjusted basic and diluted net loss per share (non-GAAP)	$(0.13)	$(0.18)

The Non-GAAP Measures for the year ended March 31, 2022 and 2021 provide management with additional insight into Tyme's results of operations from period to period by excluding certain non-operational and non-cash charges, and are calculated using the following adjustments to net loss:

a) The warrants issued as part of an equity offering on April 2, 2019 were measured at fair value using a Monte Carlo model which takes into account, as of the valuation date, factors including the current exercise price, the remaining contractual term of the warrant, the current price of the underlying stock, its expected volatility, the risk-free interest rate for the term of the warrant and the estimates of the probability of fundamental transactions occurring.

The May 2020 Warrant issued as part of the warrant exchange as described under the subheading "Historical Financings" below was measured at fair value using a Black-Scholes model which takes into account, as of the valuation date, factors including the current exercise price, the remaining contractual term of the warrant, the current price of the underlying stock, its expected volatility and the risk-free interest rate for the term of the warrant.

The warrant liability is revalued at each reporting period or upon exercise. Changes in fair value are recognized in the consolidated statements of operations and are excluded from adjusted net loss and adjusted net loss per share.

b) Tyme uses the Black-Scholes option pricing model to determine fair value of stock options granted. For employees and non-employees, the compensation expense is amortized over the requisite service period which approximates the vesting period. The expense is excluded from adjusted net loss and adjusted net loss per share.

c) Gain on warrant exchange resulted from the difference in fair value of the warrants issued as part of the equity offering on April 2, 2019 before their exchange (as described under the subheading "Historical Financings" below) and the fair value of the common stock exchange shares and the May 2020 Warrant granted pursuant to the Share Exchange Agreements and the Warrant Exchange Agreement, respectively.

Adjusted basic net loss per share is computed by dividing adjusted net loss by the weighted average number of shares of Company common stock outstanding for the period, and adjusted diluted loss per share is computed by also including common stock equivalents outstanding for the period. During the periods presented, the calculation excludes any potential dilutive common shares and any equivalents as they would have been anti-dilutive as Tyme incurred losses for the periods then ended.

Liquidity and Capital Resources

Liquidity and Capital Requirements Outlook

On February 8, 2021, Tyme closed on a registered direct offering of 40,000,000 shares of its common stock, par value $0.0001 per share, at a purchase price of $2.50 per share. The gross proceeds of the offering were $100 million, prior to deducting placement agent's fees and other offering expenses payable by Tyme, which were approximately $6.2 million.

Tyme intends to continue to use the net proceeds of this offering for the development of our clinical and preclinical assets and for general corporate purposes, capital expenditures, working capital and general and administrative expenses. Tyme may also use a portion of the net proceeds to acquire or invest in businesses, products and technologies that are complementary to its own to further diversify its product pipeline and are exploring various strategic options as described above. In addition, Tyme may also use the proceeds, and may require additional capital, to engage in potential partnerships or collaborations. Tyme's most significant funding needs are in connection with (i) participating in the investigator-initiated HoPES clinical trial of SM-88 in sarcoma, (ii) participating in OASIS, its investigator-initiated prospective open-label Phase II trial, evaluating the efficacy and safety of SM-88 with MPS for the treatment of metastatic HR+, HER2- breast cancer after treatment, (iii) conducting preclinical studies of an injectable form of SM-88, (iv) conducting preclinical studies in connection with its other preclinical pipeline products, including TYME-18 and Tumor Targeting Technology, and (v) conducting additional or related studies of other potential drug candidates. If Tyme determines to move beyond the preclinical stage for any of our preclinical product candidates or if Tyme pursues studies in other cancer types, our liquidity requirements will be increased. Additionally, if Tyme completes a material transaction resulting from its strategic evaluation process, Tyme will, among other potential payment obligations, be obligated to pay each of its executive officers a retention bonus within 20 days of such transaction.

Primarily as a result of its active clinical trials, including timing of enrollment, as well as other business developments, and based on its current operating plan, but not taking into consideration to the execution or completion of any transaction that may result from the evaluation of strategic options and diversification initiatives as described above, or from any decision to close down its trials and cease operations, Tyme currently anticipates that its quarterly cash operating expense will approximate $4.0 million to $6.0 million per quarter during fiscal year 2023. Management expects that the Tyme's net cash usage or net "cash burn" will be less than its operating costs.

As of March 31, 2022, Tyme had cash on hand of approximately $13.7 million and a working capital of approximately $71.5 million. In the first quarter of fiscal year 2022, Tyme established an investment policy and invested approximately $74.1 million in a portfolio of highly liquid investments and marketable securities. As of March 31, 2022 Tyme had marketable securities of $69.7 million and accrued interest of $0.6 million classified in other current assets. The primary objectives of Tyme's policy are to preserve capital and diversify risk, while maintaining sufficient liquidity to meet cash flow needs.

Management has concluded that substantial doubt does not exist regarding Tyme's ability to satisfy its obligations as they come due during the twelve-month period following the issuance of these financial statements. This conclusion is based on Tyme's assessment of qualitative and quantitative conditions and events, considered in aggregate as of the date of issuance of these financial statements that are known and reasonably knowable. Among other relevant conditions and events, including the ongoing COVID-19 pandemic and related government and economic responses, Tyme has considered its operational plans, liquidity sources, obligations due or expected, funds necessary to maintain Tyme's operations, and potential adverse conditions or events as of the issuance date of these financial statements.

Tyme has historically funded its operations primarily through equity offerings of its common stock. As a clinical-stage entity, without product revenues and ongoing needs to fund Tyme's clinical development activities and general operations, Tyme regularly evaluates opportunities to raise capital and obtain necessary, as well as opportunistic financing. To meet Tyme's liquidity needs, we currently expect to use existing cash balances and marketable securities in the short term, and a variety of other means as longer term funding sources, including potential issuances of debt or equity securities in public or private financings, option exercises, and partnerships and/or collaborations. The demand for the equity and debt of biopharmaceutical and biotechnology companies like Tyme is dependent upon many factors, including the general state of the financial markets. During times of extreme market volatility, capital may not be available on favorable terms, if at all. Tyme's inability to obtain such additional capital could materially and adversely affect its business operations.

While Tyme will continue to seek capital through a number of means, there can be no assurance that additional financing will be available on acceptable terms, if at all, and its negotiating position in capital generating efforts may worsen as existing resources are used. Moreover, as discussed above, should Tyme be unable to maintain compliance with Nasdaq listing requirements, its ability to raise funds and, therefore, its liquidity, could be negatively impacted. See "*Risk Factors—Risks Related to Owning Tyme Stock—Tyme may be unable to regain and maintain compliance with The Nasdaq Capital Market continued listing requirements, which could cause Tyme's common stock to be delisted from The Nasdaq Capital Market. This could result in the lack of a market for Tyme's common stock, cause a decrease in the value of an investment in Tyme, and adversely affect Tyme's business, financial condition, and results of operations.*" for additional information.

Additional equity financing, which Tyme expects to raise, may be dilutive to its stockholders; debt financing, if available, may involve significant cash payment obligations and covenants that restrict its ability to operate as a business; and its stock price may not reach levels necessary to induce option exercises. If Tyme is unable to raise the funds necessary to meet its long-term liquidity needs, Tyme may have to delay or discontinue the development of certain or all of its drug candidates or raise funds on terms that Tyme currently considers unfavorable.

From time to time, Tyme may also restructure its outstanding securities or seek to repurchase or redeem them if Tyme believes doing so would provide it with additional flexibility to raise capital or is otherwise in the best interests of Tyme.

Historical Financings

As further described above under the heading "Liquidity and Capital Requirements Outlook", on February 8, 2021, Tyme closed on a registered direct offering of 40,000,000 shares of its common stock.

On January 7, 2020, Tyme and Eagle entered into a Securities Purchase Agreement, or the Eagle SPA, pursuant to which Tyme issued and sold to Eagle 10,000,000 shares of common stock, at a price of $2.00 per share. The Eagle SPA provides that Eagle will, subject to certain conditions, make an additional payment of $20 million upon the occurrence of a milestone event, which is defined as the earlier of (i) achievement of the primary endpoint of overall survival in the TYME-88-Panc pivotal trial; (ii) achievement of the primary endpoint of overall survival in the PanCAN Precision Promise℠ SM-88 registration arm; or (iii) U.S. FDA approval of SM-88 in any cancer indication. This payment would be split into a $10 million milestone cash payment and a $10 million investment in Tyme at a 15% premium to the then prevailing market price. Eagle's shares will be restricted from sale until the earlier of three months following the milestone event or the three-year anniversary of the agreement.

On October 18, 2019, Tyme entered into an Open Market Sale Agreement℠ which was amended on August 12, 2020, or the Sale Agreement, with Jefferies LLC, or Jefferies, pursuant to which Tyme may, from time to time, sell shares of Common Stock, having an aggregate offering price of up to $30 million through Jefferies, as Tyme's sales agent, or the Jefferies ATM. Under the Sale Agreement the minimum share sales price, or Floor Price, shall not be less than $1.00 without Jefferies prior written consent. As indicated in an amendment to the Sale Agreement, the shares will be offered and sold by Tyme pursuant to its currently effective Registration Statement on Form S-3, as amended (Reg. No. 333-245033). Any sales of Common Stock pursuant to the Sales Agreement will be made by methods deemed to be an "at-the-market offering" as defined in Rule 415 promulgated under the Securities Act. Jefferies will use commercially reasonable efforts to sell the shares from time to time, based on the instructions of Tyme. Tyme will pay Jefferies a commission rate of three percent (3%) of the gross proceeds from the sales of shares of Common Stock sold pursuant to the Sale Agreement. Under the Sale Agreement, Tyme is not required to use the full available amount authorized and it may, by giving notice as specified in the Sale Agreement, terminate the Sale Agreement at any time. During the year ended March 31, 2022, Tyme did not raise any proceeds under the Jefferies ATM. During the year ended March 31, 2021, the Company raised approximately $6.1 million in gross proceeds via the sale of 4,453,939 shares of common stock

under the Jefferies ATM and incurred $0.3 million of related costs which offset such proceeds. As of March 31, 2022, there remained approximately $22.2 million of availability in the Jefferies ATM subject to the terms of the Sale Agreement.

Exchange Agreements

In May 20, 2020, Tyme entered into exchange agreements, or the Share Exchange Agreements, with the Holders of the warrants issued in April 2019, or the April 2019 Warrants. Pursuant to the Share Exchange Agreements with Holders of April 2019 Warrants to purchase 5,833,333 shares of Common Stock in the aggregate, Tyme issued an aggregate of 2,406,250 shares of Common stock, or the "Exchange Shares, in exchange for such April 2019 Warrants. Concurrently therewith, each such Holder executed and delivered to Tyme a leak-out agreement, or a Share Leak-Out Agreement, that contained trading restrictions with respect to the Exchange Shares, which (i) for the first 90 days, prohibit any sales of Exchange Shares, (ii) for the subsequent 90 days, limit sales of Exchange Shares on any day to 2.5% of that day's trading volume of Common Stock, and (iii) prohibit new short positions or short sales on Common Stock for the combined 180 day period.

Tyme also entered into an exchange agreement, or the Warrant Exchange Agreement, with another Holder of April 2019 Warrants to purchase 2,166,667 shares of Common Stock in the aggregate. Pursuant to the Warrant Exchange Agreement, Tyme issued such Holder a new warrant, or the May 2020 Warrant, to purchase the same number of shares of Common Stock. The May 2020 Warrant has the same expiration date, April 2, 2024, as the April 2019 Warrants, but has an exercise price of $1.80 and does not include the price protection, anti-dilution provisions or other restrictions on Tyme action from the April 2019 Warrants. Concurrently therewith, such Holder executed and delivered to Tyme a leak-out agreement that contains trading restrictions on sales of Common Stock issued upon exercise of the May 2020 Warrant that are substantially similar to the restrictions on Exchange Shares in the Share Leak-Out Agreement, provided that the leak-out restrictions will only apply to the first 893,750 shares of Common Stock issued pursuant to the May 2020 Warrant.

After such exchanges, the April 2019 Warrants no longer remained outstanding.

Cash Flows

Net cash used in or provided by operating, investing and financing activities from continuing operations were as follows:

	2022	2021
Net cash used in operating activities	$ (21,243,000)	$ (23,564,000)
Net cash used in investing activities	$ (72,541,000)	$ —
Net cash provided by financing activities	$ 6,000	$ 104,380,000

Operating Activities

Tyme's cash used in operating activities in the year ended March 31, 2022 totaled $21.2 million which is the sum of (i) its net loss of $23.6 million, adjusted for $2.5 million expense amortization of stock-based compensation and $1.6 million net amortization of premiums and discounts on marketable securities, partially offset by $1.8 million non-cash change in fair value of the warrant liability, and (ii) changes in operating assets and liabilities of $0.1 million.

Tyme's cash used in operating activities in the year ended March 31, 2021 totaled $23.6 million which is the sum of (i) its net loss of $29.0 million, adjusted for non-cash expenses totaling $3.9 million related to change in fair value of the warrant liability and $3.5 million expense amortization of stock-based compensation, partially offset by $2.2 million non-cash gain on warrant exchange, and (ii) changes in operating assets and liabilities of $0.3 million.

Investing Activities

During the year ended March 31, 2022, Tyme's investing activities consisted of the purchase of $95.2 million of marketable securities and the receipt of approximately $22.7 million of proceeds from maturities of marketable securities. There were no investing activities in the year ended March 31, 2021.

Financing Activities

During the year ended March 31, 2022, Tyme's financing activities consisted of the receipt of $6,000 in proceeds from the exercise of stock options.

During the year ended March 31, 2021, Tyme's finance activities consisted of the receipt of $100 million gross proceeds from a registered direct offering of 40,000,000 shares of Tyme's common stock, at a purchase price of $2.50 per share net of $6.2 million of related costs which offset such proceeds, $6.1 million in gross proceeds via sale of 4,453,939 shares of common stock under the Jefferies ATM, net of $0.3 million of related costs which partially offset such proceeds and $5.4 million proceeds through the exercise of the stock options. Tyme made payments of $518,000 on the insurance note payable related to premiums for its Director and Officer liability insurance coverage.

Seasonality

Tyme does not believe that its operations are seasonal in nature.

Contractual Obligations and Commitments

In the course of Tyme's normal business operations, it enters into agreements and arrangements with contract service providers to assist in the performance of its research and development and clinical research activities. At March 31, 2022, Tyme's obligations to contract service providers were $0.2 million in the aggregate.

Contract Service Providers

On April 1, 2020, Tyme amended the Clinical Research Funding and Drug Supply Agreement dated October 9, 2018, with PanCAN, to enroll individuals diagnosed with pancreatic cancer in a platform style clinical research study. Stage 1 of the study was initiated in the fourth quarter of fiscal year 2020. On January 26, 2022, Tyme announced the discontinuation of SM-88 with MPS in the Precision Promise trial in mPDAC upon learning from PanCAN, the trial sponsor, that it terminated the arm due to futility compared to the control of standard of care chemotherapy in second-line mPDAC. As of March 31, 2022, remaining estimated costs to close out the trial have been expensed.

Purchase Commitments

Tyme has entered into contracts with manufacturers to supply certain components used inSM-88 in order to achieve favorable pricing on supplied products. These contracts have non-cancellable elements related to the scheduled deliveries of these products in future periods. Payments are made by Tyme to the manufacturer when the products are delivered and of acceptable quality. The outstanding future contract obligations structured to match clinical supply needs for Tyme's ongoing trials and registration activity are approximately $0.9 million and $2.5 million, respectively, at March 31, 2022. Tyme expects the timing of associated payments to predominately occur through fiscal year 2023.

Leases

Tyme leases office space in New Jersey. The New Jersey lease expires in February 2023. Tyme's future minimum remaining lease payments for the New Jersey lease are approximately $39,200 due in fiscal 2023.

Executive Officers and Directors

Executive Officers and Directors of the Combined Company Following the Merger

In addition to the ten current Syros board members, (i) pursuant to the terms of the Merger Agreement, Tyme has the right to designate one board member to the board of directors of the combined company and (ii) pursuant to the terms of the Securities Purchase Agreement, two of the investors in the PIPE Financing each have the right to designate one board member to the board of directors of the combined company. The staggered structure of the current Syros board of directors will remain in place for the combined company following the completion of the merger.

The following table lists the names and ages, as of July 1, 2022, and positions of the individuals who are expected to serve as executive officers and directors of the combined company upon completion of the merger and the PIPE Financing:

Name	Age	Position
Executive Officers:		
Nancy A. Simonian, M.D.	61	President and Chief Executive Officer, Director
Conley Chee	52	Chief Commercial Officer
Jason Haas	55	Chief Financial Officer
Eric R. Olson, Ph.D.	64	Chief Scientific Officer
David A. Roth, M.D.	60	Chief Medical Officer
Kristin Stephens	49	Chief Development Officer
Non-Employee Directors:		
Srinivas Akkaraju, M.D., Ph.D.	54	Director
Mark J. Alles	63	Director
Deborah Dunsire, M.D.	60	Director
S. Gail Eckhardt, M.D.	64	Director
Marsha H. Fanucci	69	Director
Amir Nashat, Ph.D.	49	Director
Phillip A. Sharp, Ph.D.	78	Director
Peter Wirth	71	Chair of the Board of Directors
Richard A. Young, Ph.D.	68	Director

Executive Officers

Nancy A. Simonian, M.D. has been Syros' chief executive officer since July 2012. From 2001 to October 2011, Dr. Simonian was employed by Takeda and at Millennium. prior to its acquisition by Takeda, most recently as chief medical officer and senior vice president of clinical, medical and regulatory affairs. From 1995 to 2001, Dr. Simonian served at Biogen, Inc., a publicly traded biotechnology company, most recently as vice president of clinical development. She is a member of the board of directors of Seattle Genetics, Inc., a publicly traded biopharmaceutical company, the Damon Runyon Cancer Research Foundation and the Biotechnology Industry Organization. She previously served as a member of the board of directors of Evelo Biosciences, Inc. from April 2018 to June 2021. Prior to joining the biopharmaceutical industry, Dr. Simonian was on the faculty of Massachusetts General Hospital and Harvard Medical School as an assistant professor of neurology. She received a B.A. in biology from Princeton University and an M.D. from the University of Pennsylvania School of Medicine. Syros believes Dr. Simonian is qualified to serve on its board because of her role as Syros' chief executive officer, her experience in the biopharmaceutical industry and her other executive leadership and board of directors experience.

Conley Chee has been Syros' chief commercial officer since September 2021. He previously served as global head of portfolio management, global pipeline strategy and precision medicine at Novartis Oncology, or Novartis, a global pharmaceutical company from October 2018 to February 2021. In this role, Mr. Chee had strategic responsibility for shaping Novartis' overall pipeline, including driving commercial planning for the company's early-stage portfolio and diagnostics strategy for oncology. Earlier in his career at Novartis, Mr. Chee served as vice president—global head oncology lung franchise from 2015 to October 2018, as well as in multiple U.S. sales and marketing leadership roles. Prior to joining Novartis, Mr. Chee spent five years in roles of increasing responsibility at Pfizer, Inc., a global pharmaceutical company, ultimately serving as team leader of international business development. He holds a B.Sc. Pharm from the University of Alberta and an M.B.A. from the Richard Ivey School of Business at the University of Western Ontario and completed his residency in Clinical Pharmacy at the University of British Columbia.

Jason Haas has been Syros' chief financial officer since October 2021. He previously served asco-head of Americas, healthcare investment banking at Barclays from June 2016 to October 2021. Previously, he served as head of Americas, healthcare investment banking at Deutsche Bank from 2012 to June 2016. He currently serves on the board of directors of Ligand Pharmaceuticals, a public biotechnology company. Prior to his role at Deutsche Bank, he was a managing director on the healthcare investment banking team at Goldman Sachs & Co. Mr. Haas holds a B.A. in International Relations and Economics from Colgate University and an M.B.A. in Finance from Columbia Business School.

Eric R. Olson, Ph.D. has been Syros' chief scientific officer since April 2013. He previously served as research vice president for respiratory diseases at Vertex Pharmaceuticals, Inc., a biotechnology company, from 2001 to May 2013. Dr. Olson has also held positions as the director of antibacterials and molecular sciences departments at Warner-Lambert Co. as well as a research scientist focused on gene expression systems with The Upjohn Company, both of which were acquired by Pfizer Inc., a pharmaceutical company, or Pfizer. Dr. Olson serves on the boards of the Cystic Fibrosis Foundation and the National Brain Tumor Society. Dr. Olson received a B.S. in microbiology and immunology from the University of Minnesota and a Ph.D. in microbiology and immunology from the University of Michigan.

David A. Roth, M.D. has been Syros' chief medical officer since December 2015. Previously, Dr. Roth was employed by Infinity from September 2013 until September 2015, serving most recently as its executive vice president and chief medical officer and previously as its senior vice president of clinical development and medical affairs. Prior to joining Infinity, Dr. Roth was the vice president, early development in the oncology business unit of Pfizer from 2009 to August 2013. Prior to joining the pharmaceutical industry, Dr. Roth's experience included over ten years in research and clinical practice as an academic hematologist, and he served on the full-time faculty at Harvard Medical School and Beth Israel Deaconess Medical Center in Boston. Dr. Roth received his B.S. from MIT and his M.D. from Harvard Medical School in the Harvard MIT Division of Health Sciences and Technology.

Kristin Stephens has been Syros' chief development officer since June 2020. She previously served as Syros' senior vice president of product development from August 2018 to June 2020, vice president of development operations from March 2018 to August 2018, and vice president of clinical operations from October 2015 to March 2018. Prior to Syros, Ms. Stephens spent nearly ten years at Millennium and Takeda in a variety of roles with escalating responsibilities, serving most recently as vice president of global clinical operations. Earlier in her career, Ms. Stephens worked at Quintiles Strategic Research Services, Clinical Assistance Programs and Eastern Cooperative Oncology Group. Ms. Stephens earned her B.A. in mathematics and psychology at William Smith College.

Non-Employee Directors

Srinivas Akkaraju, M.D., Ph.D. has served on Syros' board of directors since June 2017. Dr. Akkaraju is a founder and managing general partner of Samsara BioCapital, a venture capital firm, a position he has held since

March 2017. From April 2013 to February 2016, Dr. Akkaraju served as a general partner of Sofinnova Ventures, a venture capital firm. From January 2009 to April 2013, Dr. Akkaraju served as managing director of New Leaf Venture Partners, a venture capital firm. Dr. Akkaraju received an M.D. and a Ph.D. in immunology from Stanford University and undergraduate degrees in biochemistry and computer science from Rice University. Dr. Akkaraju serves as a director of Intercept Pharmaceuticals, Inc., a publicly traded biotechnology company, and Jiya Acquisition Corp., a publicly traded special purpose acquisition company. Previously, he served as a director of Aravive, Inc., aTyr Pharma, Inc., Principia Biopharma Inc., Seattle Genetics, Inc., and ZS Pharma Inc., each a publicly traded biotechnology company. Syros believes that Dr. Akkaraju is qualified to serve on its board of directors because of his strong scientific background and extensive experience in private equity and venture capital investing.

Mark J. Alles has served on Syros' board of directors since December 2019. Mr. Alles served as chief executive officer of Celgene Corporation, a global biopharmaceutical company, or Celgene, from March 2016 to June 2018 and as its chairman and chief executive officer from February 2018 until its acquisition by Bristol-Myers Squibb Company in November 2019. Prior to these roles, Mr. Alles served as Celgene's president and chief operating officer from August 2014 to February 2016 and as its chief commercial officer and executive vice president, hematology & oncology from December 2012 to July 2014. Mr. Alles first joined Celgene in April 2004 and served in a number of commercial management positions of increasing responsibility at the company. Before joining Celgene, he held senior commercial management roles at Aventis Pharmaceuticals Inc. (Rhône-Poulenc Rorer) from 1993 to 2004. He is currently chairman of the board of directors of Turning Point Therapeutics, Inc., a public oncology company, and also serves on the board of directors of Antengene Corporation Limited and BioMarin Pharmaceuticals, both public biopharmaceutical companies. He is also a member of the board of directors and consulting CEO for PIKSci, Inc., a private biotechnology company. Mr. Alles received B.S. degree from Lock Haven University of Pennsylvania and served as a Captain in the United States Marine Corps. Syros believes that Mr. Alles is qualified for service on its board of directors due to his extensive executive experience and his track record of building successful global oncology organizations and commercializing innovative therapies.

Deborah Dunsire, M.D. has served on Syros' board of directors since September 2021. Dr. Dunsire is President and Chief Executive Officer of H. Lundbeck A/S, a public biopharmaceutical company, a position she has held since September 2018. She previously served as President and Chief Executive Officer and a Director of Xtuit Pharmaceuticals, Inc., a private biopharmaceutical company, from January 2017 to March 2018. Prior to her position at Xtuit, she served as President and Chief Executive Officer and a Director of FORUM Pharmaceuticals Inc., a private pharmaceutical company, from July 2013 to May 2016. Prior to FORUM, Dr. Dunsire worked for Takeda Pharmaceutical Company Limited as a corporate officer from June 2010 to June 2011 and a Director from June 2011 to June 2013. She served as President, Chief Executive Officer and a Director of Millennium Pharmaceuticals, Inc. between 2005 and 2008, when it was acquired by Takeda, and then as President and Chief Executive Officer of Millennium: The Takeda Oncology Company after the acquisition between 2008 and 2013. Prior to Millennium, Dr. Dunsire held various roles of increasing responsibility at Novartis Pharma AG between 1988 and 2005. She currently serves as a Board member of Ultragenyx Pharmaceutical Inc, a public biopharmaceutical company. She obtained an MBBCh from the University of the Witwatersrand in South Africa. Syros believes that Dr. Dunsire is qualified to serve on its board of directors due to her extensive experience in the biotechnology and pharmaceutical sectors, including service as the chief executive officer of various pharmaceutical companies.

S. Gail Eckhardt, M.D. has been a member of Syros' board of directors since September 2020. Dr. Eckhardt is a tenured Professor, inaugural Director of the Livestrong Cancer Institutes, Chair of the Department of Oncology, and Associate Dean of Cancer Programs at the University of Texas at Austin's Dell Medical School, or UT Austin. She has been a faculty member at the institution since January of 2017. Prior to joining UT Austin, Dr. Eckhardt was at the University of Colorado School of Medicine from 1999 to January 2017, where she had numerous roles and responsibilities, including Division Head of Medical Oncology, Associate Director for Translational Research at the University of Colorado Comprehensive Cancer Center and Director of the Phase I

Program and Fellowship. Dr. Eckhardt served on the Board of Directors of NuGenerex Immuno-Oncology, Inc., a public biotechnology company, from March 2020 to May 2021, and has served on the Board of Directors of OncoTex Inc., a private biotechnology company, since January 2022. She has also served on numerous committees and study sections, including the ASCO Molecular Oncology Task Force, the ASCO Board of Directors, the FDA Oncology Drugs Advisory Committee, and the National Cancer Institute (NCI) Cancer Centers Study Section. She is a member of the NCI Investigational Drug Steering Committee and serves on several external advisory boards of NCI-designated cancer centers, was a lead mentor in ASCO's Leadership Development Program and currently is a member of the Board of Directors of the Association of American Cancer Institutes. Dr. Eckhardt earned her B.S. degree in chemistry from Stephen F. Austin State University and her M.D. from the University of Texas Medical Branch in Galveston. She conducted her internship and residency in Internal Medicine at the University of Virginia Medical School, followed by a post-doctoral research fellowship in Experimental and Molecular Medicine at Scripps Research Institute in La Jolla, California, and a fellowship in Medical Oncology at the University of California San Diego. Syros believes that Dr. Eckhardt is qualified for service on its board of directors due to her expertise in the preclinical and early clinical development of novel agents and her extensive drug development experience.

Marsha H. Fanucci has been a member of Syros' board of directors since October 2015. Since 2009, Ms. Fanucci has been an independent consultant. From 2004 to 2009, she served as senior vice president and chief financial officer of Millennium Pharmaceuticals, Inc., a biopharmaceutical company, or Millennium, that was subsequently acquired by Takeda Pharmaceuticals Company, a publicly traded biopharmaceutical company, or Takeda. She previously served in various other roles at Millennium, including as vice president, finance and corporate strategy and vice president, corporate development. Ms. Fanucci is a member of the boards of directors of Alnylam Pharmaceuticals, Inc., Cyclerion Therapeutics, Inc. and Forma Therapeutics Holdings, Inc., each a publicly traded biopharmaceutical company. She previously served as a director of Momenta Pharmaceuticals, Inc. and Ironwood Pharmaceuticals, Inc., each a publicly traded biopharmaceutical company. Ms. Fanucci received her B.S. in pharmacy from West Virginia University and her M.B.A. from Northeastern University. Syros believes Ms. Fanucci is qualified to serve on its board of directors due to her expertise with public and financial accounting matters and her experience leading financial organizations in biotechnology companies.

Amir Nashat, Ph.D. has served on Syros' board of directors since January 2016. He is a managing partner at Polaris Partners, a venture capital firm, where he has worked since 2002. Dr. Nashat also serves on the advisory board of the Partners Healthcare Innovation Fund. Dr. Nashat serves on the board of directors of Scholar Rock, Inc., a biopharmaceutical company. He previously served on the boards of directors of aTyr Pharma, Inc., Bind Therapeutics, Inc., Fate Therapeutics, Inc., Receptos, Inc. and Selecta Biosciences, Inc., each a biopharmaceutical company. Dr. Nashat received a Ph.D. in chemical engineering from MIT, and an M.S. and B.S. in materials science and mechanical engineering from the University of California, Berkeley. Syros believes Dr. Nashat is qualified to serve on its board of directors because of his experience on the boards of directors of other publicly traded companies and his experience as an investor in biotechnology and life sciences companies.

Phillip A. Sharp, Ph.D. has served on Syros' board of directors since December 2012. Dr. Sharp has been an institute professor at the Massachusetts Institute of Technology, or MIT, since 1999. Much of Dr. Sharp's scientific work has been conducted at MIT's Center for Cancer Research (now the Koch Institute), which he joined in 1974 and directed from 1985 to 1991. He subsequently led the Department of Biology from 1991 to 1999 before assuming the directorship of the McGovern Institute from 2000 to 2004. Dr. Sharp is the winner of the 1993 Nobel Prize in Physiology or Medicine. Dr. Sharp is a member of the board of directors of Alnylam Pharmaceuticals, Inc. and Vir Biotechnology, Inc., each a publicly traded biopharmaceutical company. He earned his B.A. from Union College (Kentucky) and a Ph.D. in chemistry from the University of Illinois, Champaign-Urbana. He did his postdoctoral training at the California Institute of Technology. Syros believes Dr. Sharp is qualified to serve on its board of directors due to his scientific expertise and his experience as a director of a publicly traded company.

Peter Wirth has served as Chair of Syros' board of directors since January 2017. Mr. Wirth currently serves as chair of Forma Therapeutics Holdings, Inc., a publicly traded biotechnology company, as a director and senior

advisor to Zai Lab Limited, a publicly traded biopharmaceutical company based in Shanghai, China, and as a director at Kira Pharmaceuticals, Inc., and Centrexion Therapeutics Corp., each a privately held biotechnology company. Mr. Wirth was a senior executive at Genzyme Corporation, or Genzyme, from 1996 until after its acquisition by Sanofi-Aventis in 2011, most recently serving as executive vice president, legal and corporate development, chief risk officer and corporate secretary. During his time at Genzyme, Mr. Wirth had senior management responsibility for the company's legal function, corporate development function, molecular oncology division, polymer drug discovery and development division and enterprise risk management function. Mr. Wirth received his B.A. from the University of Wisconsin-Madison and his J.D. from Harvard Law School. Syros believes Mr. Wirth is qualified to serve on its board of directors due to his expertise in corporate governance and his experience in corporate strategy, product development and law in the biotechnology industry.

Richard A. Young, Ph.D. has served on Syros' board of directors since its inception in November 2011. He is also one of Syros' scientificco-founders and a member of Syros' scientific advisory board. He has been a member of the Whitehead Institute and professor of Biology at MIT since 1984. In May 2012, he was elected into the National Academy of Sciences. Dr. Young has served as an advisor to Science magazine and the World Health Organization. Dr. Young currently serves on the board of directors of Omega Therapeutics, Inc., a public biotechnology company, and on the boards of directors of Camp4 Therapeutics, Inc. and Dewpoint Therapeutics, Inc., each a private biotechnology company. Dr. Young received his Ph.D. in molecular biophysics and biochemistry from Yale University. Syros believes Dr. Young is qualified to serve on its board of directors because of his scientific expertise and his role as one of Syros' scientific co-founders.

Composition of the Board of Directors

Syros' board of directors currently consists of ten directors divided into three staggered classes, with one class to be elected at each special meeting to serve for a three-year term. The staggered structure of the board of directors will remain in place for the combined company following the completion of the merger. It is anticipated that the incoming directors will be appointed to applicable vacant director seats of the combined company board of directors.

There are no family relationships among any of the proposed combined company directors and officers.

Committees of the Board of Directors

Syros' board of directors currently has the following standing committees: audit committee, compensation committee, nominating and corporate governance committee, and research and development committee. Following the completion of the merger the combined company will continue to have the following standing committees: audit committee, compensation committee, nominating and corporate governance committee, and research and development committee.

Audit Committee

Syros' audit committee's responsibilities include:

- appointing, approving the compensation of, and assessing the independence of Syros' registered public accounting firm;
- overseeing the work of Syros' independent registered public accounting firm, including through the receipt and consideration of reports from such firm;
- reviewing and discussing with management and Syros' independent registered public accounting firm Syros' annual and quarterly financial statements and related disclosures;
- monitoring Syros' internal control over financial reporting, disclosure controls and procedures and code of business conduct and ethics;

- overseeing Syros' internal audit function, if any;
- overseeing Syros' risk assessment and risk management policies;
- establishing procedures for the receipt and retention of accounting related complaints and concerns;
- meeting independently with Syros' internal auditing staff, if any, Syros' independent registered public accounting firm and management;
- reviewing and approving or ratifying any related person transactions; and
- preparing the audit committee report required by SEC rules.

The audit committee of the combined company is expected to retain these duties and responsibilities following the completion of the merger.

In connection with the closing of the merger, the combined company's board of directors is expected to select members of the audit committee. To qualify as independent to serve on the combined company's audit committee, listing standards of Nasdaq and the applicable SEC rules require that a director not accept any consulting, advisory or other compensatory fee from the combined company, other than for service as a director, or be an affiliated person of the combined company. Syros and Tyme believe that, following the completion of the merger, the composition of the audit committee will comply with the applicable requirements of the rules and regulations of Nasdaq and the SEC.

Compensation Committee

Syros' compensation committee's responsibilities include:

- reviewing and approving, or making recommendations to Syros' board with respect to, the compensation of Syros' chief executive officer and other executive officers;
- overseeing the evaluation of Syros' senior executives;
- overseeing and administering Syros' cash and equity incentive plans;
- reviewing and making recommendations to Syros' board of directors with respect to director compensation and management succession planning;
- reviewing and discussing annually with management Syros' "Compensation Discussion and Analysis" disclosure if and to the extent such disclosure is then required by SEC rules; and
- preparing the compensation committee report if and to the extent then required by SEC rules.

The compensation committee of the combined company is expected to retain these duties and responsibilities following completion of the merger.

In connection with the closing of the merger, the combined company's board of directors is expected to select members of the compensation committee. Each member of the combined company's compensation committee is expected to be a "non-employee" director within the meaning of Rule 16b-3 of the rules promulgated under the Exchange Act and independent within the meaning of the independent director guidelines of Nasdaq. Syros and Tyme believe that, following the completion of the merger, the composition of the compensation committee will comply with the applicable requirements of the rules and regulations of Nasdaq.

Nominating and Corporate Governance Committee

Syros' nominating and corporate governance committee's responsibilities include:

- identifying individuals qualified to become members of Syros' board of directors;

- recommending to Syros' board the persons to be nominated for election as directors and to each of Syros' board's committees;
- reviewing and making recommendations to Syros' board of directors with respect to Syros' board leadership structure and board committee structure;
- making recommendations to Syros' board of directors with respect to accepting director resignations;
- developing and recommending to Syros' board corporate governance principles; and
- overseeing an annual evaluation of Syros' board.

The nominating and corporate governance committee of the combined company is expected to retain these duties and responsibilities following completion of the merger.

In connection with the closing of the merger, the combined company's board of directors is expected to select members of the nominating and corporate governance committee. Syros and Tyme believe that, after the completion of the merger, the composition of the nominating and corporate governance committee will meet the requirements for independence under, and the functioning of such nominating and corporate governance committee will comply with, any applicable requirements of the rules and regulations of Nasdaq.

Research and Development Committee

Syros' research and development committee's responsibilities include:

- reviewing Syros' current and planned R&D programs and initiatives from a scientific perspective, providing feedback to Syros' R&D management on those programs and initiatives, and from time to time providing observations and strategic recommendations to Syros' board of directors;
- serving as a sounding board for Syros' R&D organization on R&D matters;
- as requested, assisting management in identifying world-class experts to provide strategic scientific and clinical advice regarding Syros' programs; and
- identifying and discussing with Syros' board of directors significant emerging scientific and clinical issues and trends, as well as benchmarking Syros' programs and R&D activities against its competitors.

The research and development committee of the combined company is expected to retain these duties and responsibilities following completion of the merger. In connection with the closing of the merger, the combined company's board of directors is expected to select members of the research and development committee.

Compensation Committee Interlocks and Insider Participation

In connection with the closing of the merger, the combined company's board of directors is expected to select members of the compensation committee. Each member of the compensation committee is expected to be a "non-employee" director within the meaning of Rule 16b-3 of the rules promulgated under the Exchange Act and independent within the meaning of the independent director guidelines of Nasdaq. None of the proposed combined company's executive officers serves as a member of the board of directors or compensation committee of any entity that has one or more executive officers who is proposed to serve on the combined company's board of directors or compensation committee following the completion of the merger.

Director Compensation

Syros pays its non-employee directors a cash retainer for service on Syros' board of directors and for service on each committee on which the director is a member pursuant to a director compensation program that was initially adopted by Syros' board of directors effective upon completion of its initial public offering in July 2016. The

chair of each committee and the chair of the board of directors receive higher retainers for such service. In December 2019, Syros' board of directors amended the director compensation program to increase the cash retainer for its non-employee directors by $5,000, the retainer for members of the Nominating and Corporate Governance Committee by $500, and the retainer for the chair of the Nominating and Corporate Governance Committee by $1,000. These fees are payable in arrears in four equal quarterly installments on the last day of each quarter, subject to proration for any portion of such quarter that the director is not serving on Syros' board of directors, on such committee or in such position. Effective January 1, 2020, the fees paid to non-employee directors for service on the board of directors and for service on each committee of the board of directors on which the director is a member are as follows:

	Base	Incremental—Chair	Incremental—Non-Chair
Board of Directors	$40,000	$ 30,000	
Audit Committee		$ 15,000	$ 7,500
Compensation Committee		$ 10,000	$ 5,000
Research and Development Committee		$ 10,000	$ 5,000
Nominating and Corporate Governance Committee		$ 8,000	$ 4,000

In addition, under this director compensation program, Syros will grant to new non-employee directors upon their initial election to the board, an initial option to purchase 35,000 shares of Syros common stock, with an exercise price equivalent to fair market value of a share of Syros common stock at the time of grant, which option will vest as to 16.66% of the shares on the six month anniversary of the date of grant and as to the remainder of the shares in equal monthly installments thereafter until the third anniversary of the date of grant, subject to continued service, with full acceleration upon a change in control of Syros. The option will have a term of ten years.

Immediately following each special meeting of our stockholders, Syros will grant to each non-employee director who has served on its board of directors for at least six months an option to purchase 17,500 shares of Syros common stock, with an exercise price equivalent to fair market value of a share of Syros common stock at the time of grant, which option will vest as to 50% of the shares on the six-month anniversary of the date of grant and as to the remainder of the shares in equal monthly installments thereafter until the first anniversary of the date of grant, subject to continued service, with full acceleration upon a change in control of Syros. The option will have a term of ten years.

Syros also reimburses its non-employee directors for reasonable travel and out-of-pocket expenses incurred in connection with attending its board of directors and committee meetings.

Syros does not pay any compensation to its president and chief executive officer in connection with her service on the Syros board of directors. The compensation that Syros pays to its president and chief executive officer is discussed earlier in this "Syros Executive Compensation" section.

The following table sets forth information regarding compensation earned by Syros' non-employee directors during fiscal 2021.

Name	Fees Earned or Paid in Cash ($)	Option Awards ($)(1)	All Other Compensation ($)	Total ($)
Srinivas Akkaraju, M.D., Ph.D.	49,000	73,294	—	122,294
Mark J. Alles	47,500	73,294	—	120,794
Deborah Dunsire, M.D. (2)	15,353	125,829	—	141,182
S. Gail Eckhardt, M.D.	46,228	73,294	—	119,522
Marsha H. Fanucci	55,000	73,294	—	128,294

Name	Fees Earned or Paid in Cash ($)	Option Awards ($)(1)	All Other Compensation ($)	Total ($)
Amir Nashat, Ph.D.	55,500	73,294	—	128,794
Phillip A. Sharp, Ph.D.	50,000	73,294	—	123,294
Peter Wirth	80,000	73,294	—	153,294
Richard A. Young, Ph.D.	50,000	73,294	115,000 (3)	238,294

(1) The amounts reported in the "Option Awards" column reflect the aggregate grant date fair value of stock-based compensation awarded during the year computed in accordance with the provisions of ASC Topic 718. This calculation does not give effect to any estimate of forfeitures related to service-based vesting but assumes that the applicable director will perform the requisite service for the award to vest in full. See Note 12 to Syros' financial statements included elsewhere in this joint proxy statement/prospectus regarding assumptions underlying the valuation of equity awards.
(2) Dr. Dunsire was appointed to Syros' board of directors in September 2021.
(3) Represents consideration paid during fiscal 2021 pursuant to the terms of a consulting agreement Dr. Young entered with Syros that is unrelated to his service on Syros' board of directors.

As of December 31, 2021, Syros' non-employee directors held the following stock options, all of which were granted under the 2012 Plan and the Syros 2016 Plan:

Name	Option Awards
Srinivas Akkaraju, M.D., Ph.D.	79,000
Mark J. Alles	70,000
Deborah Dunsire, M.D.	35,000
S. Gail Eckhardt, M.D.	52,500
Marsha H. Fanucci	104,666
Amir Nashat, Ph.D.	90,000
Phillip A. Sharp, Ph.D.	132,857
Peter Wirth	79,000
Richard A. Young, Ph.D.	165,000

SYROS EXECUTIVE COMPENSATION

This section discusses the material elements of Syros' executive compensation policies for its "named executive officers" and the most important factors relevant to an analysis of these policies. For 2021, Syros' named executive officers are Nancy A. Simonian, M.D., its President and Chief Executive Officer, Jason Haas, its Chief Financial Officer, and David Roth, its Chief Medical Officer. In addition, this section provides qualitative information regarding the manner and context in which compensation is awarded to and earned by Syros' named executive officers and is intended to place in perspective the data presented in the following tables and the corresponding narrative.

Overview

Summary Compensation Table

The following table sets forth information regarding compensation earned by Syros' named executive officers during the years indicated.

Name and Position of Named Executive Officers	Year	Salary ($)	Option Awards ($)(1)	Non-Equity Incentive Plan Compensation ($)(2)	All Other Compensation ($)(3)	Total ($)
Nancy A. Simonian, M.D.(4)	2021	615,923	2,163,749	322,905	576	3,103,153
President & Chief Executive Officer	2020	597,692	1,503,457	429,000	360	2,530,509
Jason Haas(5)	2021	91,385	2,361,150	42,460	144	2,495,139
Chief Financial Officer	2020	—	—	—	—	—
David A. Roth, M.D.	2021	482,385	944,646	185,158	576	1,612,765
Chief Medical Officer	2020	468,269	480,697	244,400	360	1,193,726

(1) The amounts reported in the "Option Awards" column reflects the aggregate grant date fair value of stock-based compensation awarded during the year computed in accordance with the provisions of Financial Accounting Standards Board Accounting Standard Codification, or ASC, Topic 718. This calculation does not give effect to any estimate of forfeitures related to service-based vesting but assumes that the named executive officer will perform the requisite service for the award to vest in full. See Note 12 to Syros' financial statements included in its Annual Report on Form 10-K for the year ended December 31, 2021 regarding assumptions underlying the valuation of equity awards.

(2) The amounts reported in the "Non-Equity Incentive Plan Compensation" column reflect awards to Syros' named executive officers under its performance-based cash incentive program. See "*Cash Incentives*" for a description of that program. Annual cash bonus awards earned during the year is typically paid in the following year.

(3) The amounts reported in the "All Other Compensation" column reflect, for each named executive officer, the cost to Syros of life insurance premiums paid for the named executive officer.

(4) Dr. Simonian also serves as a member of Syros' board of directors but does not receive any additional compensation for her service as a director.

(5) Mr. Haas commenced employment with Syros on October 12, 2021. Amounts shown for 2021 represent compensation earned by Mr. Haas during that partial year of employment.

Narrative Disclosure to Summary Compensation Table

Syros reviews compensation for its executive officers annually. The material terms of the elements of its executive compensation program for 2021 are described below.

Syros' compensation committee sets base salaries and bonuses and grants equity incentive awards to its executive officers. In setting base salaries and bonuses and granting equity incentive awards, Syros' compensation committee considers compensation for comparable positions in the market, the historical compensation levels of Syros' executives, individual and corporate performance as compared to Syros'

expectations and objectives, Syros' desire to motivate its employees to achieve short- and long-term results that are in the best interests of Syros' stockholders, and a long-term commitment to the company. As part of this process, Dr. Simonian, as Syros' president and chief executive officer, prepares performance evaluations for the other executive officers and recommends annual salary increases, annual stock option awards and cash bonuses to the compensation committee. The compensation committee conducts a performance evaluation of Dr. Simonian. The compensation committee consults with the Syros board of directors as to the achievement of corporate objectives that drive contingent compensation awards.

During its annual compensation review, Syros' compensation committee also consults with external advisors. In the fiscal year ended December 31, 2021, or fiscal 2021, the compensation committee engaged Compensia Inc. as its independent compensation consultant to provide comparative data on executive compensation practices in Syros' industry and assess its executives' compensation relative to comparable companies.

Base Salary

Syros uses base salaries to recognize the experience, skills, knowledge and responsibilities required of all its employees, including its named executive officers. None of Syros' named executive officers is currently party to an employment agreement or other agreement or arrangement that provides for automatic or scheduled increases in base salary.

In February 2020, the compensation committee set Dr. Simonian's annualized base salary to $600,000 effective February 10, 2020. In February 2021, the compensation committee increased Dr. Simonian's annualized base salary to $618,000 effective February 22, 2021. In February 2022, the compensation committee increased Dr. Simonian's annualized base salary to $640,000 effective February 21, 2022.

Mr. Haas commenced employment with Syros in October 2021. In 2021, Syros paid him a base salary of $91,385 for his partial year of employment based on an annualized base salary of $440,000. In February 2022, the compensation committee of Syros' board of directors increased Mr. Haas's annualized base salary to $470,000 effective February 21, 2022.

In February 2020, the compensation committee set Dr. Roth's annualized base salary to $470,000 effective February 10, 2020. In February 2021, the compensation committee increased Dr. Roth's annualized base salary to $484,000 effective February 22, 2021. In February 2022, the compensation committee of Syros' board of directors increased Dr. Roth's annualized base salary to $500,000 effective February 21, 2022.

Cash Incentives

Syros has established a framework under which the compensation committee would, in its discretion, award annual performance-based cash bonuses to its executive officers for up to a specific percentage of his or her salary as a vehicle to reward achievement of value driving milestones and recognize individual performance. Dr. Simonian was eligible for a performance-based cash bonus of a percentage of her annual base salary, subject to achievement of corporate goals as determined by the compensation committee. Her bonus target was 55% of her annual base salary in the year ended December 31, 2020, or fiscal 2020, and fiscal 2021. Syros' other named executive officers are eligible for a performance-based cash bonus of a percentage of such named executive officer's base salary, 90% of which is tied to achievement of corporate goals as determined by the compensation committee, and 10% of which is tied to the achievement of individual goals as recommended by Dr. Simonian and approved by the compensation committee. The bonus target for Syros' other named executive officers was 40% of the applicable officer's annual base salary for both fiscal 2020 and fiscal 2021.

In February 2021, Syros made cash bonus awards of $429,000 to Dr. Simonian and $244,400 to Dr. Roth based on the compensation committee's assessment of achievement of corporate and individual goals during fiscal 2020, and in February 2022, Syros made cash bonus awards of $322,905 to Dr. Simonian, $42,460 to Mr. Haas

and $185,158 to Dr. Roth based on the compensation committee's assessment of achievement of corporate and individual goals during fiscal year 2021.

Equity Incentives

Although Syros does not have a formal policy with respect to the grant of equity incentive awards to its executive officers, or any formal share ownership policy or guidelines applicable to them, Syros believes that equity awards are very effective in supporting executive recruitment, motivation, and retention in a highly competitive marketplace for experienced talent, provide Syros' executive officers with a strong link to its long-term performance, create an ownership culture, and help to align the interests of Syros' executive officers and its stockholders. In addition, Syros believes that equity awards with a time-based vesting condition promote executive retention because this feature incents its executive officers to remain in its employment during the award's vesting period. Accordingly, the compensation committee periodically reviews the equity incentive compensation holdings of Syros' named executive officers and from time to time may grant equity incentive awards to them in the form of stock options and/or restricted stock unit awards. The compensation committee carefully manages Syros' share utilization and the dilutive effect of the equity incentive awards that it grants in order to ensure the long-term sustainability of its equity incentive plan. As a result of the ongoing volatility in the equity markets for development-stage companies in Syros' industry and the imperative to continue to motivate and retain Syros' executive officers through the completion of the potential value-creating clinical milestones in the future, Syros expect that the number of shares subject to the equity incentive awards granted by the compensation committee during 2022 will increase.

In February 2020, Dr. Simonian was granted an option to purchase 294,000 shares of Syros common stock and Dr. Roth was granted an option to purchase 94,000 shares of Syros common stock. These options vested as to 25% of the shares on February 28, 2021, with the remaining shares vesting in equal monthly installments thereafter through February 29, 2024, subject to the applicable officer's continued service through the applicable vesting date.

In February 2021, Dr. Simonian was granted an option to purchase 304,000 shares of Syros common stock and Dr. Roth was granted an option to purchase 119,000 shares of Syros common stock. These options vested as to 25% of the shares on February 28, 2022, with the remaining shares vesting in equal monthly installments thereafter through February 28, 2025, subject to the applicable officer's continued service through the applicable vesting date.

In October 2021, Mr. Haas was granted an option to purchase 750,000 shares of Syros common stock in connection with his appointment as its Chief Financial Officer as an inducement material to Mr. Haas' acceptance of employment with Syros in accordance with Nasdaq Listing Rule 5635(c)(4). This option vests as to 25% of the shares subject to the option on October 12, 2022, with the remaining shares vesting in equal monthly installments thereafter through October 12, 2025, subject to Mr. Haas's continued service through each applicable vesting date. The size of this equity award was driven largely by the value of new-hire equity incentive awards granted to chief financial officers at comparable companies as well as the compensation committee's desire to make Mr. Haas whole of the value of the deferred compensation he would be forfeiting upon leaving his prior employer.

Outstanding Equity Awards at Fiscal Year End 2021

The following table sets forth information regarding outstanding equity awards held by Syros' named executive officers as of December 31, 2021.

	Option Awards					Stock Awards
Current Named Executive Officers	Number of Securities Underlying Unexercised Options Exercisable (#)	Number of Securities Underlying Unexercised Options Unexercisable (#)	Option Exercise Price ($/ share)	Option Expiration Date	Number of Shares or Units of Stock That Have Not Vested (#)	Market Value of Shares or Units of Stock That Have Not Vested ($)(1)
Nancy A. Simonian, M.D.	37,666(2)	—	3.04	2/4/2025	188,000(8)	612,880
	34,838(2)	—	3.04	6/8/2025		
	21,524(2)	—	3.04	6/8/2025		
	79,165(2)	—	8.51	3/30/2026		
	75,000(2)	—	12.17	9/15/2026		
	175,000(2)	— (2)	10.90	2/9/2027		
	268,134(3)	11,878(3)	10.09	2/15/2028		
	201,872(4)	83,128(4)	6.71	2/11/2029		
	134,748(5)	159,252(5)	7.54	2/12/2030		
	— (6)	304,000(6)	11.41	2/16/2031		
Jason Haas	— (7)	750,000(7)	4.54	10/11/2031		
David A. Roth, M.D.	223,661(2)	—	9.08	12/22/2025	87,000(8)	283,620
	63,500(2)	—	10.90	2/9/2027		
	71,873(3)	3,127(3)	10.09	2/15/2028		
	53,123(4)	21,877(4)	6.71	2/11/2029		
	43,082(5)	50,918(5)	7.54	2/12/3030		
	— (6)	119,000(6)	11.41	2/16/2031		

(1) Calculated based on the closing price per share of Syros common stock on December 31, 2021, which was $3.26.
(2) This option is fully vested.
(3) This option was granted on February 16, 2018 and vested as to 25% of the shares on February 16, 2019 with the remaining shares vesting in equal monthly installments thereafter through February 28, 2022, subject to continued service.
(4) This option was granted on February 12, 2019 and vested as to 25% of the shares on February 11, 2020 with the remaining shares vesting in equal monthly installments thereafter through February 28, 2023, subject to continued service.
(5) This option was granted on February 13, 2020 and vested as to 25% of the shares on February 12, 2021 with the remaining shares vesting in equal monthly installments thereafter through February 29, 2024, subject to continued service.
(6) This option was granted on February 17, 2021 and vested as to 25% of the shares on February 17, 2022 with the remaining shares vesting in equal monthly installments thereafter through February 28, 2025, subject to continued service.
(7) This option was granted on October 12, 2021 and vests as to 25% of the shares on October 12, 2022 with the remaining shares vesting in equal monthly installments thereafter through October 12, 2025, subject to continued service.
(8) This restricted stock unit award vested in full on March 31, 2022.

Employment Agreements; Potential Payments upon Termination or Change in Control

Syros has entered into written offer letters with each of its named executive officers. These offer letters set forth the terms of the named executive officer's compensation, including his or her initial base salary, severance and annual cash bonus opportunity. In addition, the offer letters provide that the named executive officers are eligible to participate in company-sponsored benefit programs that are available generally to all of Syros' employees. In connection with the commencement of their employment with Syros, Syros' named executive officers executed its standard invention and non-disclosure agreement and non-competition and non-solicitation agreement.

Change in Control

The offer letter with Dr. Simonian provides that if her employment is terminated by Syros without cause, or by her with good reason, as such terms are defined in her offer letter, she will receive monthly severance payments equal to her then-current monthly salary rate for 12 months and payment of an incentive bonus pro-rated for the portion of the then-current calendar year during which she was employed by Syros, subject to certain conditions, including the execution of a release of all claims against Syros. In addition, in the event of a change in control of Syros, as defined in the offer letter, all unvested stock options then held by Dr. Simonian will vest in full 12 months after the change in control, or earlier if her employment is terminated by Syros without cause or by her for good reason in contemplation of, pursuant to or following a change in control, referred to as the CIC Equity Vesting.

The offer letter with each of Syros' other named executive officers provides that if his employment is terminated by Syros without cause, or by him with good reason, as such terms are defined in his offer letter, he will receive monthly severance payments equal to his then-current monthly rate of salary for nine months, subject to certain conditions, including the execution of a release of all claims against Syros. Syros' other named executive officers are also eligible for the CIC Equity Vesting.

Other Agreements

Syros has also entered into employee confidentiality, inventions,non-solicitation, and non-competition agreements with each of its named executive officers. Under the employee confidentiality, inventions, non-solicitation, and non-competition agreements, each named executive officer has agreed (1) not to compete with Syros during his or her employment and for a period of one year after the termination or cessation of his or her employment for any reason, (2) not to solicit Syros' employees during his or her employment and for a period of one year after the termination or cessation of his or her employment for any reason, (3) to protect Syros' confidential and proprietary information and (4) to assign to Syros related IP developed during the course of his or her employment.

Indemnification

Syros has entered into indemnification agreements with each of its directors and executive officers. Each of these indemnification agreements provides, among other things, that Syros will indemnify such director or executive officer to the fullest extent permitted by law for claims arising in his or her capacity as a director or executive officer, as applicable, provided that he or she acted in good faith and in a manner that he or she reasonably believed to be in, or not opposed to, Syros' best interests and, with respect to any criminal proceeding, had no reasonable cause to believe that his or her conduct was unlawful. Each of these indemnification agreements provides that in the event that Syros does not assume the defense of a claim against a director or executive officer, as applicable, Syros is required to advance his or her expenses in connection with his or her defense, provided that he or she undertakes to repay all amounts advanced if it is ultimately determined that he or she is not entitled to be indemnified by Syros.

Equity Incentive Plans

The four equity incentive plans described in this section are Syros' 2012 Equity Incentive Plan, as amended to date, or the 2012 Plan, Syros' 2016 Stock Incentive Plan, or the Syros 2016 Plan, Syros' 2016 Employee Stock Purchase Plan, or the 2016 ESPP and Syros' 2022 Inducement Stock Incentive Plan, or the 2022 Inducement Plan.

2012 Equity Incentive Plan

The 2012 Plan was adopted by Syros' board of directors and approved by its stockholders in August 2012. The 2012 Plan provides for the grant of incentive stock options, nonstatutory stock options, stock appreciation rights, awards of restricted stock, restricted stock units, other stock-based awards and cash-based awards. Syros' employees, officers, directors, consultants and advisors are eligible to receive awards under the 2012 Plan; however, incentive stock options may only be granted to Syros' employees.

The type of award granted under our 2012 Plan and the terms of such award are set forth in the applicable award agreement.

Pursuant to the terms of the 2012 Plan, Syros' board of directors (or a committee delegated by Syros' board of directors) administers the 2012 Plan and, subject to any limitations set forth in the 2012 Plan, selects the recipients of awards and determines:

- the number of shares of Syros common stock covered by options and the dates upon which the options become exercisable;
- in the event of a reorganization event pursuant to which holders of shares of Syros common stock will receive a cash payment for each share surrendered in the reorganization event, make or provide for a cash payment to the participants with respect to each award held by a participant equal to (1) the number of shares of Syros common stock subject to the vested portion of the award (after giving effect to any acceleration of vesting that occurs upon or immediately prior to such reorganization event) multiplied by (2) the excess, if any, of the cash payment for each share surrendered in the reorganization event over the exercise, measurement or purchase price of such award and any applicable tax withholdings, in exchange for the termination of such award;
- provide that, in connection with Syros' liquidation or dissolution, awards will convert into the right to receive liquidation proceeds (if applicable, net of the exercise, measurement or purchase price thereof and any applicable tax withholdings); or
- any combination of the foregoing.

Syros' board of directors is not obligated by the 2012 Plan to treat all awards, all awards held by a participant, or all awards of the same type, identically.

In the case of certain restricted stock units that are subject to Section 409A of the Internal Revenue Code of 1986, as amended, or the Code, no assumption or substitution is permitted, and the restricted stock units will instead be settled in accordance with the terms of the applicable restricted stock unit agreement.

Upon the occurrence of a reorganization event other than Syros' liquidation or dissolution, the repurchase and other rights with respect to outstanding awards of restricted stock will continue for the benefit of the successor company and will, unless Syros' board of directors may otherwise determine, apply to the cash, securities or other property which Syros common stock is converted into or exchanged for pursuant to the reorganization event. However, Syros' board of directors may provide for the termination or deemed satisfaction of such repurchase or other rights under the restricted stock award agreement or any other agreement between the participant and Syros, either initially or by amendment. Upon the occurrence of a reorganization event involving

Syros' liquidation or dissolution, all restrictions and conditions on each outstanding restricted stock award will automatically be deemed terminated or satisfied, unless otherwise provided in the agreement evidencing the restricted stock award or in any other agreement between the participant and Syros.

Syros' board of directors may, at any time, provide that any award under the 2012 Plan will become immediately exercisable in whole or in part, free of some or all restrictions or conditions, or otherwise realizable in whole or in part, as the case may be.

As of December 31, 2021, there were 711,338 shares of Syros common stock to be issued upon exercise of outstanding options under the 2012 Plan. No shares remained available for future issuance under the 2012 Plan as of December 31, 2021.

2016 Stock Incentive Plan

Syros' board of directors has adopted, and its stockholders have approved, the 2016 Stock Incentive Plan, or the Syros 2016 Plan, which became effective immediately prior to the effectiveness of the registration statement filed in connection with Syros' initial public offering. The Syros 2016 Plan provides for the grant of incentive stock options, nonstatutory stock options, stock appreciation rights, awards of restricted stock, restricted stock units and other stock-based awards. Upon effectiveness of the Syros 2016 Plan, the number of shares of Syros common stock reserved for issuance under the Syros 2016 Plan was the sum of (1) 3,120,000 shares plus; (2) the number of shares reserved for issuance (up to 2,112,203 shares) equal to the sum of the number of shares of Syros common stock then available for issuance under the 2012 Plan and the number of shares of Syros common stock subject to outstanding awards under the 2012 Plan that expire, terminate or are otherwise surrendered, cancelled, forfeited or repurchased by us at their original issuance price pursuant to a contractual repurchase right; plus (3) an annual increase, to be added the first day of each fiscal year, beginning with the fiscal year ending December 31, 2017 and continuing until, and including, the fiscal year ending December 31, 2026, equal to the lowest of 1,600,000 shares of Syros common stock, 4.0% of the number of shares of Syros common stock outstanding on the first day of the fiscal year and an amount determined by Syros' board of directors. Syros' employees, officers, directors, consultants and advisors are eligible to receive awards under the Syros 2016 Plan, however, incentive stock options may only be granted to Syros' employees.

Pursuant to the terms of the Syros 2016 Plan, Syros' board of directors (or a committee delegated by Syros' board of directors) administers the plan and, subject to any limitations set forth in the plan, will select the recipients of awards and determine:

- the number of shares of Syros common stock covered by options and the dates upon which those options become exercisable;
- the type of options to be granted;
- the duration of options, which may not be in excess of ten years;
- the exercise price of options, which price must be at least equal to the fair market value of Syros common stock on the date of grant;
- the methods of payment of the exercise price of options; and
- the number of shares of Syros common stock subject to and the terms and conditions of any stock appreciation rights, awards of restricted stock, restricted stock units or other stock-based awards, including conditions for repurchase, measurement price, issue price and repurchase price and performance conditions (though the measurement price of stock appreciation rights must be at least equal to the fair market value of Syros common stock on the date of grant and the duration of such awards may not be in excess of ten years), if any.

If Syros' board of directors delegates authority to an executive officer to grant awards under the Syros 2016 Plan, the executive officer will have the power to make awards to all of Syros' employees, except executive officers.

Syros' board of directors will fix the terms of the awards to be granted by such executive officer, including the exercise price of such awards (or a formula for establishing such price), and the maximum number of shares subject to awards that such executive officer may make.

In the event of any stock split, reverse stock split, stock dividend, recapitalization, combination of shares, reclassification of shares,spin-off or other similar change in capitalization or event, or any dividend or distribution to holders of Syros common stock other than an ordinary cash dividend, Syros is required by the Syros 2016 Plan to make equitable adjustments (or make substitute awards, if applicable), in a manner determined by Syros' board, to:

- the number and class of securities available under the Syros 2016 Plan;
- the share counting rules under the Syros 2016 Plan;
- the number and class of securities and exercise price per share of each outstanding option;
- the share and per-share provisions and measurement price of each outstanding stock appreciation right;
- the number of shares and repurchase price per share subject to each outstanding restricted stock award or restricted stock unit award; and
- the share and per-share related provisions and purchase price, if any, of each outstanding other stock-based award.

Upon a merger or other reorganization event (as defined in the Syros 2016 Plan), Syros' board of directors, may, on such terms as Syros' board determines (except to the extent specifically provided otherwise in an applicable award agreement or other agreement between the participant and Syros), take any one or more of the following actions pursuant to the Syros 2016 Plan, as to all or any (or any portion of) outstanding awards, other than awards of restricted stock:

- provide that all outstanding awards will be assumed or substantially equivalent awards will be substituted by the acquiring successor corporation (or an affiliate thereof);
- upon written notice to a participant, provide that all of the participant's unvested and/or unexercised awards will terminate immediately prior to the consummation of such reorganization event unless exercised by the participant;
- provide that outstanding awards will become exercisable, realizable or deliverable, or restrictions applicable to an award will lapse, in whole or in part, prior to or upon such reorganization event;
- in the event of a reorganization event pursuant to which holders of shares of Syros common stock will receive a cash payment for each share surrendered in the reorganization event, make or provide for a cash payment to the participants with respect to each award held by a participant equal to (1) the number of shares of Syros common stock subject to the vested portion of the award (after giving effect to any acceleration of vesting that occurs upon or immediately prior to such reorganization event) multiplied by (2) the excess, if any, of the cash payment for each share surrendered in the reorganization event over the exercise, measurement or purchase price of such award and any applicable tax withholdings, in exchange for the termination of such award;
- provide that, in connection with Syros' liquidation or dissolution, awards will convert into the right to receive liquidation proceeds (if applicable, net of the exercise, measurement or purchase price thereof and any applicable tax withholdings); or
- any combination of the foregoing.

Syros' board of directors is not obligated by the Syros 2016 Plan to treat all awards, all awards held by a participant, or all awards of the same type, identically.

In the case of certain restricted stock units, no assumption or substitution is permitted, and the restricted stock units will instead be settled in accordance with the terms of the applicable restricted stock unit agreement.

Upon the occurrence of a reorganization event other than Syros' liquidation or dissolution, the repurchase and other rights with respect to outstanding awards of restricted stock will continue for the benefit of the successor company and will, unless Syros' board of directors may otherwise determine, apply to the cash, securities or other property which Syros common stock is converted into or exchanged for pursuant to the reorganization event. However, Syros' board of directors may provide for the termination or deemed satisfaction of such repurchase or other rights under the restricted stock award agreement or any other agreement between the participant and Syros, either initially or by amendment. Upon the occurrence of a reorganization event involving Syros' liquidation or dissolution, all restrictions and conditions on each outstanding restricted stock award will automatically be deemed terminated or satisfied, unless otherwise provided in the agreement evidencing the restricted stock award or in any other agreement between the participant and Syros.

Syros' board of directors may at any time provide that any award under the Syros 2016 Plan will become immediately exercisable in whole or in part, free of some or all restrictions or conditions, or otherwise realizable in whole or in part, as the case may be.

Except with respect to certain actions requiring stockholder approval under the Code or Nasdaq rules, Syros' board of directors may amend, modify or terminate any outstanding award under the Syros 2016 Plan, including but not limited to, substituting therefor another award of the same or a different type, changing the date of exercise or realization, and converting an incentive stock option into a nonstatutory stock option, subject to certain participant consent requirements. Unless Syros' stockholders approve such action, the Syros 2016 Plan provides that Syros may not (except as otherwise permitted in connection with a change in capitalization or reorganization event):

- amend any outstanding stock option or stock appreciation right granted under the Syros 2016 Plan to provide an exercise or measurement price per share that is lower than the then-current exercise or measurement price per share of such outstanding award;
- cancel any outstanding option or stock appreciation right (whether or not granted under the Syros 2016 Plan) and grant in substitution therefor new awards under the Syros 2016 Plan (other than substitute awards permitted in connection with a merger or consolidation of an entity with Syros or Syros' acquisition of property or stock of another entity) covering the same or a different number of shares of Syros common stock and having an exercise or measurement price per share lower than the then-current exercise or measurement price per share of the cancelled award;
- cancel in exchange for a cash payment any outstanding option or stock appreciation right with an exercise or measurement price per share above the then-current fair market value of Syros common stock; or
- take any other action that constitutes a "repricing" within the meaning of Nasdaq rules.

No award may be granted under the Syros 2016 Plan after ten years from the effectiveness of the Syros 2016 Plan. Syros' board of directors may amend, suspend or terminate the Syros 2016 Plan at any time, except that stockholder approval will be required to comply with applicable law or stock market requirements.

As of December 31, 2021, 4,798,230 shares were reserved for issuance upon the exercise of outstanding options under the Syros 2016 Plan, and 2,238,206 shares remained available for future issuance under the Syros 2016 Plan. If Syros' stockholders approve the adoption of the Syros Pharmaceuticals, Inc. 2022 Equity Incentive Plan, which is the subject of Syros Proposal No. 4, and such plan is adopted, then no further awards will be made pursuant to the Syros 2016 Plan.

2016 Employee Stock Purchase Plan

Syros' board of directors has adopted, and its stockholders have approved, the 2016 Employee Stock Purchase Plan, or the 2016 ESPP, which became effective upon the closing of Syros' initial public offering. The 2016 ESPP is administered by Syros' board of directors or by a committee appointed by its board of directors. The 2016 ESPP initially provided participating employees with the opportunity to purchase up to an aggregate of 586,666 shares of Syros common stock. The number of shares of Syros common stock reserved for issuance under the 2016 ESPP will automatically increase on the first day of each fiscal year, commencing on January 1, 2017 and ending on December 31, 2025, in an amount equal to the least of (i) 1,173,333 shares of Syros common stock, (ii) 1.0% of the total number of shares of Syros common stock outstanding on the first day of the applicable year, and (iii) an amount determined by Syros' board of directors.

All of Syros' employees or employees of any designated subsidiary, as defined in the 2016 ESPP, are eligible to participate in the 2016 ESPP, provided that:

- such person is customarily employed by Syros or a designated subsidiary for more than 20 hours a week and for more than five months in a calendar year;
- such person has been employed by Syros or by a designated subsidiary for at least six months prior to enrolling in the 2016 ESPP; and
- such person was Syros' employee or an employee of a designated subsidiary on the first day of the applicable offering period under the 2016 ESPP.

No employee may purchase shares of Syros common stock under the 2016 ESPP and any of our other employee stock purchase plans in excess of $25,000 of the fair market value of Syros common stock (as of the date of the option grant) in any calendar year. In addition, no employee may purchase shares of Syros common stock under the 2016 ESPP that would result in the employee owning 5% or more of the total combined voting power or value of Syros stock or the stock of any of Syros' subsidiaries.

Syros may make offerings to its eligible employees to purchase stock under the 2016 ESPP beginning at such time as Syros' board of directors may determine. Each offering will consist of a six-month offering period during which payroll deductions will be made and held for the purchase of Syros common stock at the end of the offering period. Syros' board of directors may, at its discretion, choose a different period of not more than 12 months for offerings.

On the commencement date of each offering period, each eligible employee may authorize up to a maximum of 15% of his or her compensation to be deducted by Syros during the offering period. Each employee who continues to be a participant in the 2016 ESPP on the last business day of the offering period will be deemed to have exercised an option to purchase from us the number of whole shares of Syros common stock that his or her accumulated payroll deductions on such date will pay for, not in excess of the maximum numbers set forth above. Under the terms of the 2016 ESPP, the purchase price shall be determined by Syros board of directors for each offering period and will be at least 85% of the applicable closing price of Syros common stock. If Syros board of directors does not make a determination of the purchase price, the purchase price will be 85% of the lesser of the closing price of Syros common stock on the first business day of the offering period or on the last business day of the offering period.

An employee who is not a participant on the last day of the offering period is not entitled to purchase shares under the 2016 ESPP, and the employee's accumulated payroll deductions will be refunded. An employee's rights under the 2016 ESPP terminate upon voluntary withdrawal from an offering under the 2016 ESPP at any time, or when the employee ceases employment for any reason.

Syros is required to make equitable adjustments to the number and class of securities available under the 2016 ESPP, the share limitations under the 2016 ESPP, and the purchase price for an offering period under the 2016

ESPP to reflect stock splits, reverse stock splits, stock dividends, recapitalizations, combinations of shares, reclassifications of shares, spin-offs and other similar changes in capitalization or events or any dividends or distributions to holders of Syros common stock other than ordinary cash dividends.

In connection with a merger or other reorganization event, as defined in the 2016 ESPP, Syros' board of directors or a committee of Syros' board of directors may take any one or more of the following actions as to outstanding options to purchase shares of Syros common stock under the 2016 ESPP on such terms as Syros' board or committee determines:

- provide that options shall be assumed, or substantially equivalent options shall be substituted, by the acquiring or succeeding corporation (or an affiliate thereof);
- upon written notice to employees, provide that all outstanding options will be terminated immediately prior to the consummation of such reorganization event and that all such outstanding options will become exercisable to the extent of accumulated payroll deductions as of a date specified by Syros' board or committee in such notice, which date shall not be less than ten days preceding the effective date of the reorganization event;
- upon written notice to employees, provide that all outstanding options will be cancelled as of a date prior to the effective date of the reorganization event and that all accumulated payroll deductions will be returned to participating employees on such date;
- in the event of a reorganization event under the terms of which holders of Syros common stock will receive upon consummation thereof a cash payment for each share surrendered in the reorganization event, change the last day of the offering period to be the date of the consummation of the reorganization event and make or provide for a cash payment to each employee equal to (1) the cash payment for each share surrendered in the reorganization event times the number of shares of Syros common stock that the employee's accumulated payroll deductions as of immediately prior to the reorganization event could purchase at the applicable purchase price, where the acquisition price is treated as the fair market value of Syros common stock on the last day of the applicable offering period for purposes of determining the purchase price and where the number of shares that could be purchased is subject to the applicable limitations under the 2016 ESPP minus (2) the result of multiplying such number of shares by the purchase price; and/or
- provide that, in connection with Syros' liquidation or dissolution, options shall convert into the right to receive liquidation proceeds (net of the purchase price thereof).

Syros' board of directors may at any time, and from time to time, amend or suspend the 2016 ESPP or any portion thereof. Syros will obtain stockholder approval for any amendment if such approval is required by Section 423 of the Code. Further, Syros' board of directors may not make any amendment that would cause the 2016 ESPP to fail to comply with Section 423 of the Code. The 2016 ESPP may be terminated at any time by Syros' board of directors. Upon termination, Syros will refund all amounts in the accounts of participating employees.

2022 Inducement Stock Incentive Plan

Syros' board of directors adopted the 2022 Inducement Stock Incentive Plan, or the 2022 Inducement Plan, on January 25, 2022. The 2022 Inducement Plan became effective on such date. The approval of Syros stockholders was not required as a condition to the effectiveness of the 2022 Inducement Plan.

The 2022 Inducement Plan provides for the grant of nonstatutory stock options, stock appreciation rights, awards of restricted stock, restricted stock units and other stock-based awards. Subject to adjustment in connection with a change in capitalization, the number of shares of Syros common stock reserved for issuance under the 2022 Inducement Plan is 1,000,000. Awards under the 2022 Inducement Plan may only be granted to persons who

(a) were not previously an employee or director of Syros or (b) are commencing employment with Syros following a bona fide period of non-employment, in either case as an inducement material to the individual's entering into employment with Syros and in accordance with the requirements of Nasdaq Stock Market Rule 5635(c)(4). Neither consultants nor advisors are eligible to participate in the 2022 Inducement Plan. Promptly following the grant of an award under the 2022 Inducement Plan, Syros must disclose in a press release the material terms of the grant, the number of shares involved, and, if required by law or the rules of Nasdaq, the identity of the participant.

Pursuant to the terms of the 2022 Inducement Plan, Syros' board of directors administers the plan. Syros' board of directors has the authority to grant awards and to adopt, amend and repeal such administrative rules, guidelines and practices relating to the 2022 Inducement Plan as it deems advisable. Syros' board of directors may construe and interpret the terms of the 2022 Inducement Plan and any award agreements entered into under the 2022 Inducement Plan. Syros' board of directors may correct any defect, supply any omission or reconcile any inconsistency in the 2022 Inducement Plan or any award thereunder in the manner and to the extent it deems expedient. All decisions by the Syros board of directors with respect to the 2022 Inducement Plan and any awards thereunder will be made in Syros' board of directors' sole discretion and will be final and binding on all persons having or claiming any interest in the 2022 Inducement Plan or in any such award. To the extent permitted by applicable law, Syros' board of directors may delegate any or all of its powers under the 2022 Inducement Plan to one or more committees or subcommittees of its board of directors. All references in this description of the 2022 Inducement Plan to the Syros board of directors means the Syros board of directors or any such committee or subcommittee.

In the event of any stock split, reverse stock split, stock dividend, recapitalization, combination of shares, reclassification of shares,spin-off or other similar change in capitalization or event, or any dividend or distribution to holders of Syros common stock other than an ordinary cash dividend, Syros is required by the 2022 Inducement Plan to make equitable adjustments (or make substitute awards, if applicable), in a manner determined by Syros' board of directors, to:

- the number and class of securities available under the 2022 Inducement Plan;
- the share counting rules under the 2022 Inducement Plan;
- the number and class of securities and exercise price per share of each outstanding option;
- the share and per-share provisions and measurement price of each outstanding stock appreciation right;
- the number of shares and repurchase price per share subject to each outstanding restricted stock award or restricted stock unit award; and
- the share and per-share related provisions and purchase price, if any, of each outstanding other stock-based award.

In connection with a reorganization event (as defined in the 2022 Inducement Plan), Syros' board of directors, may, on such terms as Syros' board of directors determines (except to the extent specifically provided otherwise in an applicable award agreement or other agreement between the participant and Syros), take any one or more of the following actions pursuant to the 2022 Inducement Plan, as to all or any (or any portion of) outstanding awards, other than awards of restricted stock:

- provide that all outstanding awards will be assumed or substantially equivalent awards will be substituted by the acquiring or succeeding corporation (or an affiliate thereof);
- upon written notice to a participant, provide that all of the participant's unvested and/or unexercised awards will terminate immediately prior to the consummation of such reorganization event unless exercised by the participant (to the extent then exercisable) within a specified period following the date of such notice;

- provide that outstanding awards will become exercisable, realizable or deliverable, or restrictions applicable to an award will lapse, in whole or in part, prior to or upon such reorganization event;
- in the event of a reorganization event pursuant to which holders of shares of Syros common stock will receive a cash payment for each share surrendered in the reorganization event, make or provide for a cash payment to the participants with respect to each award held by a participant equal to (1) the number of shares of Syros common stock subject to the vested portion of the award (after giving effect to any acceleration of vesting that occurs upon or immediately prior to such reorganization event) multiplied by (2) the excess, if any, of the cash payment for each share surrendered in the reorganization event over the exercise, measurement or purchase price of such award and any applicable tax withholdings, in exchange for the termination of such award;
- provide that, in connection with Syros' liquidation or dissolution, awards will convert into the right to receive liquidation proceeds (if applicable, net of the exercise, measurement or purchase price thereof and any applicable tax withholdings); and
- any combination of the foregoing.

In taking the foregoing actions, Syros' board of directors is not obligated by the 2022 Inducement Plan to treat all awards, all awards held by a participant, or all awards of the same type, identically.

In the case of certain restricted stock units, no assumption or substitution is permitted, and the restricted stock units will instead be settled in accordance with the terms of the applicable restricted stock unit agreement.

Upon the occurrence of a reorganization event other than Syros' liquidation or dissolution, the repurchase and other rights with respect to outstanding awards of restricted stock will continue for the benefit of the successor company and will, unless Syros' board of directors may otherwise determine, apply to the cash, securities or other property which Syros common stock is converted into or exchanged for pursuant to the reorganization event in the same manner and to the same extent as they applied to such restricted stock. However, Syros' board of directors may provide for the termination or deemed satisfaction of such repurchase or other rights under the restricted stock award agreement or any other agreement between the participant and Syros, either initially or by amendment. Upon the occurrence of a reorganization event involving Syros' liquidation or dissolution, all restrictions and conditions on each outstanding restricted stock award will automatically be deemed terminated or satisfied, unless otherwise provided in the agreement evidencing the restricted stock award or in any other agreement between the participant and Syros.

Syros' board of directors may at any time provide that any award under the 2022 Inducement Plan will become immediately exercisable in whole or in part, free of some or all restrictions or conditions, or otherwise realizable in whole or in part, as the case may be.

Except with respect to option or stock appreciation right repricings, Syros' board of directors may amend, modify or terminate any outstanding award under the 2022 Inducement Plan, including but not limited to, substituting therefor another award of the same or a different type, and changing the date of exercise or realization, provided that no amendment that would require Syros stockholder approval under the rules of Nasdaq may be made effective unless and until Syros stockholders approve such amendment and subject to certain participant consent requirements. Unless Syros' stockholders approve such action, the 2022 Inducement Plan provides that Syros may not (except as otherwise permitted in connection with a change in capitalization or reorganization event):

- amend any outstanding stock option or stock appreciation right granted under the 2022 Inducement Plan to provide an exercise or measurement price per share that is lower than the then-current exercise or measurement price per share of such outstanding award;
- cancel any outstanding option or stock appreciation right (whether or not granted under the 2022 Inducement Plan) and grant in substitution therefor new awards under the 2022 Inducement Plan

covering the same or a different number of shares of Syros common stock and having an exercise or measurement price per share lower than the then-current exercise or measurement price per share of the cancelled award;

- cancel in exchange for a cash payment any outstanding option or stock appreciation right with an exercise or measurement price per share above the then-current fair market value of Syros common stock; or
- take any other action that constitutes a "repricing" within the meaning of Nasdaq rules.

Syros' board of directors may amend, suspend or terminate the 2022 Inducement Plan or any portion thereof at any time provided that no amendment that would require Syros stockholder approval under the rules of Nasdaq may be made effective unless and until Syros stockholders approve such amendment. Unless otherwise specified in the amendment, any such amendment to the 2022 Inducement Plan adopted will apply to, and be binding on the holders of, all awards outstanding under the 2022 Inducement Plan at the time the amendment is adopted, provided Syros' board of directors determines that such amendment, taking into account any related action, does not materially and adversely affect the rights of participants under the 2022 Inducement Plan.

As of June 30, 2022, 647,600 shares remained available for future issuance under the 2022 Inducement Plan.

401(k) Plans

Syros maintains a 401(k) retirement plan that is intended to be a tax-qualified defined contribution plan under Section 401(k) of the Internal Revenue Code. In general, all of Syros' employees are eligible to participate, beginning on the first day of the month following commencement of their employment. The 401(k) plan includes a salary deferral arrangement pursuant to which participants may elect to reduce their current compensation by up to the statutorily prescribed limit, equal to $19,500 in each of 2020 and 2021, and have the amount of the reduction contributed to the 401(k) plan. Participants over the age of 50 are entitled to an additional catch-up contribution up to the statutorily prescribed limit, equal to $6,500 in each of 2020 and 2021. Syros makes matching contributions at a rate of 100% of each employee's contribution up to a maximum matching contribution of 2% of the employee's compensation and 50% of each employee's contribution in excess of 2% up to a maximum of 6% of the employee's compensation.

Health and Welfare Benefits

All of Syros' employees are eligible to participate in its employee benefit plans, including Syros' medical, dental, life and disability insurance plans, in each case on the same basis as all of Syros' other employees.

EXECUTIVE COMPENSATION OVERVIEW

Tyme is a "smaller reporting company" as defined by the SEC, and is therefore not required to provide, and does not purport to provide, all of the disclosures required for a "Compensation and Discussion Analysis" as set forth in rules promulgated by the SEC. Tyme is, however, providing a brief overview of its executive compensation program in order to aid its stockholders' understanding of how its business and performance affects executive compensation decisions.

Objectives of Tyme's Compensation Program

Tyme's compensation program has been designed to attract, motivate and retain quality executive officers who will manage and lead Tyme and will advance it toward achievement of its corporate and strategic goals. The program is also intended to be fair and equitable to Tyme's executive officers and stockholders. Tyme also strives to increase the value of Tyme, align the interests of its executive officers with those of its stockholders, and to reward its executive officers, at reasonable cost, for achievements and advances of Tyme's goals.

General

Tyme's executive officer compensation program consists of the following elements:

- Base salary;
- Cash Incentive Bonus Plan;
- Stock option awards; and
- Employee benefits.

The amounts of compensation awarded for each element of Tyme's compensation program (*i.e.*, base salary, bonuses and stock options) are reviewed in connection with Tyme's performance. Each of these elements is described in more detail below. In May 2018, Tyme engaged an independent compensation consultant, Pearl Meyer to help perform a comprehensive review of Tyme's executive compensation practices and policies. As a result of this review, Tyme implemented several changes to its compensation structure. To date, compensation has generally been determined based on negotiations with employees during the hiring process and available resources. Pearl Meyer was again engaged as an independent compensation consultant in fiscal year 2022. As Tyme continues to review its policies with Pearl Meyer, Tyme has continued to formalize and further develop its approach to compensation and to implement compensation policies going forward.

The Role of the Board, the Compensation Committee and Management

Tyme's Compensation Committee is responsible for determining the recommended compensation of its executive officers, including the Tyme Named Executive Officers (defined further below), except its Chief Executive Officer. The Compensation Committee annually evaluates the CEO's performance and Tyme's performance against its pre-established goals and makes recommendations to the independent members of the Tyme board about the CEO's performance and compensation.

The Tyme board then considers the Compensation Committee's recommendations as part of its review and approval of the CEO's compensation. The members of the Compensation Committee are currently Messrs. DeGolyer (chairman), Carberry and Michels. Each of the current members is an "independent director" under Nasdaq listing standards and a "Non-Employee Director" within the meaning of Section 16 of the Exchange Act.

The Compensation Committee advises Tyme's board concerning its compensation philosophy and policies, in general, and, in particular, reviews and approves, or recommends to the Tyme board for review and approval, the

compensation of Tyme's Chief Executive Officer and other executive officers and of members of the Tyme board In conducting its work, the Compensation Committee consults with the Chief Executive Officer, other members of management, and may consult third-party compensation consultants. Recommendations and decisions made by the Compensation Committee are reported to the full Board for approval or ratification, as appropriate.

Compensation Consultant Role in Executive Compensation

While the Compensation Committee or Tyme board ultimately makes all executive compensation decisions, the Compensation Committee engages the services of outside advisors for assistance. Since 2018, the Compensation Committee has directly engaged Pearl Meyer as its independent compensation consultant.

The Compensation Committee has utilized Pearl Meyer throughout these periods to provide independent, objective analysis, advice and information and to generally assist the Compensation Committee in the performance of its duties. The Compensation Committee will typically request information and recommendations directly from the compensation consultant as it deems appropriate to structure and evaluate Tyme's compensation programs, practices and plans. As part of its engagement, at the direction of the Compensation Committee, the compensation consultant will work, and exchange information, with Tyme's internal legal counsel in its work on the Compensation Committee's behalf. The Compensation Committee assesses the compensations consultant's independence each year, considering the amount of fees paid to the consultant, the consultant's policies designed to prevent conflicts of interest, any stock owned by the consultant, and other factors deemed relevant to the committee.

Elements of Compensation

Base Salary

Annual base salaries compensate Tyme's executive officers for fulfilling the requirements of their respective positions and provide them with a level of cash income predictability and stability with respect to a portion of their total compensation. Tyme believes that the level of an executive officer's base salary should reflect the executive's performance, experience and breadth of responsibilities, its understanding of salaries for similar positions within its industry and any other factors relevant to that particular job.

Base salaries are typically negotiated at the outset of an executive's employment. Salary levels are considered annually as part of Tyme's performance review process, but also in cases including promotion or other change in the job responsibilities of an executive officer. For Tyme Named Executive Officers, initial base salaries generally are established in connection with negotiation of an offer of employment and employment agreement. Increases in base salary have several elements. In addition to promotion and increased responsibilities, merit and Company-wide general increases are also taken into consideration. Salaries of the Tyme Named Executive Officers for fiscal year 2022 and certain prior years are also reported in the Summary Compensation Table.

The following table shows the base salary for each of the Tyme Named Executive Officers for fiscal 2021 and fiscal 2022 and as approved for fiscal 2023:

Name	2021	Increase	2022	Increase	2023
Richard Cunningham	$550,000	2.4%	$563,000	4.0%	$585,520
James Biehl	$465,750	2.0%	$475,065	4.0%	$494,068
Frank L. Porfido	(2)	(2)	$370,000	3.2%	$381,759
Steve Hoffman	$569,250	—	$500,000	—	N/A(3)

(1) Mr. Cunningham joined Tyme in fiscal year 2021.
(2) Mr. Porfido joined Tyme during fiscal year 2022 and his increase waspro-rated for partial year of service.
(3) In connection with his stepping down as Chief Executive Officer in November 2020, Mr. Hoffman agreed to reduce his salary to $500,000 beginning in fiscal year 2022. Mr. Hoffman's employment ended on March 21, 2022.

Cash Incentive Plan

Tyme has a Cash Incentive Plan to motivate and reward its executives for achievements related to corporate performance for each fiscal year. Each year, the Tyme board, after recommendation by the Compensation Committee, approves:

- Corporate performance measures and goals;
- Target incentive bonus opportunity for each executive officer, including each Tyme Named Executive Officer, defined as a percentage of his or her annual salary;
- Funding levels for actual Cash Incentive Plan awards; and
- Individual awards for the Tyme Named Executive Officers, except for the CEO's award, which is approved by the Tyme board.

Each year, the Tyme board upon the recommendation of the Compensation Committee, establishes major corporate objectives for the coming fiscal year related to clinical activities, operations and administration which are referred to throughout this joint proxy statement/prospectus as the Corporate Objectives. The Tyme board believes the Corporate Objectives will contribute to the long-term success of Tyme by aligning with and driving the execution of Tyme's business strategy. For fiscal 2022, the corporate objectives related to awarding incentive bonus payments consisted of:

- Publish Part 1 Pancreatic Data.
- Initiate Oasis (HR+/HER2-) study
- Achieve clinical enrollment objectives
- Present Sarcoma Updated Response Data at ASCO
- Conduct pre-clinical research to support clinical development strategy
- Meet or beat approved financial budget

Each year, the Compensation Committee recommends, and the Tyme board approves and establishes, the target cash incentive opportunity for each executive officer assuming full achievement against the Corporate Objectives. For fiscal 2022, the target cash incentive opportunity for each of the Tyme Named Executive Officer was considered to be within the competitive range of market data provided to the Compensation Committee by Pearl Meyer. The following table shows the amount of the target incentive for each Tyme Named Executive Officer as of March 31, 2022 as a percentage of salary and the dollar amount:

Name	Target Incentive 2022	Target Incentive Bonus 2022
Richard Cunningham	50%	$ 281,500
James Biehl	40%	$ 190,026
Frank L. Porfido	40%	$ 148,000
Steve Hoffman	50%	$ 250,000

At the end of the fiscal year, the Compensation Committee reviews and approves the level of Tyme's achievement against the Corporate Objectives, except for the CEO's achievement, which is approved by the entire Tyme board excluding the CEO. In addition to its assessment of achievement against each Corporate Objective, the Compensation Committee also considers Tyme's "stretch" goals or above target objectives achieved. Also, the Compensation Committee may consider Tyme's performance as a whole during the fiscal year, including matters not included in the Corporate Objectives. In reviewing Tyme's level of achievement against the Corporate Objectives, the Compensation Committee recommended incentive bonus funding level at 80%. In making this determination, the committee considered the achievement of Corporate Objectives at target, but also the discontinued trials that occurred during the fiscal year and their impact on Tyme's performance as a whole. In

consultation with Pearl Meyer, the Compensation Committee conducted an extensive review of the incentive compensation of similar profile companies that experienced discontinued trials. Based upon this review and other factors, the Compensation Committee reduced the total payout percentage to 80% of target.

Following the determination of the corporate achievement, the Compensation Committee considers the performance of each Tyme Named Executive Officer in arriving at the individual awards, if any, to be made. The Compensation Committee's determination of Tyme's level of achievement against the Corporate Objectives is the basis for establishing the funding available for awards. Notwithstanding these determinations, the Compensation Committee and the Tyme board can determine individual awards that are above or below the corporate level of achievement based on their evaluation of that individual's performance. The Compensation Committee believes this flexibility is an important tool to aid in the retention of key talent, reward significant achievement by individual employees, motivate employees and recognize management decision-making focused on generating long-term value for stockholders over short-term achievement of the Corporate Objectives. In fiscal year 2022, the Compensation Committee considered the achievement of the Corporate Objectives as discussed above and each Tyme Named Executive Officer's individual performance in determining each Named Executive Officer's incentive bonus award. In determining the amount of each Tyme Named Executive Officer's award, the Compensation Committee and the Tyme board also considered a Tyme Named Executive Officer's performance against individual goals and the CEO's input with respect to the performance of Tyme and the other executive officers.

The following table shows the achievement of the cash incentive bonus for each Tyme Named Executive Officer as of March 31, 2022 as a percentage of the target incentive bonus amount and the dollar amount except for Mr. Hoffman whose payments in connection with his termination of employment are discussed below under "Hoffman Release Agreement":

Name	Achievement Incentive Bonus 2022	Incentive Bonus ($)
Richard Cunningham	80%	$225,200
James Biehl	80%	$152,021
Frank L. Porfido	80%	$ 94,071(1)

(1) Mr. Porfido joined Tyme on June 14, 2021 and his target incentive award is prorated for the partial year of service.

Stock Option Grants

Tyme provides stock option grants to its executives to complement cash salaries and cash incentives, incentivize new hires to achieve its corporate and strategic goals, and align executive compensation with the long-term interests of its stockholders and stock value. Tyme historically provided stock option grants to the Tyme Named Executive Officers upon their initial hiring, as negotiated in their employment agreements. The Compensation Committee has the discretion to grant stock option compensation to promote high performance and achievement of Tyme's corporate objectives by its executives. In granting these awards, the Compensation Committee may establish any conditions or restrictions it deems appropriate in accordance with the 2015 Equity Incentive Plan. In addition, Tyme's CEO, as sole member of Tyme's Non-Executive Equity Incentive Committee, established by the Compensation Committee, has limited discretionary authority to grant stock options under the 2015 Equity Incentive Plan to Tyme's non-executive employees and consultants, subject to certain volume limitations.

In fiscal 2022, Mr. Cunningham, Mr. Biehl and Mr. Porfido were awarded stock options; however, in light of his significant share ownership, Mr. Hoffman was not awarded stock options.

Benefits Plans

Tyme believes that establishing competitive benefit packages for its employees is an important factor in attracting and retaining highly qualified personnel. Tyme maintains broad-based benefits that are provided to all

employees, including medical insurance, dental insurance, vision insurance, basic life and personal accident insurance, long and short-term disability insurance, medical flexible spending accounts, adoption assistance and commuter benefits. Tyme obtains certain of these benefits through Insperity. All of Tyme's executive officers are eligible to participate in all of its employee benefit plans, in each case on the same basis as other employees. Tyme generally does not offer the Tyme Named Executive Officers any material compensation in the form of perquisites, but any perquisites provided to the Tyme Named Executive Officers and described in the footnotes to the Summary Compensation Table are offered to encourage the long-term retention of its executives.

2022 Retention Agreements

On April 28, 2022, Tyme entered into retention agreements with each of its executive officers, including, Richard Cunningham, Frank L. Porfido, Jonathan Eckard and James Biehl. The agreements provide for a retention cash bonus in an amount equal to the officer's respective bonus for the fiscal year ending March 31, 2023, to be payable within 20 days following the closing of the merger should it occur on or before March 31, 2023, provided that such officer remains employed as of the closing of the merger and, provided, further, that if such officer is terminated without Cause or terminates the officer's employment for Good Reason (as such terms are defined in each officer's respective employment agreement) prior to the closing of the merger, such officer will still be entitled to the retention bonus, payable within 20 days following the closing of the merger.

Limits on Hedging and Pledging

As part of Tyme's insider trading policy, all employees, including executive officers, and members of its board of directors are prohibited from engaging in hedging transactions involving our securities, including short sales and purchases or sales of puts, calls or other derivative securities. Tyme's insider trading policy also prohibits certain types of pledges of its securities by all employees, including executive officers, and members of the Tyme board, specifically purchases of its securities on margin, borrowing against its securities held in a margin account or pledging its securities as collateral for a loan, with an exception for transactions with the pre-approval of Tyme's Chief Compliance Officer.

Tax Considerations

The applicability of Section 162(m) of the Code may affect the tax deductibility of certain portions of the Tyme Named Executive Officers' compensation. Under Section 162(m) of the Code, the Tax Act eliminates the performance-based compensation exception such that all compensation over one million dollars paid to "covered employees" would be nondeductible. Notwithstanding the changes to the tax deductibility requirements of Section 162(m) of the Code, Tyme continues to believe that a meaningful portion of its executive officers' compensation should be tied to measures of performance of its business.

Tyme does not usually consider the tax consequences to the Tyme Named Executive Officers of cash compensation or of equity-based compensation, though it considers the tax treatment to Tyme for non-qualified options and the non-qualifying disposition of qualified options to be favorable.

Consideration of Advisory Vote on Executive Compensation

Tyme held an advisory vote on executive compensation at the 2020 annual meeting of stockholders (otherwise known as "Say-on-Pay" votes) with over 90% of the votes cast voting to approve the executive compensation of Tyme's then-named executive officers. At Tyme's 2018 annual meeting of stockholders, the stockholders voted to recommend an advisory vote on Tyme's compensation once every two years and Tyme has followed this recommendation. While Say-on-Pay votes are not binding on Tyme, the Compensation Committee and the Tyme board will consider the outcome of Tyme's Say-on-Pay votes when making future compensation decisions for its executive officers.

Use of External Data

In consultation with Pearl Meyer, Tyme has established the following nineteen companies as its peer group for fiscal year 2022. Tyme evaluates this group in conjunction with its review of peer compensation data, which is comprised principally of oncology focused non-commercial, biotechnology and pharmaceuticals companies with products generally in Phase II or Phase III clinical trials that Pearl Meyer has deemed to be most comparable to us in market capitalization, employee head count and research and development expense.

Actinium Pharmaceuticals, Inc.	MEI Pharma, Inc.
Calithera Biosciences, Inc.	Mustang Bio, Inc.
Cardiff Oncology, Inc.*	OncternalTherapeutics, Inc*
Checkpoint Therapeutics, Inc.	PDS Biotechnology Corporation*
Corvus Pharmaceuticals, Inc.	Pieris Pharmaceuticals, Inc.
Evelo Biosciences, Inc.	Sesen Bio, Inc.
Geron Corporation	Syndax Pharmaceuticals, Inc.
Infinity Pharmaceuticals, Inc.	Syros Pharmaceuticals, Inc.
Leap Therapeutics, Inc.	

* Indicates a new peer group company in fiscal year 2022.

Tyme compares its executive compensation program and amounts of compensation against its peer group. Tyme generally targets total cash compensation, comprised of base salary and target annual incentive bonuses, to be competitive with the 50th percentile of the market. For fiscal year 2022, the total cash compensation for the Tyme Named Executive Officers generally fell within a competitive range of Tyme's target positioning. In addition, Tyme generally grants stock options within a competitive range of the market. Tyme sizes equity grants based on market data that expresses the awards as a percent of common shares outstanding, although in the future Tyme may change its approach to base the size of equity grants on dollar value. This sizing approach is helpful to ensure that the dilutive effects of the grants are reasonable. In total, Tyme believes that the compensation for the Tyme Named Executive Officers was reasonable given its corporate performance and Tyme's financial circumstances. As indicated above, the Tyme peer group is subject to change over time, and Tyme expects that the Compensation Committee and it will continue to periodically review and update the list.

EXECUTIVE COMPENSATION

The following table sets forth, with respect to Tyme's fiscal years ended March 31, 2022 and 2021, all compensation earned by or paid to all persons who served as Chief Executive Officer of Tyme at any time during such periods, and Tyme's two most highly compensated executive officers other than the Chief Executive Officer who were serving as executive officers at the end of the last completed fiscal year, or collectively, the Tyme Named Executive Officers.

Except as noted below, no compensation in the form of stock, options or other equity were granted or issued to any of the persons set forth in the following table during the periods indicated as compensation.

Summary Compensation Table

Name and Principal Position	Year	Salary ($)	Bonus ($)	Option Awards ($)(1)	Nonequity Incentive Plan Compensation ($)	All Other Compensation ($)(2)	Total ($)
Richard Cunningham, Chief Executive Officer(3)	2022	564,083	—	554,176	225,200	621	1,344,080
	2021	193,750	75,000	1,495,344	87,000	218	1,851,312
James Biehl, Chief Legal Officer	2022	474,677	—	554,176	152,021	9,190	1,190,064
	2021	465,750	—	362,673	171,396	8,379	1,008,198
Frank L. Porfido, Chief Financial Officer(5)	2022	295,720	—	803,555	94,071	23,295	1,216,641
Steve Hoffman, former Chief Executive Officer and former Chief Science Officer(4)	2022	486,111	—	—	—	2,111,493	2,597,604
	2021	569,250	—	—	245,916	4,496	819,662

(1) Amounts shown do not reflect compensation actually received by the Tyme Named Executive Officer. Instead, the amounts reported above in the "Option Awards" column represents the aggregate grant date fair value of option awards granted in the respective fiscal years, as determined in accordance with ASC 718. These values have been determined based on assumptions set forth in Note 12 to the Tyme Consolidated Financial Statements.

(2) All Other Compensation includes health insurance premium payments for fiscal year 2022 and 2021 as compensation. For 2022, Tyme made health insurance premium payments in the amount of $621 for Mr. Cunningham (Mr. Cunningham has not elected to receive health insurance through Tyme and receives only the minimal benefits provided as a matter of course to all employees), $4,738 for Mr. Hoffman, $9,190 for Mr. Biehl and $10,479 for Mr. Porfido. For 2022, pursuant to his Release Agreement, Mr. Hoffman also received $2,105,366 severance, and Mr. Porfido received $12,816 for consulting services prior to hire date. Additionally, Mr. Hoffman received $1,389 for his service on the Tyme board from his resignation date until the end of the fiscal year. For 2021, Tyme made health insurance premium payments in the amount of $218 for Mr. Cunningham, $4,496 for Mr. Hoffman, and $8,379 for Mr. Biehl.

(3) Mr. Cunningham was appointed as Chief Executive Officer on November 23, 2020 and received a sign-on bonus of $75,000.

(4) Mr. Hoffman also served as Tyme's Chief Executive Officer during the periods presented until November 23, 2020.

(5) Mr. Porfido was hired on June 14, 2021, accordingly salary and nonequity incentive plan reflect a partial year of service.

Outstanding Equity Awards as of March 31, 2022

As of March 31, 2022, the following equity awards were outstanding for the benefit of the Tyme Named Executive Officers. This table provides information about outstanding unexercised stock options held as of March 31, 2022 by each of the Tyme Named Executive Officers that remain outstanding.

Name	Option Grant Date	Number of Securities Underlying Unexercised Options		Option Exercise Price ($)	Option Expiration Date
		Exercisable (#)	Unexercisable(#)		
Richard Cunningham	11/25/2020(1)	625,000	1,375,000	1.03	11/24/2030
	6/14/2021(1)	93,750	406,250	1.43	6/13/2031
James Biehl	03/28/2017(3)	25,000	—	2.95	03/28/2027
	05/24/2018(4)	75,000	—	2.90	05/24/2028
	09/13/2018(5)	500,000	—	2.42	09/08/2028
	05/03/2019(5)	232,100	21,100	1.56	05/02/2029
	05/07/2020(1)	157,500	202,500	1.39	05/06/2030
	6/14/2021(1)	93,750	406,250	1.43	6/13/2031
Frank L. Porfido	6/14/2021(1)	135,936	589,064	1.43	6/13/2031
Steve Hoffman	05/09/2016(2)	500,000	—	8.75	06/21/2022

(1) The option vests quarterly over 4 years.
(2) The option vests 1/36th of the total grant every month after the date of grant.
(3) This option vested 3/4th during quarter ended March 31, 2017 and 1/4th during quarter ended March 31, 2018.
(4) The option vested during quarter ended June 30, 2018.
(5) The option vests quarterly over 3 years.

Option Exercises and Stock Vested During the Fiscal Year Ended March 31, 2022

No stock options were exercised by any Tyme Named Executive Officer during the fiscal year ended March 31, 2022. Tyme has not made stock awards.

Employment Agreements

Richard Cunningham

On November 24, 2020, Tyme entered into an employment agreement with its Chief Executive Officer, Richard Cunningham. Under this agreement, the chief executive officer will be entitled to an annual base salary and such target incentive award bonuses as Tyme's board may determine, from time to time, in its sole discretion. The base salary is reviewed annually by Tyme's Compensation Committee and board; provided that the base salary may not be decreased from its then current level due to any board review. The employment agreement has a term of four years. If employment is terminated by Tyme without Cause or by the executive for Good Reason, the executive will be entitled to receive (A)(i) base salary as in effect at the time of such termination to the extent such amount has accrued through the termination date and remains unpaid, (ii) any earned but unpaid incentive award as of the termination date, (iii) any unpaid unreimbursed expenses as of the termination date ((A)(i) through (iii) above, the "Accrued Obligations") and (B) in return for a timely executed and delivered release, (i) an aggregate amount equal to one year of his base salary, which will be payable in the same amounts and at the same intervals as if the employment period had not ended, (ii) immediate vesting of the portion of all his time-vesting equity awards under Tyme's 2015 Equity Incentive Plan that would have vested in the 12-month period following the termination date and (iii) if he timely elects continued coverage pursuant to COBRA, payment of his share of the premium cost at the same rate as for active employees of Tyme for the 12-month period following the termination date.

If the employment is terminated by Tyme without Cause or by the executive for Good Reason, in each case, upon or within 12 months following the consummation of a Change in Control, then the executive will be entitled to

(A) the Accrued Obligations; and (B) in return for a timely executed and delivered release, (i) an amount equal to one-and-a-half times one year of base salary, which will be payable in the same amounts and at the same intervals as if the employment period had not ended, (ii) an amount equal to one-and-a-half times his target incentive award for the year in which the termination date occurs (or if it has not yet been established, the target incentive award established for the immediately preceding year), which will be payable in the same manner and at the same time that Tyme pays other Tyme executive incentive awards under the Cash Incentive Plan after the termination date, (iii) immediate vesting of all his time-based equity awards under the 2015 Equity Incentive Plan and (iii) if he timely elects continued coverage pursuant to COBRA, payment of his share of the premium cost at the same rate as for active employees of Tyme for the 18-month period following the termination date.

If the employment is terminated for "Cause," or in the case of the executive's death or disability, the executive will only be entitled to his base salary through the termination date, plus any accrued and unpaid incentive award as of the termination date. For purposes of these employment agreements, "Cause" means any one of the following: the executive's: (i) breach of the employment agreement, (ii) conviction of, guilty plea to, or confession of guilt of, a felony, (iii) materially fraudulent, dishonest or illegal conduct in the performance of services for or on behalf of Tyme or any of its affiliates, (iv) any repeated conduct by the executive in material violation of Tyme written policy (v) any conduct that is materially detrimental to the reputation of Tyme or any of its affiliates, (vi) misappropriation of funds of Tyme or any of its affiliates, (vii) gross negligence or willful misconduct or willful failure to comply with written directions of the Tyme board which directions are within the scope of executive's duties, or (viii) engaging in discrimination, sexual or other harassment, retaliation, or any conduct involving an act of moral turpitude. "Good Reason" means a material diminution in the executive's authority, title, duties or responsibilities, the failure of Tyme to make all payments due to the executive under the applicable agreement or otherwise, or the relocation of the executive's primary office to a location more than 50 miles from the company office.

James Biehl

On September 10, 2018, Tyme entered into an employment agreement with its Chief Legal Officer, James Biehl. Under this agreement, the chief legal officer will be entitled to an annual base salary and such performance bonuses as Tyme's board of directors may determine, from time to time, in its sole discretion. The base salary is reviewed annually by Tyme's Compensation Committee and board of directors; provided that the base salary may not be decreased from its then current level due to any Tyme board review. The employment agreement has a term of two and a half years, provided, however, that, commencing on the six month anniversary of the date of the agreement and on each subsequent six month anniversary thereafter, the term will automatically be extended by six months, such that, at any time during the term of the agreement, the remaining employment term will never be less than two years and one day. If employment is terminated by Tyme without Cause or by the executive for Good Reason, the executive will be entitled to receive (A)(i) base salary as in effect at the time of such termination to the extent such amount has accrued through the termination date and remains unpaid, (ii) any fully earned and declared but unpaid performance bonus as of the termination date and (iii) any unpaid unreimbursed expenses as of the termination date ((A)(i) through (iii) above, the "Accrued Obligations") and (B) in return for a timely executed and delivered release, (i) an aggregate amount equal to the sum of his base salary that he would have received from the termination date through the agreement expiration date, which will be payable in the same amounts and at the same intervals as if the employment period had not ended, (ii) immediate vesting of the portion of all his time-vesting equity awards under Tyme's 2015 Equity Incentive Plan (unless the board determines the executive was negligent in the performance of his duties) and (iii) if he timely elects continued coverage pursuant to COBRA, payment of his share of the premium cost at the same rate as for active employees of Tyme for the 12-month period following the termination date.

If the employment is terminated for "Cause," or in the case of the executive's death or disability, the executive will only be entitled to the Accrued Obligations. For purposes of these employment agreements, "Cause" means any one of the following: the executive's: (i) material breach of the employment agreement, (ii) conviction of, guilty plea to, or confession of guilt of, a felony involving Tyme, (iii) materially fraudulent, dishonest or illegal

conduct in the performance of services for or on behalf of Tyme or any of its affiliates, (iv) any repeated conduct by the executive in material violation of Company written policy (v) any conduct that is materially detrimental to the reputation of Tyme or any of its affiliates, (vi) misappropriation of funds of Tyme or any of its affiliates, (vii) gross negligence or willful misconduct or willful failure to comply with written directions of the Tyme board which directions are within the scope of executive's duties, or (viii) conduct involving an act of moral turpitude. "Good Reason" means a material diminution in the executive's authority, title, duties or responsibilities, the failure of Tyme to make all payments due to the executive under the applicable agreement or otherwise, or the relocation of the executive's primary office to a location more than 25 miles from the company office.

Frank Porfido

On May 11, 2021, Tyme entered into an employment agreement with its Chief Financial Officer, Frank Porfido. Under this agreement, the chief financial officer will be entitled to an annual base salary and is also eligible to earn an annual target incentive award under Tyme's Cash Incentive Plan, determined by the Compensation Committee. If employment is terminated by Tyme without Cause or by the executive for Good Reason, the executive will be entitled to receive (A)(1) his base salary as in effect at the time of such termination to the extent such amount has accrued through the termination date and remains unpaid, (ii) any fully earned and declared but unpaid target incentive award as of the termination date, and (iii) any unpaid unreimbursed expenses as of the termination date (collectively, (A)(i) – (iii), the "Accrued Obligations"); and (B) in return for a timely executed and delivered release, (i) an amount equal to three fourths of his annual base salary, which will be payable at the same intervals as if the employment period had not ended, and (ii) if he timely elects continued coverage pursuant to COBRA, payment of his share of the premium cost for the 9-month period following the termination date (the "COBRA Payments"). Should Mr. Porfido be terminated upon or within 12 months of a "Change in Control," Mr. Porfido would be entitled to the (i) Accrued Obligations, and (ii) in return for a timely executed and delivered release, (a) an amount equal to one year of his base salary, which will be payable in the same amounts and at the same intervals as if the employment period had not ended, (b) an amount equal to one times the target incentive award for the applicable fiscal year, (c) immediate vesting of the portion of all his time-based equity awards under Tyme's 2015 Equity Incentive Plan, and (d) if he timely elects continued coverage, COBRA Payments for a twelve-month period.

If the employment is terminated for "Cause," or in the case of the executive's death or disability, the executive will only be entitled to the Accrued Obligations. "Cause" means any one of the following: the executive's: (i) material breach of the employment agreement, (ii) conviction of, guilty plea to, or confession of guilt of, a felony involving Tyme, (iii) materially fraudulent, dishonest or illegal conduct in the performance of services for or on behalf of Tyme or any of its affiliates, (iv) any repeated conduct by the executive in material violation of Tyme written policy (v) any conduct that is materially detrimental to the reputation of Tyme or any of its affiliates, (vi) misappropriation of funds of Tyme or any of its affiliates, (vii) gross negligence or willful misconduct or willful failure to comply with written directions of the Tyme board which directions are within the scope of executive's duties, or (viii) engagement in discrimination, sexual or other harassment, retaliation, or any conduct involving an act of moral turpitude. "Good Reason" means a material diminution in the executive's authority, title, duties or responsibilities, the failure of the Company to make all payments due to the executive under the applicable agreement or otherwise, or the relocation of the executive's primary office to a location more than 50 miles from Tyme's office.

Change in Control

For purposes of Messrs. Cunningham's and Porfido's employment agreements, a "Change in Control" is deemed to occur when and only when any of the following events first occurs: (A) any person becomes the beneficial owner, directly or indirectly, of securities of Tyme representing 50% or more of the combined voting power of Tyme's then outstanding voting securities; (B) members of the Incumbent Board (as defined in Tyme's 2015 Equity Incentive Plan) cease to constitute a majority of the Board without the approval of the remaining members of the Incumbent Board; or (C) any merger (other than a merger where Tyme is the survivor and there is no

accompanying Change in Control under clauses (A) or (B), consolidation, liquidation or dissolution of Tyme, or the sale of all or substantially all of the assets of Tyme. Notwithstanding the foregoing, a Change in Control is not deemed to have occurred pursuant to clause (A) solely because 50% or more of the combined voting power of Tyme's outstanding securities is acquired by one or more employee benefit plans maintained by Tyme or by any other employer, the majority interest in which is held, directly or indirectly, by Tyme.

Hoffman Release Agreement

In connection with Mr. Hoffman stepping down as Chief Executive Officer and continuing as Chief Science Officer, his employment agreement was amended and restated on November 24, 2020. Under this amended and restated agreement, he was entitled to an annual base salary of $500,000 in fiscal year 2022, $450,000 in fiscal year 2023 and thereafter as Tyme's board of directors may determine, from time to time, in its sole discretion. Mr. Hoffman was also entitled to a target incentive award of 50% of base salary for fiscal year 2022, 40% of base salary for fiscal year 2023, and thereafter in such amounts as Tyme's board of directors may determine, from time to time, in its sole discretion, provided such target incentive award could never be below 40% of Mr. Hoffman's then-current base salary. The employment agreement had a term of five years; provided, however, that, commencing on the first anniversary of the date of the agreement and on each anniversary thereafter, the term was automatically extended by one year, such that, at any time during the term of the agreement, the remaining employment term would never be less than four years and one day. If employment is terminated by Tyme without Cause or by the executive for Good Reason, Mr. Hoffman would be entitled to receive (i) base salary as in effect at the time of such termination to the extent such amount has accrued through the termination date and remains unpaid, (ii) any earned but unpaid incentive award as of the termination date, (iii) in return for a timely executed and delivered release, an aggregate amount equal to the sum of base salary the executive would have received from the date of such termination through the then applicable expiration date, which will be payable in the same amounts and at the same intervals as if the employment period had not ended, and (iv) any unpaid expenses as of the termination date.

Tyme and Mr. Hoffman entered into a Release Agreement, dated March 24, 2022, pursuant to which Mr. Hoffman resigned and received the severance that would have been payable under his employment agreement for a termination by Tyme without Cause or by him for Good Reason, but such amount was paid in a lump sum payment following the expiration (without revocation) of a required 7-day revocation period under New Jersey law. As is customary, the agreement also placed confidentiality obligations on Mr. Hoffman and included mutual non-disparagement obligations and a mutual release.

DIRECTOR COMPENSATION

Tyme has adopted a director compensation policy fornon-employee directors. Under the current compensation policy, each of Tyme's non-employee directors is entitled to receive annual cash compensation in the amount of $50,000, to be paid on a quarterly basis, as well as stock option awards as follows:

- Upon an initial election of a director to the Tyme board of directors, each new director will receive a grant of options to purchase 176,000 shares of Tyme Common Stock under the Tyme 2016 Stock Option Plan for Non-Employee Directors, as amended and restated August 24, 2021, or the Tyme 2016 Plan, which shares will vest in equal quarterly increments over a three-year period from the date of grant rather than over a one-year period; and
- An annual grant of options to purchase 88,000 shares of Tyme Common Stock under the Tyme 2016 Plan. The award vests in equal quarterly increments over a one-year period from the date of grant.

From time to time, Tyme's non-employee directors have in the past deferred and may in the future defer the right to receive cash payable pursuant to its non-employee director compensation policy to conserve cash resources. In

the future, they may elect to receive the cash award in the form of stock options also to conserve cash reserves. Directors serving on a committee are also entitled to additional cash compensation as follows:

Committee	Annual Cash Retainer
Audit	Chair: $15,000 Member: $7,500
Compensation	Chair: $12,500 Member: $6,250
Nominating and Corporate Governance	Chair: $8,250 Member: $4,125
Strategic Planning	Chair: $8,250 Member: $4,125

The independent chairman of the Tyme's board of directors also receives an additional annual cash retainer of $25,000.

Director Compensation Table

The table below includes information about the compensation paid tonon-employee directors with respect to the fiscal year ending March 31, 2022. Mr. Cunningham, who serves as a Tyme employee and on Tyme's board, did not receive any compensation for board service. As noted in the Summary Compensation Table, above, Mr. Hoffman received $1,389 for his board service from his resignation date until the end of the fiscal year. Beginning in fiscal year 2023, as a non-employee director, Mr. Hoffman will receive cash compensation for board service in the same amounts as othernon-employee directors.

Name(1)	Fees Paid or Earned in Cash ($)	Option Awards(2) ($)	All Other Compensation ($)	Total Compensation ($)
Christine Baker	1,250	57,831	—	59,081
David Carberry	75,375	72,866	—	148,241
Donald W. DeGolyer	74,125	72,866	—	146,991
Douglas A. Michels	93,469	72,866	—	166,335
Dr. Gerald Sokol	50,000	72,866	—	122,866
Timothy C. Tyson	65,865	72,866	—	138,731

(1) The table immediately below indicates each director's outstanding option awards as of the fiscal year end.
(2) This column lists the aggregate grant date fair value of options awarded to directors pursuant to the Tyme 2016 Plan, computed in accordance with FASB Accounting Standards Codification (ASC) Topic 718. These values have been determined based on assumptions set forth in Note 12 to the Tyme Consolidated Financial Statements.

Outstanding Equity Awards for Non-Employee Directors as of March 31, 2022

The following table sets forth information regarding unexercised stock options for each Tyme director outstanding as of March 31, 2022. Tyme has not awarded stock grants or other equity incentive awards and as such have not made any disclosures regarding such awards.

Name	Number of Securities Underlying Unexercised Options Exercisable (#)	Number of Securities Underlying Unexercised Options Unexercisable (#)	Option Exercise Price ($)	Option Expiration Date
Christine Baker	—	212,888	0.35	03/22/2032
David Carberry	25,000	—	2.95	03/28/2027
	75,000	—	2.90	05/24/2028
	50,000	—	2.33	08/26/2028
	50,000	—	1.18	08/22/2029
	65,000	—	1.22	08/19/2030
	44,000	44,000	1.10	08/23/2031
Donald W. DeGolyer	100,000	—	2.90	05/24/2028
	50,000	—	2.33	08/26/2028
	50,000	—	1.18	08/22/2029
	65,000	—	1.22	08/19/2030
	44,000	44,000	1.10	08/23/2031
Douglas A. Michels	145,833	—	2.71	10/01/2028
	50,000	—	1.18	08/22/2029
	65,000	—	1.22	08/19/2030
	44,000	44,000	1.10	08/23/2031
Dr. Gerald Sokol	25,000	—	8.75	05/09/2026
	75,000	—	2.90	05/24/2028
	50,000	—	2.33	08/26/2028
	50,000	—	1.18	08/22/2029
	65,000	—	1.22	08/19/2030
	44,000	44,000	1.10	08/23/2031
Timothy C. Tyson	50,958	—	4.10	11/21/2022
	25,000	—	8.75	05/09/2026
	75,000	—	2.90	05/24/2028
	50,000	—	2.33	08/26/2028
	50,000	—	1.18	08/22/2029
	65,000	—	1.22	08/19/2030
	44,000	44,000	1.10	08/23/2031

In addition to the compensation arrangements, including employment, termination of employment and change in control arrangements, with Syros' and Tyme's directors and executive officers, including those discussed in the sections titled "*Management Following the Merger*," "*Syros Executive Compensation*" and "*Tyme Executive Compensation*," the following is a description of each transaction involving Syros since January 1, 2020, each transaction involving Tyme since April 1, 2020 and each currently proposed transaction in which:

- either Syros or Tyme has been or are to be a participant;
- the amounts involved exceeded or will exceed the lesser of $120,000 and 1% of the average of Syros' or Tyme's total assets at year end for the last two completed fiscal years, as applicable; and
- any of Syros' or Tyme's directors, executive officers or holders of more than 5% of Syros' or Tyme's capital stock, or an affiliate or immediate family member of the foregoing persons, had or will have a direct or indirect material interest.

Syros Transactions

Certain related party transactions involving Syros' directors and executive officers are described in more detail in the section entitled "*The Merger—Interests of Syros Directors and Executive Officers in the Merger*" beginning on page 186 of this joint proxy statement/prospectus.

December 2020 Private Placement

In December 2020, Syros completed a private placement of 10,312,500 shares of Syros common stock and, in lieu of Syros common stockpre-funded warrants to purchase an aggregate of 1,000,000 shares of Syros common stock, and, in each case, accompanying warrants to purchase an aggregate of up to 2,828,125 additional shares of Syros common stock (or pre-funded warrants to purchase Syros common stock in lieu thereof) at a price of $8.00 per share and accompanying warrant (or $7.99 per pre-funded warrant and accompanying warrant). Samsara BioCapital, L.P., a venture capital firm, purchased 625,000 shares of Syros common stock and accompanying warrants to purchase 156,250 shares of Syros common stock (or pre-funded warrants to purchase common stock in lieu thereof) in this private placement at an aggregate purchase price of $5.0 million. Srinivas Akkaraju, M.D., Ph.D., who serves on the Syros board of directors, is one of the managers of Samsara BioCapital GP, LLC, which is the general partner of Samsara BioCapital, L.P.

Consulting Agreement with Dr. Young

Richard A. Young, Ph.D., who serves on the Syros board of directors, earned $115,000 during each of fiscal 2021 and fiscal 2020 pursuant to the terms of a consulting agreement he entered with Syros that is unrelated to his service as a member of Syros' board of directors.

Investors' Rights Agreement

Prior to its expiration in June 2021, Syros was a party to an amended and restated investors' rights agreement, dated as of October 9, 2014, with the purchasers of preferred stock prior to Syros' initial public offering, including ARCH Venture Fund VII, L.P., entities affiliated with FMR LLC, entities affiliated with Flagship Ventures, entities affiliated with Polaris Partners (of which Amir Nashat, who serves on Syros' board of directors, is a managing partner), Nancy A. Simonian, M.D., who serves as President and Chief Executive Officer and as a director of Syros, and Phillip A. Sharp, Ph.D., who serves on Syros' board of directors. The investors' rights agreement provided these holders the right to demand that Syros file a registration statement or request that their shares be covered by a registration statement that Syros was otherwise filing.

PIPE Financing

As discussed elsewhere in this joint proxy statement/prospectus, on July 3, 2022, Syros entered into the Securities Purchase Agreement with several institutional accredited investors pursuant to which Syros agreed to issue and sell to the investors in the PIPE Financing an aggregate of 63,871,778 shares of Syros common stock, and in lieu of shares of Syros common stock to certain investors, Pre-Funded Warrants to purchase an aggregate of 74,267,400 shares of Syros common stock, and, in each case, accompanying Warrants, to purchase an aggregate of up to 138,139,178 additional shares of common stock (or Pre-Funded Warrants to purchase common stock in lieu thereof) at a price of $0.94 per share and accompanying Warrant (or $0.9399 per Pre-Funded Warrant and accompanying Warrant), for an aggregate purchase price of approximately $130 million, before deducting estimated offering expenses payable by Syros not inclusive of any exercise of the Warrants. The closing of the PIPE Financing contemplated by the Securities Purchase Agreement is conditioned upon the satisfaction or waiver of the conditions to the closing of the merger as well as certain other conditions, as set forth in the Securities Purchase Agreement. The following table summarizes the shares of Syros common stock that members of Syros' board of directors or officers of Syros, or their affiliates, and holders of more than 5% of Syros' outstanding capital stock agreed to purchase in the PIPE Financing.

Name of Stockholder	Shares of Syros Common Stock	Pre-Funded Warrants in Lieu of Shares of Common Stock	Accompanying PIPE Warrants	Total Purchase Price ($)
Flagship Pioneering Fund VIII, L.P. (1)	7,000,000	14,200,000	21,200,000	19,926,580.00
Invus Public Equities, L.P.	10,638,297	—	10,638,297	9,999,999.18
Ally Bridge MedAlpha Master Fund L.P.	5,319,148	—	5,319,148	4,999,999.12
Entities affiliated with Bain Capital Life Sciences, L.P.	5,319,400	5,319,400	10,638,800	9,999,940.06
Samsara BioCapital, L.P. (2)	6,914,893	—	6,914,893	6,499,999.42

(1) Douglas Cole, M.D., a general partner of Flagship Pioneering Fund VIII, L.P., is the spouse of Nancy Simonian, M.D., President, Chief Executive Officer and member of the Syros board of directors.

(2) Srinivas Akkaraju, M.D., Ph.D., a member of the Syros board of directors, is one of the managers of Samsara BioCapital GP, LLC, which is the general partner of Samsara BioCapital, L.P., a venture capital firm.

Tyme Transactions

Director Independence

Tyme's board of directors has reviewed the independence of its directors under the applicable Nasdaq standards. Based upon this review, Tyme's board of directors has determined that Ms. Baker, Dr. Sokol and Messrs. Carberry, DeGolyer, Michels and Tyson meet the Nasdaq definition of independent and that each member of the Audit Committee, Compensation Committee and Nominating and Corporate Governance Committee meets the heightened independence standards under Nasdaq and SEC rules.

After review of all relevant transactions or relationships between each director, or any of his family members, and Tyme, its senior management and its independent registered public accounting firm, Tyme's board of directors has affirmatively determined that all of its directors are independent directors within the meaning of the applicable Nasdaq listing standards, as currently in effect, excluding Messrs. Hoffman and Cunningham. Mr. Cunningham serves as the Chief Executive Officer of Tyme and Mr. Hoffman was an executive officer until March 21, 2022 and remains a significant stockholder.

Indemnification Agreements

Tyme has entered into indemnification agreements with each of its directors and officers. These indemnification agreements may require Tyme, among other things, to indemnify Tyme's directors and officers for some

expenses, including attorneys' fees, judgments, fines and settlement amounts incurred by a director or officer in any action or proceeding arising out of his or her service as one of Tyme's directors or officers, or any of its subsidiaries or any other company or enterprise to which the person provides services at Tyme's request.

Policies and Procedures for Related Person Transactions

Although Tyme does not have a formal, written related person transaction policy, pursuant to its charter, Tyme's Audit Committee is responsible for reviewing and approving, as appropriate, all transactions with related persons. In reviewing and approving any such transactions, Tyme's Audit Committee considers all relevant facts and circumstances, including, but not limited to, whether the transaction is on terms comparable to those that could be obtained in an arm's length transaction and the extent of the related person's interest in the transaction.

Certain Relationships and Related Transactions

As a smaller reporting company, SEC rules require Tyme to disclose any transaction for the last two completed fiscal years or any currently proposed transaction in which Tyme is a participant and in which any related person has or will have a direct or indirect material interest involving an amount in excess of $120,000 or one percent of the average of the Tyme's total assets at year end for the last two fiscal years. A related person is any executive officer, director, nominee for director or holder of 5% or more of Tyme's Common Stock or an immediate family member of any of those persons.

In accordance with such SEC rules, in addition to other disclosures contained elsewhere in this joint proxy statement/prospectus, Tyme notes the following related party transactions that occurred during such period:

Tyme was provided legal service by Faegre Drinker Biddle & Reath LLP, or Faegre Drinker, which, prior to February 1, 2020, was Drinker Biddle & Reath LLP, or DBR. James Biehl, Tyme's Chief Legal Officer, held the consulting role "Senior Counsel" with Faegre Drinker until December 31, 2021. During the year ending March 31, 2022, Tyme incurred approximately $0.5 million in legal charges payable to Faegre Drinker, and Tyme had approximately $153,000 and $289,000 in accounts payable and accrued expenses payable to Faegre Drinker at March 31, 2022 and June 30, 2022, respectively. During the year ending March 31, 2021, Tyme incurred approximately $0.6 million in legal charges payable to Faegre Drinker, and Tyme had approximately $87,000 and $101,000 in accounts payable and accrued expenses payable to Faegre Drinker at March 31, 2021 and June 30, 2021, respectively.

As noted above in *"Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters,"* Michael Demurjian, who beneficially owns more than five percent of Tyme's voting securities, resigned as an executive officer and director of Tyme effective March 15, 2019. In connection with his resignation, he entered into a Release Agreement, dated March 15, 2019, or the Release Agreement, pursuant to which he is entitled to certain severance payments subject to his compliance with obligations and restrictions under the agreement. Mr. Demurjian is entitled to continued payment of his current base salary through March 5, 2024 pursuant to the terms of his employment agreement with Tyme, dated March 5, 2015. Additionally, his vested stock options will remain exercisable until March 5, 2024, and he has forfeited all unvested stock options. Mr. Demurjian has also agreed, among other things, not to compete with Tyme and not to solicit Tyme's employees, officers, managers or full-time consultants until March 5, 2024. The Release Agreement also places confidentiality and non-disparagement obligations upon Mr. Demurjian and includes a release of all claims against Tyme. Tyme likewise has a non-disparagement obligation, ending on March 5, 2024. Tyme paid Mr. Demurjian $450,000 of his severance during the 2022 fiscal year and paid $450,000 of his severance during the 2021 fiscal year. Additionally, on April 18, 2022, Tyme and Michael Demurjian entered into a Voting Agreement, pursuant to which Mr. Demurjian agreed to vote all shares of Tyme common stock beneficially owned by him in accordance with the Tyme board of directors' recommendation with respect to any matter presented to Tyme's stockholders for a period of two years from the date of the agreement.

In connection with entering into the Release Agreement with Mr. Hoffman discussed in the section titled *"Tyme Executive Compensation"* in this joint proxy statement/prospectus, on the same date, Tyme and Mr. Hoffman also entered into a Voting Agreement, pursuant to which Mr. Hoffman agreed to vote all shares of Tyme common stock beneficially owned by him in accordance with Tyme's board of directors recommendation with respect to any matter presented to the stockholders for a period of one year from the date of the agreement.

On July 3, 2022, Eagle, a holder of more than 5% of Tyme's outstanding common stock, and each of Tyme's directors and officers, except Mr. Hoffman, entered into a Support Agreement with Syros and Tyme, in which Eagle and each such director and executive officer agreed, to, among other things, vote all of their shares of Tyme common stock owned as of the record date for the Tyme special meeting (i) in favor of the adoption of the proposals required for the merger, (ii) against any competing acquisition proposal, and (iii) against any proposal, action or agreement that would reasonably be expected to impede, interfere with, delay or postpone, prevent or otherwise impair the merger or the other transactions contemplated by the merger Agreement. Each of Tyme's executive officers and each of Tyme's directors, other than Mr. Hoffman, has also entered into a lock-up agreement in connection with the merger.

The Merger

On July 3, 2022, Syros Pharmaceuticals, Inc., a Delaware corporation ("Syros"), Tack Acquisition Corp., a Delaware corporation and a wholly owned subsidiary of Syros ("Merger Sub"), and Tyme Technologies, Inc., a Delaware corporation ("Tyme"), entered into an Agreement and Plan of Merger (the "Merger Agreement"), pursuant to which, among other matters, and subject to the satisfaction or waiver of the conditions set forth in the Merger Agreement, Merger Sub will merge with and into Tyme, with Tyme continuing as a wholly owned subsidiary of Syros and the surviving corporation of the merger (the "Merger"). The Merger, together with the PIPE Financing (defined below), is intended to be tax free for U.S. federal income tax purposes to Tyme stockholders.

Subject to the terms and conditions of the Merger Agreement, at the closing of the Merger, (a) each then outstanding share of Tyme common stock will be converted into the right to receive a number of shares of Syros common stock (subject to the payment of cash in lieu of fractional shares and subject to adjustment in the event of any reverse stock split that may be effectuated by Syros in connection with the transactions) calculated in accordance with the Merger Agreement (the "Exchange Ratio"); and (b) each then outstanding Tyme stock option and warrant to purchase Tyme common stock will be assumed by Syros, subject to adjustment as set forth in the Merger Agreement.

Upon the closing of the Merger, Syros expects to issue approximately 74.3 million shares of Syros common stock to Tyme stockholders, assuming that Tyme net cash as of the closing of the Merger is approximately $62.3 million and Tyme stockholders are expected to receive approximately 0.4312 shares of Syros common stock for each share of Tyme common stock. The number of shares to be issued in the Merger and the Exchange Ratio will be subject to adjustment based on the amount of Tyme's net cash at the closing of the Merger and the number of shares of Tyme common stock outstanding at the closing of the Merger.

PIPE Financing

On July 3, 2022, Syros entered into a securities purchase agreement (the "Securities Purchase Agreement") with several institutional accredited investors, pursuant to which Syros agreed to issue and sell to the investors in a private placement (the "PIPE Financing") an aggregate of 63.9 million shares of Syros common stock, par value $0.001 per share (the "Shares"), and, in lieu of Shares to certain investors, pre-funded warrants to purchase an aggregate of 74.3 million shares of common stock (the "Pre-Funded Warrants"), and, in each case, accompanying warrants (the "Warrants") to purchase an aggregate of up to 138.1 million additional shares of common stock (or Pre-Funded Warrants to purchase common stock in lieu thereof) at a price of $0.94 per share and accompanying Warrant (or $0.9399 per Pre-Funded Warrant and accompanying Warrant). The price per Pre-Funded Warrant and accompanying Warrant represents the price of $0.94 per share and accompanying Warrant to be sold in the PIPE Financing, minus the $0.0001 per share exercise price of each such Pre-Funded Warrant. The exercise price of the Warrants is $1.034 per share, or if exercised for a Pre-Funded Warrant in lieu thereof, $1.0339 per Pre-Funded Warrant (representing the Warrant exercise price of $1.034 per share minus the $0.0001 per share exercise price of each such Pre-Funded Warrant). The Warrants are exercisable beginning six months after the closing date of the PIPE Financing and prior to five years after the closing date of the PIPE Financing. The Pre-Funded Warrants are exercisable at any time after their original issuance and will not expire.

The PIPE Financing is expected to close substantially concurrently with the Merger, subject to the satisfaction of specified customary closing conditions and contingent upon, among other things, the closing of the Merger. The Company expects to receive aggregate gross proceeds from the PIPE Financing of approximately $130.0 million, before deducting estimated offering expenses payable by the Company and not inclusive of any exercise of the Warrants. The Company expects the net proceeds from the PIPE Financing to be used to advance the Company's

clinical development pipeline, business development activities, working capital and for general corporate purposes.

Oxford Finance Loan Agreement Amendment

Also on July 3, 2022, Syros entered into an amendment (the "Loan Amendment") to its Loan and Security Agreement (the "Loan Agreement") with Oxford Finance LLC, in its capacity as lender (in such capacity, the "Lender") and collateral agent (in such capacity, the "Agent"). Pursuant to the Loan Amendment, the Lender and Agent have agreed to modify the Loan Agreement in order to, among other things, (i) consent to the entry into the Merger Agreement, and subject to certain conditions, the consummation of the Merger; (ii) upon the consummation of the Merger and the PIPE Financing and the receipt of proceeds therefrom and subject to the payment of certain fees, extend the interest only period end date from March 1, 2023 to March 1, 2024 and extend the maturity date from February 1, 2025 to February 1, 2026; and (iii) upon the achievement of certain milestones and subject to the payment of certain fees, further extend the interest only period end date to September 1, 2024 and maturity date to August 1, 2026.

Pro Forma Financial Information

In the unaudited pro forma combined financial statements, the Merger is expected to be accounted for as a recapitalization under U.S. GAAP because the primary assets of Tyme at the effective date are expected to be primarily cash and marketable securities. Syros was determined to be the accounting acquirer based upon the terms of the Merger and other factors including: (1) Syros stockholders will own a substantial majority of the voting rights of the combined organization; (2) Syros will designate a majority of the initial members of the board of directors of the combined organization; and (3) Syros senior management will hold all key positions in senior management of the combined organization.

The unaudited pro forma combined balance sheet data as of March 31, 2022 gives effect to the PIPE Financing, the Loan Amendment and the Merger as if they took place on March 31, 2022. The unaudited pro forma combined statements of operations data for the twelve months ended December 31, 2021 and the three months ended March 31, 2022 give effect to the Merger and the Loan Amendment as if they took place on January 1, 2021. Syros and Tyme have different fiscal year ends. Syros' fiscal year ends on December 31, whereas Tyme's fiscal year ends on March 31. The unaudited pro forma condensed combined statement of operations for the twelve months ended December 31, 2021 combines the historical statements of operations of Syros and Tyme for the twelve months ended December 31, 2021. The historical statement of operations for Tyme for the twelve months ended December 31, 2021, was derived from Tyme's unaudited condensed statement of operations for the three months ended March 31, 2021 and the unaudited condensed statement of operations for the nine months ended December 31, 2021. The historical statement of operations for Tyme for the three months ended March 31, 2022 is Tyme's unaudited condensed statement of operations for the three months ended March 31, 2022, which was derived from the fourth quarter of the audited statement of operations for the year ended March 31, 2022.

The adjustments presented on the unaudited pro forma condensed combined financial statements have been identified and presented to provide relevant information necessary for an accurate understanding of the combined organization upon consummation of the Merger. The unaudited pro forma condensed combined financial information is based on assumptions and adjustments that are described in the accompanying notes. The unaudited pro forma condensed combined financial information is for illustrative purposes only. The financial results may have been different had the companies always been combined. The unaudited pro forma condensed combined financial information should not be relied upon as being indicative of the historical results that would have been achieved had the companies always been combined or the future results that the combined organization will experience. The actual amounts recorded as of the completion of the Merger may differ materially from the information presented in these unaudited pro forma combined financial statements as a result of the amount of cash used by Tyme between the signing of the Merger Agreement and the closing of the

Merger, the timing of closing of the Merger, and other changes in the amounts or estimated fair value of Tyme's assets and liabilities prior to the completion of the Merger.

The unaudited pro forma combined financial statements, including the notes thereto, should be read in conjunction with:

- The accompanying notes to the unaudited pro forma condensed combined financial information;
- The audited historical consolidated financial statements of Syros as of and for the year ended December 31, 2021, and 2020 and the related notes set forth in the Annual Report on Form 10-K filed with the SEC on March 15, 2022, included elsewhere in this prospectus;
- The unaudited historical consolidated financial statements of Syros as of and for the three months ended March 31, 2022, and the related notes set forth in the Quarterly Report on Form 10-Q filed with the SEC on May 16, 2022, included elsewhere in this prospectus;
- The audited historical consolidated financial statements of Tyme as of and for the year ended March 31, 2022, and 2021 and the related notes set forth in the Annual Report on Form 10-K filed with the SEC on May 25, 2022, included elsewhere in this prospectus;
- The disclosures contained in the sections titled "Syros Management's Discussion and Analysis of Financial Condition and Results of Operations," and "Tyme Management's Discussion and Analysis of Financial Condition and Results of Operations of Tyme," included elsewhere in this prospectus.

The unaudited pro forma condensed combined financial information has been presented for illustrative purposes only and does not necessarily reflect what the combined entity's financial condition or results of operations would have been had the Merger occurred on the dates indicated. Further, the unaudited pro forma condensed combined financial information also may not be useful in predicting the future financial condition and results of operations of the combined entity. The actual financial position and results of operations may differ significantly from the pro forma amounts reflected herein due to a variety of factors. The unaudited pro forma transaction accounting adjustments represent management's estimates based on information available as of the date of this unaudited pro forma condensed combined financial information and are subject to change as additional information becomes available and analyses are performed.

The combined entity believes that its assumptions and methodologies provide a reasonable basis for presenting all the significant effects of the transactions based on information available to management at this time and that the unaudited pro forma transaction accounting adjustments give appropriate effect to those assumptions and are properly applied in the unaudited pro forma condensed combined financial information.

Unaudited Pro Forma Condensed Combined Balance Sheet
As of March 31, 2022
(in thousands, except share and per share data)

	Historical						
	Syros (I)	Tyme (II)	Reclassifications	PIPE Financing	Loan Amendment	Merger Accounting Adjustments	Pro Forma Combined
Assets							
Current assets:							
Cash and cash equivalents	$ 69,575	$ 13,739	$ —	$122,053(d)	$ (300)(e)	$ (4,404)(f)	$ 200,663
Marketable securities	40,686	60,612	—	—	—	—	101,298
Contract assets	3,182	—	—	—	—	—	3,182
Prepaid clinical costs	—	481	(481)(a)	—	—	—	—
Prepaid expenses and other current assets	3,034	4,064	481(a)	—	—	—	7,579
Total current assets	116,477	78,896	—	122,053	(300)	(4,404)	312,722
Property and equipment, net	12,554	—	—	—	—	—	12,554
Marketable securities—noncurrent	2,638	9,081	—	—	—	—	11,719
Other long-term assets	3,155	—	—	—	—	—	3,155
Restricted cash	3,086	—	—	—	—	—	3,086
Right-of-use asset—operating lease	13,900	38	—	—	—	—	13,938
Right-of-use assets—financing leases	271	—	—	—	—	—	271
Total assets	$ 152,081	$ 88,015	$ —	$122,053	$ (300)	$ (4,404)	$ 357,445
Liabilities and stockholders' equity							
Current liabilities:							
Accounts payable	$ 2,841	$ 3,803	$ —	$ —	$ —	$ —	$ 6,644
Accrued expenses	13,249	—	3,545(b)	—	—	6,258(i)	23,052
Severance payable	—	2,612	(2,612)(b)	—	—	—	—
Accrued bonuses	—	933	(933)(b)	—	—	—	—
Deferred revenue	7,773	—	—	—	—	—	7,773
Financing lease obligations, current portion	274	—	—	—	—	—	274
Operating lease obligation, current portion	1,789	37	—	—	—	—	1,826
Debt, current portion	1,667	—	—	—	(1,667)(e)	—	—
Total current liabilities	27,593	7,385	—	—	(1,667)	6,258	39,569
Financing lease obligations, net of current portion	12	—	—	—	—	—	12
Operating lease obligation, net of current portion	22,378	—	—	—	—	—	22,378
Warrant liability	581	124	—	85,650(d)	—	—	86,355
Debt, net of debt discount, long term	38,775	—	—	—	1,367(e)	—	40,142
Severance payable, net of current portion	—	422	(422)(c)	—	—	—	—
Other long term liabilities	—	—	422(c)	—	—	—	422
Total liabilities	89,339	7,931	—	85,650	(300)	6,258	188,878
Commitments and contingencies							
Stockholders' equity:							
Common stock	61	17	—	64(d)	—	59(h)	201
Additional paid-in capital—common stock	551,679	241,031	—	39,435(d)	—	(171,424)(f),(g),(h),(i)	660,721
Accumulated other comprehensive loss	(273)	(544)	—	—	—	544(h)	(273)
Accumulated deficit	(488,725)	(160,420)	—	(3,096)(d)	—	160,159(g),(h)	(492,082)
Total stockholders' equity	62,742	80,084	—	36,403	—	(10,662)	168,567
Total liabilities and stockholders' equity	$ 152,081	$ 88,015	$ —	$122,053	$ (300)	$ (4,404)	$ 357,445

Pro Forma notes

(I) Derived from the unaudited condensed consolidated balance sheet of Syros as of March 31, 2022.
(II) Derived from the audited consolidated balance sheet of Tyme as of March 31, 2022.

Unaudited Pro Forma Condensed Combined Statements of Operations
Year Ended December 31, 2021
(in thousands, except share and per share data)

	Historical						
	Syros (I)	Tyme (II)	Reclassifications	PIPE Financing	Loan Amendment	Merger Accounting Adjustments	Pro Forma Combined
Revenue	$ 23,488	$ —	$ —	$ —	$ —	$ —	$ 23,488
Operating expenses:							
Research and development	99,872	14,695	506(a)	—	—	38(c)	115,111
General and administrative	23,036	9,449	70(a)	3,096(e)	—	223(c)	35,874
Severance expense	—	576	(576)(a)	—	—	—	—
Total operating expenses	122,908	24,720	—	3,096	—	261	150,985
Loss from operations	**(99,420)**	**(24,720)**	**—**	**(3,096)**	**—**	**(261)**	**(127,497)**
Change in fair value of warrant liability	16,682	706	—	—	—	—	17,388
Interest income	87	—	—	—	—	—	87
Interest expense	(3,907)	(76)	—	—	116(b)	—	(3,867)
Other income (expense)	—	98	—	—	—	—	98
Net loss applicable to common stockholders	**$ (86,558)**	**$ (23,992)**	**$ —**	**$ (3,096)**	**$ 116**	**$ (261)**	**$ (113,791)**
Net loss per share applicable to common stockholders—basic and diluted	**$ (1.38)**	**$ (0.15)**					**$ (0.41)**
Weighted-average number of common shares used in net loss per share applicable to common stockholders—basic and diluted	**62,534,978**	**163,849,671**					**274,929,768(d)**

Pro Forma notes

(I) Derived from the audited consolidated statement of operations of Syros for the year ended December 31, 2021.

(II) Derived from the audited consolidated statement of operations of Tyme for the year ended March 31, 2022, adjusted to December 31, 2021 year end by adding amounts from the unaudited consolidated condensed statement of operations for the three months ended March 31, 2021 and deducting amounts from the unaudited consolidated condensed statement of operations for the three months ended March 31, 2022.

Unaudited Pro Forma Condensed Combined Statements of Operations
Three Months Ended March 31, 2022
(in thousands, except share and per share data)

	Historical				
	Syros (I)	Tyme (II)	Reclassifications	Loan Amendment	Pro Forma Combined
Revenue	$ 5,467	$ —	$ —	$ —	$ 5,467
Operating expenses:					
Research and development	25,171	2,487	1,646(a)	—	29,304
General and administrative	6,949	2,376	537(a)	—	9,862
Severance expense	—	2,183	(2,183)(a)	—	—
Total operating expenses	32,120	7,046	—	—	39,166
Loss from operations	**(26,653)**	**(7,046)**	**—**	—	**(33,699)**
Change in fair value of warrant liability	2,448	188	—	—	2,636
Interest income	35	—	—	—	35
Interest expense	(976)	(13)	—	11(b)	(978)
Other income (expense)	—	56	—	—	56
Net loss applicable to common stockholders	**$ (25,146)**	**$ (6,815)**	**$ —**	**$ 11**	**$ (31,950)**
Net loss per share applicable to common stockholders—basic and diluted	**$ (0.40)**	**$ (0.04)**	**$ —**	**$ —**	**$ (0.12)**
Weighted-average number of common shares used in net loss per share applicable to common stockholders—basic and diluted	**63,061,423**	**172,206,894**			**275,456,213**(d)

Pro Forma notes

(I) Derived from the unaudited condensed consolidated statement of operations of Syros for the three months ended March 31, 2022.
(II) Derived from the unaudited condensed consolidated statement of operations of Tyme for the three months ended March 31, 2022, which are the fourth quarter of the audited consolidated statement of operations of Tyme for the year ended March 31, 2022.

NOTES TO UNAUDITED PRO FORMA CONDENSED COMBINED FINANCIAL STATEMENTS

Note 1—Basis of Presentation

The Merger is expected to be accounted for as a recapitalization because Syros has been determined to be the legal and accounting acquirer under Financial Accounting Standards Board's Accounting Standards Codification Topic 805, Business Combinations ("ASC 805"). The determination is primarily based on the evaluation of the following facts and circumstances taking into consideration:

- The pre-combination equity holders of Syros will hold the relative majority of voting rights in the combined entity;
- The pre-combination equity holders of Syros will have the right to appoint the majority of the directors on the combined entity board of directors;
- Senior management of Syros will comprise the senior management of the combined entity;
- Operations of Syros will comprise the ongoing operations of the combined entity; and
- Upon effectiveness of the Merger, the primary assets of Tyme at the effective date are expected to be primarily cash, cash equivalents and marketable securities.

Under the recapitalization accounting model, the Merger will be treated as Syros issuing stock for the net assets of Tyme, and any excess of consideration transferred over the fair value of the net assets of Tyme following determination of the actual purchase consideration will be reflected as a reduction to equity. The assets and liabilities of Tyme will be recorded, as of the completion of the Merger, at their fair value which is expected to approximate carrying value because of the short-term nature of the instruments. Syros has preliminarily concluded that the fair value of any intangible assets of Tyme is immaterial.

One-time direct and incremental transaction costs incurred prior to, or concurrent with, the closing of the Merger are reflected in the unaudited pro forma condensed combined balance sheet as a direct reduction to the combined entity's additional paid-in capital and are assumed to be cash-settled, except for the severance provision, stock-based compensation expense and the PIPE Financing costs attributable to the issuance of the Warrants.

The unaudited pro forma condensed combined financial information was prepared in accordance with Article 11 of SECRegulation S-X as amended by the final rule, Release No. 33-10786 "Amendments to Financial Disclosures about Acquired and Disposed Businesses." The historical financial information of Syros and Tyme include transaction accounting adjustments to illustrate the estimated effect of the Merger, the Loan Amendment and the PIPE Financing and certain other adjustments to provide relevant information necessary for an understanding of the combined entity upon consummation of the transactions described herein. The pro forma adjustments are subject to further adjustments as additional information becomes available and as additional analyses are conducted following the completion of the Merger, the Loan Amendment and the PIPE Financing. There can be no assurances that these additional analyses will not result in material changes to the estimates of fair value and the accounting for the transactions.

The unaudited pro forma condensed combined financial information does not reflect the income tax effects of the pro forma adjustments. Given the combined entity is expected to incur significant losses, a full valuation allowance is anticipated and therefore no income taxes are estimated for purposes of the unaudited pro forma condensed combined financial information.

Management will perform a comprehensive review of the two entities' accounting policies and may identify differences between the accounting policies of the two entities which, when conformed, could have a material impact on the financial statements of the post-combination company. Based on its initial analysis, management did not identify any differences that would have a material impact on the unaudited pro forma condensed combined financial information. As a result, the unaudited pro forma condensed combined financial information does not assume any differences in accounting policies.

Note 2—Shares of Syros Common Stock Issued to Tyme Stockholders upon Closing of the Merger

The number of shares of common stock Syros will issue to Tyme shareholders, for purposes of these pro forma combined financial statements as of March 31, 2022, is calculated pursuant to the terms of the Merger Agreement, using an Exchange Ratio that assumes Tyme has approximately $62.3 million of cash as of the Merger closing, assuming it had occurred on March 31, 2022, as follows:

	(in thousands, except share and per share amounts)
Estimated number of shares of the combined company to be owned by Tyme stockholders(1)	74,255,612
Multiplied by the assumed price per share of Syros common stock(2)	$0.94
Estimated fair value of shares of combined company to be owned by Tyme stockholders	$69,800
Estimated fair value of assumed Tyme equity awards attributable topre-combination service(3)	$861
Estimated purchase price(4)	$70,661

(1) Represents the number of shares of the combined company that Tyme stockholders would own as of the closing of the Merger pursuant to the Merger Agreement, which, for purposes of these pro forma financial statements, is calculated as 172,206,894 of Tyme shares outstanding as of July 5, 2022, converted into Syros shares using the Exchange Ratio calculated as of July 5, 2022. The final Exchange Ratio will be measured on the Merger closing date.

(2) $0.94 is the 5-day period average closing trading price of Syros common stock calculated using closing prices from June 27, 2022 through July 1, 2022.

(3) Represents the portion of the acquisition-date fair value of assumed Tyme equity awards that are attributable topre-combination service. This amount will be determined based on the closing trading price of Tyme common stock on the Merger closing date, the number of Tyme equity awards outstanding on the Merger closing date, and the period of service provided by the holders of the awards prior to the Merger closing date.

(4) As the Merger is expected to be accounted for as a recapitalization, any difference between the estimated purchase price and the fair value of the net assets of Tyme, which are expected to be primarily comprised of cash, cash equivalents and marketable securities, are reflected within equity.

Note 3—Adjustments to Unaudited Pro Forma Combined Balance Sheet as of March 31, 2022

The following pro forma adjustments included in the pro forma condensed combined balance sheet assume that the Merger was consummated on March 31, 2022, and are based on preliminary estimates that could change materially as additional information is obtained.

(a) To reclassify Prepaid clinical costs to Prepaid expenses and other current assets, to conform with Syros consolidated financial statements presentation.

(b) To reclassify Accrued bonuses and Severance payable to Accrued expenses, to conform with Syros consolidated financial statements presentation.

(c) To rename Accrued severance, net of current portion, to Other long term liabilities in connection with the reclassification of (b) above.

(d) To reflect the issuance of 63.9 million Shares, par value $0.001 per share, and in lieu of Shares to certain investors,Pre-Funded Warrants to purchase an aggregate of 74.3 million shares of common stock at an exercise price of $1.034 per share and accompanying Warrants. The aggregate purchase

price for the securities to be sold in the PIPE Financing is $130.0 million. The net proceeds from the PIPE Financing are estimated to be $122.1 million, less transaction costs of $7.9 million, of which $3.1 million was allocated to the Warrants, based on its relative fair value, and expensed. The fair value of the Warrants was $85.7 million, determined using the Black-Scholes valuation model (see Note 6 below).

Syros shares of common stock outstanding at March 31, 2022	62,801,296
Estimated number of shares of common stock to be issued to Tyme stockholders	74,255,612
Shares of common stock expected to be issued in PIPE Financing	63,871,778
Total estimated number of shares to be outstanding after the Merger and PIPE Financing	200,928,686
Par value per share	$ 0.001
Par value (in thousands)	$ 201

(e) To reflect the modification to the senior secured loan facility with Oxford Finance LLC, including the estimated payment of debt issuance costs of $0.3 million that will be reflected as a reduction to the debt balance and the reclassification of the current portion of debt to long-term.

(f) To reflect the payment of costs that are deemed to be direct and incremental costs of the Merger. These amounts are reflected as a reduction to additional paid-in capital as part of the recapitalization accounting as they reduce the net cash proceeds from the Merger.

(g) To record (1) $0.9 million of consideration transferred related to thepre-combination service of the replacement awards granted to Tyme by Syros and (2) the post-combination stock-based compensation expense of $0.3 million as an increase in additional paid-in capital and accumulated deficit related to the modification of certain awards extending the exercise period from 90 days to two years for certain awards.

(h) To reflect the elimination of Tyme's historical equity and remaining accumulated deficit, and to record Tyme's net assets acquired as an adjustment to additional paid-in capital.

(i) To record the severance provision of $6.3 million for Tyme's personnel that will be incurred upon termination of employment without cause or upon resignation for good reason before the Merger as part of liabilities assumed by Syros from Tyme. The severance provision adjustment is based upon preliminary assumptions that are subject to further refinement as additional information is obtained.

Note 4—Adjustments to Unaudited Pro Forma Combined Statements of Operations for the Year Ended December 31, 2021 and the Three Months Ended March 31, 2022

The following pro forma adjustment included in the pro forma condensed combined statement of operations assumes that the Merger was consummated on January 1, 2021, and is based on preliminary estimates that could change materially as additional information is obtained.

(a) Certain amounts from the historical consolidated financial statements of Tyme have been reclassified to conform to Syros' presentation.

(b) To reflect the effect of the Loan Amendment on interest expense.

(c) For the year ended December 31, 2021, to record the post-combination stock-based compensation expense of $0.3 million related to the modification of certain awards extending the exercise period from 90 days to two years.

(d) The pro forma combined basic and diluted earnings per share have been adjusted to reflect the pro forma net income for the year ended December 31, 2021 and the three months ended March 31, 2022. In addition, the number of shares used in calculating the pro forma combined basic and diluted net loss per share has been adjusted to reflect the estimated total number of shares of common stock of the combined company that would be outstanding as of the Merger closing date. For the year ended December 31, 2021 and the three months ended March 31, 2022, the pro forma weighted average shares outstanding has been calculated as follows:

	Three Months Ended March 31, 2022	Year Ended December 31, 2021
Syros weighted-average shares outstanding	63,061,423	62,534,978
Estimated shares of common stock expected to be issued to Tyme shareholders upon consummation of the Merger	74,255,612	74,255,612
Shares of common stock expected to be issued in the PIPE Financing	63,871,778	63,871,778
Pre-funded warrants expected to be issued in the PIPE Financing	74,267,400	74,267,400
Pro forma weighted-average shares outstanding	275,456,213	274,929,768

(e) To reflect the $3.1 million of PIPE Financing transaction costs allocated to the Warrants based on its relative fair value and expensed.

Note 5—Accounting for the PIPE Financing and PIPE Warrants

The common stock, Pre-Funded Warrants, and Warrants should be accounted for as separate freestanding financial instruments, as they are separately exercisable and legally detachable.

The Company preliminarily concluded that the Pre-Funded Warrants are equity-classified because they do not appear to be liabilities under ASC 480 as they neither embody an obligation to buy back the Company's shares, nor embody an obligation to issue a variable number of shares. Further, they are expected to meet the criteria within ASC 480 that would entitle all holders of the Pre-Funded Warrants to receive the same consideration as all other holders of the Company's common stock upon occurrence of a fundamental transaction, which does not preclude equity classification. However, the Company is currently finalizing its evaluation of the accounting, which is subject to change.

The Warrants meet the definition of a liability under ASC 480, because they embody an obligation to transfer cash equal to the Black Scholes Value upon occurrence of certain fundamental transactions. As such they will be recorded at their fair value at issuance date and mark-to-market at each reporting period. The fair value of the Warrants as of March 31, 2022 was determined using the Black-Scholes valuation model with the following assumptions:

Expected term (in years)	5
Risk-free interest rate	2.88%
Expected volatility	85.83%
Expected dividend rate	0.00%
Stock price	$ 0.91
Exercise price	$ 0.94

The assumptions used to calculate the pro formaPre-Funded Warrants and Warrants values are based on information as of July 1, 2022. The pro forma combined financial statements include an estimate for transaction costs of $7.9 million, of which $3.1 million was allocated to the Warrants based on its relative fair value and expensed. All assumptions and estimates are preliminary and are subject to change based on the information and circumstances as of the consummation of the Merger.

Note 6—Accounting for Stock Based Compensation Arrangements

Most Tyme stock options granted under the Tyme stock option plans (whether or not then exercisable) that are outstanding prior to the effective time of the Merger will become options to purchase Syros common stock. After the effective time, all outstanding and unexercised Tyme stock options assumed by Syros may be exercised solely for shares of Syros common stock. The number of shares of Syros common stock issuable upon the exercise of such options is equal to the number of shares of Tyme common stock subject to the unexercised portion of such Tyme option immediately prior to the effective time multiplied by the Exchange Ratio (rounded down to the nearest whole share number), at an exercise price per share equal to the exercise price per share of such Tyme option immediately prior to the effective time divided by the Exchange Ratio (rounded up to the nearest whole cent). The amendment of the terms of the Tyme stock options will be treated as a modification of the awards. Refer to the sections entitled "*The Merger Agreement—Merger Consideration*" and "*The Merger Agreement—Treatment of Tyme Equity Awards and Warrants*" beginning on pages 203 and 204, respectively, of this joint proxy statement/prospectus for further information regarding the Exchange Ratio.

Vesting of all unvested Tyme equity awards issued and outstanding will be accelerated at the effective time of the Merger, and all such equity awards issued and outstanding at the time of the merger that are held by continuing service providers will be assumed by Syros and will remain issued and outstanding. For accounting purposes, since the original awards provided for acceleration of vesting upon a change of control, the entire fair value-based measure of the replaced awards is attributable to precombination service and included in the consideration transferred. In addition, the exercise period for certain of Tyme's stock options will be extended to two years (from 90 days). For accounting purposes, the extension of the exercise periods will result in a one-time charge in the combined company's postcombination financial statements equal to the difference in the fair value of the options immediately prior to and immediately following the modification of the exercise period.

DESCRIPTION OF SYROS CAPITAL STOCK

The following description of the common stock of Syros, which is the only security of Syros registered under Section 12 of the Exchange Act, summarizes certain information regarding the Syros common stock in Syros' restated certificate of incorporation, as amended, Syros' amended and restated bylaws and applicable provisions of the DGCL, and is qualified by reference to Syros' restated certificate of incorporation and amended and restated by-laws, which are incorporated by reference as Exhibits 3.1 and 3.2, respectively, to this joint proxy statement/prospectus.

Authorized Capital Stock

Syros' authorized capital stock consists of 200,000,000 shares of Syros common stock and 10,000,000 shares of Syros preferred stock, par value $0.001 per share.

Common Stock

Holders of Syros common stock are entitled to one vote for each share held on all matters submitted to a vote of Syros stockholders and do not have cumulative voting rights. An election of directors by Syros stockholders is determined by a plurality of the votes cast by the stockholders entitled to vote on the election. Other matters are decided by the affirmative vote of Syros stockholders having a majority in voting power of the votes cast by the stockholders present or represented and voting on such matter, except as otherwise disclosed below. Holders of Syros common stock are entitled to receive proportionately any dividends as may be declared by Syros' board of directors, subject to any preferential dividend rights of outstanding Syros preferred stock.

In the event of Syros' liquidation or dissolution, the holders of Syros common stock are entitled to receive proportionately all assets available for distribution to Syros stockholders after the payment of all debts and other liabilities and subject to the prior rights of any outstanding Syros preferred stock. Holders of Syros common stock have no preemptive, subscription, redemption or conversion rights, and there are no sinking fund provisions applicable to Syros common stock. The rights, preferences and privileges of holders of Syros common stock are subject to and may be adversely affected by the rights of the holders of shares of any series of Syros preferred stock that Syros may designate and issue in the future.

Warrants

2019 Warrants. In April 2019, Syros completed two concurrent underwritten public offerings of Syros' equity securities, in connection with which Syros sold certain Class A warrants, which we refer to as the Syros 2019 Warrants, to purchase an aggregate of 2,118,344 shares of Syros common stock. Each Syros 2019 Warrant has an exercise price of $8.625 per share and will expire on October 10, 2022. The Syros 2019 Warrants and the shares of Syros common stock underlying such Syros 2019 Warrants have been registered pursuant to a Form S-3 shelf registration statement which was filed with the SEC and declared effective on July 31, 2017, and as of June 22, 2020, any such Syros 2019 Warrants and shares of Syros common stock underlying such Syros 2019 Warrants that remained unsold were included on a Form S-3 shelf registration statement which was filed with the SEC and declared effective on June 22, 2020. As of December 31, 2021, 2,117,094 Syros 2019 Warrants are outstanding and remain unexercised.

Oxford Warrants. On February 12, 2020, Syros entered into the Loan Agreement with Oxford, pursuant to which a term loan was funded on February 12, 2020, which we refer to as the First Tranche, and another term loan was funded on December 23, 2020, which we refer to as the Second Tranche. In connection with the funding of the First Tranche, Syros issued Oxford warrants to purchase 27,548 shares of Syros common stock at an exercise price per share of $7.26 that will expire on February 12, 2025, which we refer to as the First Tranche Warrants. In connection with the funding of the Second Tranche, Syros issued Oxford warrants to purchase 17,389 shares of Syros common stock at an exercise price of $11.50 per share that will expire on December 23, 2025, which we

refer to as the Second Tranche Warrants. As of December 31, 2021, 27,548 First Tranche Warrants and 17,389 Second Tranche Warrants, which we refer to collectively as the Oxford Warrants, are outstanding and remain unexercised.

Pre-Funded 2020 Warrants and 2020 Warrants. On December 8, 2020, through a private placement, Syros issued 10,312,500 shares of Syros common stock, and, in lieu of shares of Syros common stock, pre-funded warrants, which we refer to as the Pre-Funded 2020 Warrants, to purchase an aggregate of 1,000,000 shares of Syros common stock, and, in each case, accompanying warrants, which we refer to as the Syros 2020 Warrants, to purchase an aggregate of up to 2,828,125 additional shares of Syros common stock (or Syros Pre-Funded 2020 Warrants to purchase Syros common stock in lieu thereof) at an exercise price of $8.00 per share and accompanying Syros 2020 Warrant (or $7.99 per Pre-Funded 2020 Warrant and accompanying Syros 2020 Warrant). The price per Pre-Funded 2020 Warrant and accompanying Syros 2020 Warrant represents the price of $8.00 per share and accompanying Syros 2020 Warrant minus the $0.01 per share exercise price of each such Pre-Funded 2020 Warrant. The exercise price of the Syros 2020 Warrants is $11.00 per share, or if exercised for a Pre-Funded 2020 Warrant in lieu thereof, $10.99 per Pre-Funded 2020 Warrant (representing the Syros 2020 Warrant exercise price of $11.00 per share minus the $0.01 per share exercise price of each such Pre-Funded 2020 Warrant). The Syros 2020 Warrants are exercisable at any time during the period beginning on June 8, 2021 and ending on December 8, 2025. The Pre-Funded 2020 Warrants are exercisable at any time after their original issuance and will not expire. The shares of Syros common stock underlying the Pre-Funded 2020 Warrants and the Syros 2020 Warrants have been registered for resale on a Form S-3 resale registration statement which was filed with the SEC and declared effective on January 19, 2021. As of December 31, 2021, 1,000,000 Pre-Funded 2020 Warrants and 2,828,125 Syros 2020 Warrants are outstanding and remain unexercised.

Syros has authorized and reserved for issuance all shares of Syros common stock issuable upon exercise of each of the Syros 2019 Warrants, the Oxford Warrants, the Pre-Funded 2020 Warrants and the Syros 2020 Warrants, which are referred to collectively in this section as the Syros Warrants. The number of shares of Syros common stock to be received upon the exercise of each Syros Warrant may be adjusted from time to time upon the occurrence of certain events, including but not limited to the payment of a dividend or other distribution in respect of Syros common stock, subdivisions, reclassifications or combinations of the Syros common stock. The securities receivable upon exercise of each Syros Warrant may be adjusted in the event of any reorganization, consolidation, merger, liquidation or similar event.

Anti-Takeover Effects of Delaware Law and Syros' Charter and Bylaws

Delaware law and Syros' restated certificate of incorporation and amended and restated bylaws contain provisions that could have the effect of delaying, deferring or discouraging another party from acquiring control of Syros. These provisions, which are summarized below, are expected to discourage coercive takeover practices and inadequate takeover bids. These provisions are also designed to encourage persons seeking to acquire control of us to first negotiate with Syros' board of directors.

Staggered Board; Removal of Directors. Syros' restated certificate of incorporation and amended and restatedby-laws divide Syros' board of directors into three classes with staggered three-year terms. In addition, a director may only be removed for cause and only by the affirmative vote of the holders of at least 75% of the votes that all of Syros' stockholders would be entitled to cast in an annual election of directors. Any vacancy on Syros' board of directors, including a vacancy resulting from an enlargement of Syros' board of directors, may only be filled by vote of a majority of Syros' directors then in office. The classification of Syros' board of directors and the limitations on the removal of directors and filling of vacancies could make it more difficult for a third party to acquire, or discourage a third party from seeking to acquire, control of Syros.

Stockholder Action by Written Consent; Special Meetings Syros' restated certificate of incorporation provides that any action required or permitted to be taken by Syros' stockholders must be effected at a duly called annual or special meeting of such holders and may not be effected by any consent in writing by such holders. Syros'

restated certificate of incorporation and amended and restated bylaws also provide that, except as otherwise required by law, special meetings of Syros' stockholders can only be called by Syros' chairman of the board, Syros' chief executive officer or Syros' board of directors.

Advance Notice Requirements for Stockholder Proposals. Syros' amended and restated bylaws establish an advance notice procedure for stockholder proposals to be brought before an annual meeting of Syros' stockholders, including proposed nominations of persons for election to Syros' board of directors. Stockholders at a Syros annual meeting may only consider proposals or nominations specified in the notice of meeting or brought before the meeting by or at the direction of Syros' board of directors or by a Syros stockholder of record on the record date for the meeting who is entitled to vote at the meeting and who has delivered timely written notice in proper form to Syros' secretary of the stockholder's intention to bring such business before the meeting. These provisions could have the effect of delaying until the next stockholder meeting stockholder actions that are favored by the holders of a majority of Syros' outstanding voting securities.

Delaware Business Combination Statute. Syros is subject to Section 203 of the DGCL. Subject to certain exceptions, Section 203 prevents a publicly held Delaware corporation from engaging in a "business combination" with any "interested stockholder" for three years following the date that the person became an interested stockholder, unless the interested stockholder attained such status with the approval of Syros' board of directors or unless the business combination is approved in a prescribed manner. A "business combination" includes, among other things, a merger or consolidation involving Syros and the "interested stockholder" and a sale involving Syros and the "interested stockholder" of 10% or more of Syros' assets. In general, an "interested stockholder" is any entity or person beneficially owning 15% or more of Syros' outstanding voting stock and any entity or person affiliated with or controlling or controlled by such entity or person.

Amendment of Syros' restated certificate of incorporation and amended and restated bylaws. The DGCL provides generally that the affirmative vote of a majority of the shares entitled to vote on any matter is required to amend a corporation's certificate of incorporation or bylaws, unless a corporation's certificate of incorporation or bylaws, as the case may be, requires a greater percentage. Syros' amended and restated bylaws may be amended or repealed by a majority vote of Syros' board of directors or by the affirmative vote of the holders of at least 75% of the votes that all of Syros' stockholders would be entitled to cast in any annual election of directors. In addition, the affirmative vote of the holders of at least 75% of the votes that all of Syros' stockholders would be entitled to cast in any annual election of directors is required to amend or repeal or to adopt any provisions inconsistent with any of the provisions of Syros' restated certificate of incorporation described above under "*—Staggered Board; Removal of Directors*" and "*—Stockholder Action by Written Consent; Special Meetings.*"

Authorized but Unissued Shares

The authorized but unissued shares of Syros common stock and Syros preferred stock are available for future issuance without stockholder approval, subject to any limitations imposed by the listing requirements of The Nasdaq Global Select Market. These additional shares may be used for a variety of corporate finance transactions, acquisitions and employee benefit plans. The existence of authorized but unissued and unreserved Syros common stock and Syros preferred stock could make it more difficult or discourage an attempt to obtain control of Syros by means of a proxy contest, tender offer, merger or otherwise.

COMPARISON OF THE RIGHTS OF HOLDERS OF SYROS STOCK AND TYME STOCK

If the merger is completed, Tyme stockholders will receive shares of Syros common stock pursuant to the terms of the Merger Agreement. Immediately prior to the closing of the merger, Syros' restated certificate of incorporation will be amended to increase the authorized shares of Syros common stock, as set forth in the form of certificate of amendment attached as *Annex H* to this joint proxy statement/prospectus.

Syros and Tyme are both incorporated under the laws of the State of Delaware. The rights of Syros stockholders and Tyme stockholders are generally governed by the DGCL. Upon completion of the merger, Tyme stockholders will become Syros stockholders, and their rights will be governed by the DGCL, the second amended and restated bylaws of Syros and the restated certificate of incorporation of Syros.

The material differences between the current rights of Tyme stockholders under the Tyme amended and restated certificate of incorporation, as amended, and amended and restated bylaws and their rights as Syros stockholders, after the merger, under the Syros restated certificate of incorporation and the second amended and restated bylaws, both as will be in effect immediately following the completion of the merger, are summarized below. The summary below does not purport to be complete and is subject to, and qualified in its entirety by reference to, the DGCL and the governing corporate instruments that are subject to amendment in accordance with their terms. You should carefully read this entire document and the other referenced documents, including the governing corporate instruments, for a more complete understanding of the differences between being a stockholder of Syros or Tyme before the merger and being a stockholder of the combined company following the completion of the merger. For more information on how to obtain these documents, see the section titled "*Where You Can Find More Information*" beginning on page 445 of this joint proxy statement/prospectus.

Syros	**Tyme**
Organizational Documents	
The rights of Syros stockholders are governed by Syros' restated certificate of incorporation, Syros' second amended and restated bylaws and the DGCL.	The rights of Tyme stockholders are governed by Tyme's amended and restated certificate of incorporation, as amended, Tyme's amended and restated bylaws and the DGCL.
Authorized Capital Stock Syros is authorized to issue two classes of capital stock which are designated, respectively, "common stock" and "preferred stock." The total number of shares that Syros is authorized to issue is 210,000,000 (which would increase to 710,000,000 if Syros Proposal No. 2 is adopted), of which 200,000,000 (which would increase to 700,000,000 if Syros Proposal No. 2 is adopted) shares are common stock, par value $0.001 per share, and 10,000,000 shares are preferred stock, par value $0.001 per share. The number of authorized shares of preferred stock may be increased or decreased (but not below the number of shares then outstanding) by the affirmative vote of the holders of a majority of the voting power of the capital stock of Syros entitled to vote thereon, voting as a single class, irrespective of the provisions of Section 242(b)(2) of the DGCL. The number of authorized shares of common stock may be increased or decreased (but not below the number of shares thereof then outstanding) by the affirmative vote	Tyme is authorized to issue two classes of capital stock which are designated, respectively, "common stock" and "preferred stock." The total number of shares that Tyme is authorized to issue is 310,000,000, of which 300,000,000 shares are common stock, par value $0.0001 per share, and 10,000,000 shares are preferred stock, par value $0.0001 per share.

Syros	Tyme
of the holders of a majority of the stock of Syros entitled to vote, irrespective of the provisions of Section 242(b)(2) of the DGCL.	
Common Stock Syros' authorized common stock consists of 200,000,000 shares of common stock, which would increase to 700,000,000 if Syros Proposal No. 2 is approved by Syros' holders.	Tyme's authorized common stock consists of 300,000,000 shares of common stock.
Each holder of a share of Syros common stock is entitled to one vote for each such share held of record on the applicable record date on each matter voted on at a meeting of stockholders.	Each holder of a share of Tyme common stock is entitled to one vote for each such share held of record on the applicable record date on each matter voted on at a meeting of stockholders.
Preferred Stock Syros' authorized preferred stock consists of 10,000,000 shares of preferred stock. No shares of Syros preferred stock are currently outstanding.	Tyme's authorized preferred stock consists of 10,000,000 shares of preferred stock. No shares of Tyme preferred stock are currently outstanding.
Number and Qualification of Directors The Syros board of directors consists of one or more members, and the number of directors is fixed from time to time by resolution of the Syros board of directors. The Syros board of directors currently consists of ten members. Directors of Syros need not be stockholders of Syros.	The Tyme board of directors consists of one or more members, and the number of directors is fixed from time to time by resolution of the Tyme board of directors in its sole discretion. The Tyme board of directors currently consists of eight members. No decrease in the authorized number of directors constituting the Tyme board of directors will shorten the term of any incumbent director. Directors of Tyme need not be stockholders of Tyme.
Structure of Board of Directors; Term of Directors; Election of Directors Other than any directors elected by the separate vote of the holders of any series of Syros preferred stock, the Syros board of directors is divided into three classes, designated as Class I, Class II and Class III, respectively. Directors are assigned to each class in accordance with a resolution or resolutions adopted by the Syros board of directors. At the first annual meeting of stockholders following the effectiveness of Syros' initial public offering, the term of office of the Class I directors expired and Class I directors were elected for a full term of three years. At the second annual meeting of stockholders following Syros' initial public offering, the term of office of the Class II directors expired and Class II directors were elected for a full term of three years. At the third annual meeting of stockholders following Syros' initial public offering, the term of office of the Class III directors expired and Class III directors were elected for a full term of three years. At each succeeding annual meeting of stockholders,	Other than any directors elected by the separate vote of the holders of any series of Tyme preferred stock, the Tyme board of directors is divided into three classes, designated as Class I, Class II and Class III, respectively. Directors are assigned to each class in accordance with a resolution or resolutions adopted by the Tyme board of directors. At the first annual meeting of stockholders following the effectiveness of Tyme's initial public offering, the term of office of the Class I directors expired and Class I directors were elected for a full term of three years. At the second annual meeting of stockholders following Tyme's initial public offering, the term of office of the Class II directors expired and Class II directors were elected for a full term of three years. At the third annual meeting of stockholders following Tyme's initial public offering, the term of office of the Class III directors expired and Class III directors were elected for a full term of three years. At each

Syros	Tyme
directors are elected for a full term of three years to succeed the directors of the class whose terms expire at such annual meeting.	succeeding annual meeting of stockholders, directors are elected for a full term of three years to succeed the directors of the class whose terms expire at such annual meeting.
Removal of Directors Subject to the special rights of the holders of one or more series of Syros preferred stock to elect directors, or except as otherwise provided by the DGCL, the Syros board of directors or any individual director may be removed from office at any time, but only for cause and only by the affirmative vote of the holders of at least seventy-five percent (75%) of the voting power of all the then outstanding shares of voting stock of Syros entitled to vote at an election of directors.	Subject to the special rights of the holders of one or more series of Tyme preferred stock to elect directors, or except as otherwise provided by the DGCL or the Tyme amended and restated certificate of incorporation, as amended, the Tyme board of directors or any individual director may be removed from office at any time, but only for cause and only by the affirmative vote of the holders of at least a majority of the voting power of all the then outstanding shares of voting stock of Tyme entitled to vote at an election of directors, voting together as a single class.
Vacancies on the Board of Directors Any director may resign at any time by delivering a resignation in writing or by electronic transmission to Syros at its principal executive office or to its Chairman of the Board, the Chief Executive Officer, the President or the Secretary. Such resignation shall be effective upon receipt unless it is specified to be effective at some later time or upon the happening of some later event.	Any director may resign at any time. Such resignation shall be made in writing or by electronic transmission and shall take effect at the time specified therein, or, if no time is specified, at the time of its receipt by Tyme's Chairman of the Board, if any, the Chief Executive Officer, if any, the President or the Secretary. The acceptance of a resignation shall not be necessary to make it effective unless so specified therein.
Any vacancy on Syros' board of directors, including a vacancy resulting from an enlargement of Syros' board of directors, may only be filled by vote of a majority of Syros' directors then in office, although less than a quorum, or by a sole remaining director and shall not be filled by the stockholders.	Vacant directorships, including newly created seats, may only be filled by a majority of the directors of Tyme then in office, although less than a quorum, by a sole remaining director, if applicable, or only in the case where there are no directors then in office, by the stockholders of Tyme.
Stockholder Action by Written Consent No action may be taken by the stockholders except at an annual or special meeting of stockholders called in accordance with Syros' second amended and restated by-laws, and no action may be taken by the stockholders by written consent in lieu of a meeting.	Action may be taken by the stockholders at an annual or special meeting of stockholders called in accordance with Tyme's amended and restated bylaws, or by the written consent of the Tyme stockholders entitled to vote thereon.
Quorum Unless otherwise provided by law or Syros' restated certificate of incorporation, at each meeting of stockholders the holders of a majority of the shares of stock entitled to vote at the meeting, present in person, by means of remote communication in a manner, if any, authorized by Syros' board of directors in its sole	Unless otherwise provided by law or Tyme's amended and restated certificate of incorporation, as amended, at each meeting of stockholders the holders of at least one-third (1/3) of the shares of stock entitled to vote at the meeting, present in person or represented by proxy, will constitute a quorum for

Syros	Tyme
discretion, or represented by proxy, will constitute a quorum for the transaction of business. If a quorum fails to attend any meeting, the chairperson of the meeting or the holders of the shares entitled to vote who are present or represented at such meeting may adjourn the meeting.	the transaction of business. If a quorum fails to attend any meeting, the chairperson of the meeting or the holders of a majority of the shares entitled to vote who are present, in person or by proxy, at the meeting may adjourn the meeting.
Special Meetings of Stockholders Special meetings of stockholders for any purpose or purposes may be called at any time by only the board of directors, the Chair of the Syros board of directors, or the Chief Executive Officer.	Special meetings of the stockholders can be called only by a resolution of the Tyme board of directors in its sole and absolute discretion.
The Syros board of directors will determine the time and place, if any, of such special meeting. Special meetings may not be called by any other person or persons.	The Tyme board of directors will determine the time and place, if any, of such special meeting. Special meetings may not be called by any other person or persons.
Notice of Stockholder Meetings Notice of all meetings of stockholders is to be given in writing or by electronic transmission in the manner provided by law and Syros' second amended and restated bylaws, stating the place, if any, date and time of the meeting, the means of remote communications, if any, by which stockholders and proxyholders may be deemed to be present in person and vote at such meeting, and in the case of a special meeting, the purpose or purposes of the meeting. Unless otherwise required by applicable law, such notice is to be given not less than ten nor more than 60 days before the date of the meeting to each stockholder of record entitled to vote at such meeting.	Meetings of the stockholders for the election of Tyme's directors or for any other purpose shall be held on such date, at such time and at such place, either within or without the State of Delaware, as shall be designated from time to time by Tyme's board of directors and stated in the notice of the meeting or in a duly executed waiver of notice thereof. Tyme's board of directors may determine, in its sole discretion, that (a) stockholders may, by means of remote communication, participate in a meeting of stockholders and be deemed present in person and vote thereat and/or (b) a meeting of stockholders may be held not at any place, but may instead be held solely by means of remote communication, both as provided in the DGCL. Unless otherwise required by applicable law or Tyme's amended and restated certificate of incorporation, as amended, such notice is to be given not less than ten nor more than 60 days before the date of the meeting to each stockholder of record entitled to vote at such meeting.
Advance Notice Requirements for Stockholder Proposals Nominations of persons for election to the Syros board of directors and the proposal of business other than nominations to be considered by the stockholders may be made at an annual meeting of stockholders only as (i) specified in the notice of meeting (or any supplement thereto) given by or at the direction of the Syros board of directors, (ii) otherwise properly brought before the meeting by or at the direction of Syros' board of directors or (iii) properly brought before the meeting by a stockholder.	Nominations of persons for election to the Tyme board of directors and the proposal of business other than nominations to be considered by the stockholders may be made at an annual meeting of stockholders only (i) as specified in the notice of meeting (or any supplement thereto) given by or at the direction of Tyme's board of directors, (ii) otherwise properly brought before the meeting by or at the direction of Tyme's board of directors or (iii) otherwise properly brought before the meeting by a stockholder of record.

Syros	Tyme
Amendment of Certificate of Incorporation The affirmative vote of holders of at least seventy-five percent (75%) of the votes that all of Syros' stockholders would be entitled to cast in any annual election of directors is required to amend, repeal or adopt any provisions inconsistent with certain provisions of Syros' restated certificate of incorporation, including provisions relating to the size of the board, removal of directors, amendment requirements for the restated certificate of incorporation and second amended and restated bylaws, and actions by written consent. Notwithstanding any other provisions of Syros' restated certificate of incorporation, Syros' second amended and restated bylaws, or any provision of law which might otherwise permit a lesser vote or no vote, stockholders may vote to amend Syros' amended and restated certificate of incorporation pursuant to Section 242 of the DGCL.	The affirmative vote of holders of at least a majority of the then-outstanding shares of voting stock will be required to amend Tyme's amended and restated certificate of incorporation, as amended. Notwithstanding any other provisions of Tyme's amended and restated certificate of incorporation, as amended, Tyme's amended and restated bylaws, or any provision of law which might otherwise permit a lesser vote or no vote, stockholders may vote to amend Tyme's amended and restated certificate of incorporation, as amended, pursuant to Section 242 of the DGCL.
Amendment of Bylaws The affirmative vote of holders of at least seventy-five percent (75%) of the votes that all of Syros' stockholders would be entitled to cast in any annual election of directors, is required to adopt, amend or repeal Syros' second amended and restated bylaws.	The affirmative vote of a majority of Tyme's stockholders entitled to vote is required to alter, amend or repeal Tyme's amended and restated bylaws. The Tyme board of directors also has the power to adopt, amend or repeal Tyme's amended and restated bylaws by the approval of a majority of the authorized number of directors without prior notice to or approval by its stockholders.
Limitation on Director Liability The liability of the Syros directors for monetary damages is and will be eliminated to the fullest extent under applicable law. If applicable law is amended to authorize corporate action further eliminating or limiting the personal liability of directors, then the liability of a director to Syros will be eliminated or limited to the fullest extent permitted by applicable law as so amended.	The liability of the Tyme directors for monetary damages is and will be eliminated to the fullest extent under applicable law. If applicable law is amended to authorize corporate action further eliminating or limiting the personal liability of directors, then the liability of a director to Tyme will be eliminated or limited to the fullest extent permitted by applicable law as so amended.
Indemnification To the fullest extent permitted by applicable law, Syros is authorized to provide indemnification of (and advancement of expenses to) any person who was or is a party or threatened to be made a party to any threatened, pending or completed action, suit or proceeding, whether civil, criminal, administrative or investigative, by reason of the fact that he or she is or was, or has agreed to become, a director or officer of Syros, or is or was serving, or has agreed to serve, at the request of	To the fullest extent permitted by applicable law, Tyme is authorized to provide indemnification of (and advancement of expenses to) directors, officers, employees and agents of Tyme (and any other persons to which applicable law permits Tyme to provide indemnification) through provisions of Tyme's amended and restated bylaws, agreements with such agents or other persons, vote of stockholders or disinterested directors or otherwise in

Syros	Tyme
Syros, as a director, officer, partner, employee or trustee of, or in a similar capacity with, another corporation, partnership, joint venture, trust or other enterprise (including any employee benefit plan, and any other persons to which applicable law permits Syros to provide indemnification) agreements with such agents or other persons, vote of stockholders or disinterested directors or otherwise in excess of the indemnification and advancement otherwise permitted by such applicable law. If applicable law is amended to authorize corporate action further eliminating or limiting the personal liability of directors, then the liability of a director to Syros will be eliminated or limited to the fullest extent permitted by applicable law as so amended.	excess of the indemnification and advancement otherwise permitted by such applicable law. If applicable law is amended to authorize corporate action further eliminating or limiting the personal liability of directors, then the liability of a director to Tyme will be eliminated or limited to the fullest extent permitted by applicable law as so amended.
Conversion Rights There are no conversion rights associated with any outstanding capital stock of Syros.	There are no conversion rights associated with any outstanding capital stock of Tyme.
Right of First Refusal Syros does not have a right of first refusal in place.	Tyme does not have a right of first refusal in place.
Right of Co-Sale Syros does not have a right of co-sale in place.	Tyme does not have a right of co-sale in place.
Preemptive Rights Syros stockholders do not have preemptive rights. Thus, if additional shares of Syros common stock are issued, the current holders of Syros common stock will own a proportionately smaller interest in a larger number of outstanding shares of common stock to the extent that they do not participate in the additional issuance.	Tyme stockholders do not have preemptive rights. Thus, if additional shares of Tyme common stock are issued, the current holders of Tyme common stock will own a proportionately smaller interest in a larger number of outstanding shares of common stock to the extent that they do not participate in the additional issuance.
Distributions to Stockholders Dividends upon Syros capital stock, subject to the provisions of Syros' restated certificate of incorporation and applicable law, if any, may be declared by the Syros board of directors pursuant to law at any regular or special meeting. Dividends may be paid in cash, in property, or in shares of the capital stock, subject to the provisions of Syros' restated certificate of incorporation and applicable law. The Syros board of directors may fix a record date for the determination of holders of Syros common stock entitled to receive payment of a dividend or distribution declared thereon, which record date is not to precede the date upon which the resolution fixing the record date is adopted, and which record date may not be more than 60 days prior to the date fixed for the payment thereof.	Dividends upon Tyme capital stock, subject to the provisions of Tyme's amended and restated certificate of incorporation, as amended, and applicable law, if any, may be declared by the Tyme board of directors pursuant to law at any regular or special meeting. Dividends may be paid in cash, in property, or in shares of the capital stock, subject to the provisions of Tyme's amended and restated certificate of incorporation, as amended, and applicable law. The Tyme board of directors may fix a record date for the determination of holders of Tyme common stock entitled to receive payment of a dividend or distribution declared thereon, which record date is not to precede the date upon which the resolution fixing the record date is adopted, and

Syros	Tyme
	which record date may not be more than 60 days prior to the date fixed for the payment thereof.
Exclusive Forum Unless Syros consents in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware (or, if the Court of Chancery of the State of Delaware does not have jurisdiction, the federal district court for the District of Delaware) shall, to the fullest extent permitted by law, be the sole and exclusive forum for (i) any derivative action or proceeding brought on behalf of Syros; (ii) any action asserting a claim of breach of a fiduciary duty owed by any director, officer, other employee or stockholder of Syros to Syros or Syros stockholders; (iii) any action asserting a claim arising pursuant to any provision of the DGCL or as to which the DGCL confers jurisdiction on the Court of Chancery of the State of Delaware; or (iv) any action asserting a claim arising pursuant to any provision of Syros' restated certificate of incorporation or second amended and restated bylaws (in each case, as they may be amended from time to time) or governed by the internal affairs doctrine.	Unless Tyme consents in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware (or, if the Court of Chancery of the State of Delaware does not have jurisdiction, the federal district court for the District of Delaware) will be the sole and exclusive forum for (i) any derivative action or proceeding brought on behalf of Tyme; (ii) any action asserting a claim of breach of a fiduciary duty owed by any director, officer, employee or agent of Tyme to Tyme or Tyme stockholders; (iii) any action asserting a claim against Tyme arising pursuant to any provision of the DGCL, Tyme's amended and restated certificate of incorporation, as amended, or Tyme's amended and restated bylaws; or (iv) any action asserting a claim against Tyme governed by the internal affairs doctrine.
Registration Rights Syros is party to three registration rights agreements, which are dated December 4, 2020, July 3, 2022 and July 3, 2022, respectively. Under each of these registration rights agreements, certain investors of Syros have certain registration rights, including for Syros to file a registration statement on Form S-3, or a shelf registration statement.	Under the registration rights agreement, dated January 7, 2020, Eagle has certain registration rights, including for Tyme to file a registration statement on Form S-3, or a shelf registration statement, or request that their shares be covered by a registration statement that Tyme is otherwise filing, so-called "piggyback" registration rights.
Stock Transfer Restrictions Applicable to Stockholders Shares of Syros are transferable in the manner prescribed by the DGCL.	Shares of Tyme are transferable in the manner prescribed by the DGCL.

PRINCIPAL STOCKHOLDERS OF SYROS

Except where specifically noted, the following information and all other information contained in this joint proxy statement/prospectus does not give effect to the proposed Syros reverse stock split.

The following table and accompanying footnotes set forth certain information with respect to the beneficial ownership of Syros common stock at June 30, 2022 for:

- each person, or group of affiliated persons, who is known by Syros to beneficially own more than 5% of Syros common stock;
- each of Syros' named executive officers;
- each of Syros' directors; and
- all of Syros' executive officers and directors as a group.

Beneficial ownership prior to the completion of the merger and the PIPE Financing is based on 62,989,020 shares of Syros common stock outstanding as of June 30, 2022.

Syros has determined beneficial ownership in accordance with the rules of the SEC. These rules generally attribute beneficial ownership of securities to persons who possess sole or shared voting power or investment power with respect to those securities. In addition, these rules require that Syros includes shares of common stock issuable pursuant to the vesting of restricted stock units and the exercise of stock options and warrants that are either immediately exercisable or exercisable within 60 days of June 30, 2022. These shares are deemed to be outstanding and beneficially owned by the person holding those options or warrants for the purpose of computing the percentage ownership of that person, but they are not treated as outstanding for the purpose of computing the percentage ownership of any other person. Unless otherwise indicated, the persons or entities identified in this table have sole voting and investment power with respect to all shares shown as beneficially owned by them, subject to applicable community property laws.

Except as otherwise noted below, the address for persons listed in the table is c/o Syros Pharmaceuticals, Inc., 35 CambridgePark Drive, 4th Floor, Cambridge Massachusetts 02140.

Name of Beneficial Owner	Shares of Common Stock Beneficially Owned	+	Common Stock Underlying Options and Other Rights Acquirable Within 60 Days	=	Total Beneficial Ownership: Shares Beneficially Owned	Total Beneficial Ownership: Percentage of Shares Beneficially Owned
5% Stockholders						
Entities affiliated with FMR LLC	5,797,876		—		5,797,876 (1)	9.20%
Entities affiliated with Bain Capital Life Sciences, L.P.	5,504,661 (2)		875,393 (3)		6,380,054	9.99%
Ally Bridge MedAlpha Master Fund L.P.	3,539,895 (4)		390,625 (5)		3,930,520	6.20%
Entities affiliated with Invus Public Equities, L.P.	3,500,000		—		3,500,000 (6)	5.56%
Named Executive Officers and Directors						
Nancy Simonian, M.D.	852,723 (7)		1,238,054		2,090,777	3.26%
Jason Haas	—		—		—	*
David A. Roth, M.D.	59,719		527,115		586,834	*
Srinivas Akkaraju, M.D., Ph.D.	1,899,616 (8)		368,250 (9)		2,267,866	3.58%
Mark J. Alles	10,000		66,110		76,110	*
Deborah Dunsire, M.D.	—		10,692		10,692	*
S. Gail Eckhardt, M.D.	—		39,860		39,860	*
Marsha H. Fanucci	—		104,666		104,666	*
Amir Nashat, Ph.D.	1,586,653 (10)		90,000		1,676,653	2.66%
Phillip A. Sharp, Ph.D.	266,666 (11)		132,857		399,523	*
Peter Wirth	—		79,000		79,000	*
Richard A. Young, Ph.D.	321,711		90,000		411,711	*
All Current Executive Officers and Directors as a Group (15 persons)	5,087,707		3,480,190		8,567,897	12.89%

* Represents beneficial ownership of less than 1% of Syros' outstanding common stock.

(1) FMR LLC, or FMR, and Abigail P. Johnson, a director, the chair and the chief executive officer of FMR, each report beneficially owning and having sole dispositive power over 5,797,876 of the shares listed herein. FMR reports sole voting power over 5,797,042 of the shares listed herein. Members of the Johnson family, including Ms. Johnson, are the predominant owners, directly or through trusts, of Series B voting common shares of FMR, representing 49% of the voting power of FMR. The Johnson family group and all other Series B shareholders have entered into a shareholders' voting agreement under which all Series B voting common shares will be voted in accordance with the majority vote of Series B voting common shares. Accordingly, through their ownership of voting common shares and the execution of the shareholders' voting agreement, members of the Johnson family may be deemed under the Investment Company Act of 1940, or the 1940 Act, to form a controlling group with respect to FMR. FMR has an address at 245 Summer Street, Boston, MA 02210. For information regarding FMR, Syros has relied, without independent investigation, on the Schedule 13G/A filed by FMR with the SEC on April 11, 2022.

(2) Bain Capital Life Sciences Fund II, L.P., or BCLS II, reports holding shared voting and dispositive power over 4,907,011 shares, and BCIP Life Sciences Associates, LP, or BCIPLS, and, together with BCLS II, the Bain Capital Life Science Entities) reports holding shared voting and dispositive power over 597,650 shares. Bain Capital Life Sciences Investors, LLC, or BCLSI, is the ultimate general partner of BCLS II and governs the investment strategy and decision-making process with respect to investments held by BCIPLS. As a result, BCLSI may be deemed to share voting and dispositive power with respect to the shares of common stock held by the Bain Capital Life Sciences Entities. The address of the Bain Capital Life

Sciences Entities is c/o Bain Capital Life Sciences, LP, 200 Clarendon Street, Boston, MA 02116. For information regarding the Bain Capital Life Science Entities, Syros has relied, without independent investigation, on the Schedule 13G/A filed by the Bain Capital Life Science Entities with the SEC on February 14, 2022.

(3) BCLS II owns warrants to purchase 1,114,286 shares of common stock (orpre-funded warrants in lieu thereof) and pre-funded warrants to purchase 891,429 shares of common stock, and BCIPLS owns warrants to purchase 135,714 shares of common stock (or pre-funded warrants in lieu thereof) and pre-funded warrants to purchase 108,571 shares of common stock. The Bain Capital Life Science Entities are prohibited from exercising such warrants and pre-funded warrants, if, as a result of such exercise, the Bain Capital Life Science Entities would beneficially own more than 9.99% of the total number of shares of common stock then issued and outstanding immediately after giving effect to the exercise. For information regarding the Bain Capital Life Science Entities, Syros has relied, without independent investigation, on the Schedule 13G/A filed by the Bain Capital Life Science Entities with the SEC on February 14, 2022.

(4) Ally Bridge MedAlpha Master Fund L.P., or Ally Bridge, reports holding shared voting and dispositive power with respect to all of the shares listed herein. Mr. Fan Yu is the sole shareholder of ABG Management Ltd., which is the sole member of Ally Bridge Group (NY) LLC, which manages Ally Bridge's investments. As such, each of the foregoing entities and Mr. Fan Yu may be deemed to share beneficial ownership of the shares held of record by Ally Bridge. Each of them disclaims any such beneficial ownership. The address of Ally Bridge is c/o Ally Bridge Group (NY) LLC, 430 Park Avenue, 12th Floor, New York, NY 10022. For information regarding Ally Bridge, Syros has relied, without independent investigation, on the Schedule 13G/A filed by Ally Bridge with the SEC on February 11, 2022.

(5) Ally Bridge owns warrants to purchase 390,625 shares of common stock (orpre-funded warrants in lieu thereof). For information regarding Ally Bridge, Syros has relied, without independent investigation, on the Schedule 13G/A filed by Ally Bridge with the SEC on February 11, 2022.

(6) Invus Public Equities, L.P., or Invus Public Equities, directly holds the 3,500,000 shares of common stock. Invus Public Equities Advisors, LLC, or Invus PE Advisors, as the general partner of Invus Public Equities, controls Invus Public Equities and, accordingly, may be deemed to beneficially own the shares held by Invus Public Equities. The Geneva branch of Artal International S.C.A, or Artal International, as the managing member of Invus PE Advisors, controls Invus PE Advisors, and, accordingly, may be deemed to beneficially own the shares that Invus PE Advisors may be deemed to beneficially own. Artal International Management S.A., or Artal International Management, as the managing partner of Artal International, controls Artal International and, accordingly, may be deemed to beneficially own the shares that Artal International may be deemed to beneficially own. Artal Group S.A., or Artal Group, as the sole stockholder of Artal International Management, controls Artal International Management and, accordingly, may be deemed to beneficially own the shares that Artal International Management may be deemed to beneficially own. Westend S.A., or Westend, as the parent company of Artal Group, controls Artal Group and, accordingly, may be deemed to beneficially own the shares that Artal Group may be deemed to beneficially own. Stichting Administratiekabntoor Westland, or Stichting, as the majority stockholder of Westend, controls Westend and, accordingly, may be deemed to beneficially own the shares that Westend may be deemed to beneficially own. Mr. Amaury Wittouck, or Mr. Wittouck, as the sole member of the board of the Stichting, controls the Stichting and, accordingly, may be deemed to beneficially own the shares that the Stichting may be deemed to beneficially own. The address for Invus Public Equities and Invus PE Advisors is 750 Lexington Avenue, 30th Floor, New York, NY 10022. The address for Artal International, Artal International Management, Artal Group, Westend and Mr. Wittouck is Valley Park, 44, Rue de la Vallée, L-2661, Luxembourg. The address for Stichting is Claude Debussylaan, 46, 1082 MD Amsterdam, The Netherlands. For information regarding Invus Public Equities, Invus PE Advisors, Artal International, Artal International Management, Artal Group, Westend, Stichting, and Mr. Wittouck, Syros has relied, without independent investigation, on the Schedule 13G filed by such parties with the SEC on February 11, 2022.

(7) Consists of (i) 692,723 shares of common stock held by Dr. Simonian, (ii) 80,000 shares of common stock held of record by the Douglas and Nancy Cole Family Trust f/b/o Bennett H. Cole, and (iii) 80,000 shares of common stock held of record by the Douglas and Nancy Cole Family Trust f/b/o William B. Cole.

(8) Consists of 1,899,616 shares owned by Samsara BioCapital, L.P., or Samsara LP. The general partner of Samsara LP is Samsara BioCapital GP, LLC, or Samsara LLC. The managers of Samsara LLC are Srinivas Akkaraju and Michael Dybbs. These individuals may be deemed to have shared voting and investment power of the shares held by Samsara LP and may be deemed to beneficially own certain shares held by Samsara LP. Dr. Akkaraju disclaims beneficial ownership of these shares, except to the extent of his pecuniary interest therein.

(9) Includes warrants to purchase 289,250 shares of common stock that are owned by Samsara LP and are currently exercisable. Dr. Akkaraju disclaims beneficial ownership of such warrants and the shares of common stock underlying them, except to the extent of his pecuniary interest therein.

(10) Consists of 1,538,333 shares of common stock held by Polaris Partners VII, L.P. and 48,320 shares of common stock held by Polaris Entrepreneurs' Fund VII, L.P. The general partner of Polaris Partners VII, L.P. and Polaris Entrepreneurs' Fund VII, L.P. is Polaris Management Co. VII, L.L.C., or Polaris Management, and Polaris Management may be deemed to have sole voting and investment power over such shares. Polaris Management disclaims beneficial ownership of these shares, except to the extent of its pecuniary interest therein. Amir Nashat, a managing member of Polaris Management, may be deemed to have voting and investment power over such shares. The address of such stockholders is One Marina Park Drive, 10th Floor, Boston, MA 02210. For information regarding Polaris Partners VII, L.P. Syros has relied, without independent investigation, on the Schedule 13D/A filed by Polaris Management with the SEC on February 14, 2019.

(11) Consists of (i) 146,666 shares of common stock held of record by Dr. Sharp, (ii) 40,000 shares of common stock held of record by Ann H. Sharp and Christine S. Carey, as Trustees of the Phillip A. Sharp 2008 Irrevocable Trust f/b/o Christine S. Carey, (iii) 40,000 shares of common stock held of record by Ann H. Sharp and Helena S. Gordon, as Trustees of the Phillip A. Sharp 2008 Irrevocable Trust f/b/o Helena H. Sharp, and (iv) 40,000 shares of common stock held of record by Ann H. Sharp and Sarah S. Brokaw, as Trustees of the Phillip A. Sharp 2008 Irrevocable Trust f/b/o Sara S. Brokaw.

PRINCIPAL STOCKHOLDERS OF TYME

As of July 1, 2022, Tyme had 172,206,894 shares of Tyme common stock outstanding. The following tables set forth certain information regarding the ownership of shares of Tyme's common stock as of the close of business on that date, by:

- each person known by Tyme to beneficially own more than 5% of the outstanding shares of each class of Tyme stock;
- each of the Tyme directors;
- each of the Tyme Named Executive Officers who currently serve in such roles; and
- all of the Tyme directors and executive officers as a group.

Beneficial ownership data below includes stock options and warrants that are exercisable within sixty days after July 1, 2022, or Currently Exercisable.

The following table sets forth certain information regarding the beneficial ownership of the Tyme common stock for each Tyme director and Named Executive Officer for fiscal year 2022 and all Tyme directors and executive officers of Tyme as a group. The number of shares of Tyme common stock beneficially owned is as of July 1, 2022.

	Amount and Nature of Beneficial Ownership		
Name and Address of Beneficial Owner	Tyme Common Stock Owned	Options Exercisable Within 60 Days of Record Date	Percentage
Tyme Named Executive Officers and Directors(1)			
Christine Baker	—	51,555	0.0%
James Biehl(2)	105,150	2,190,837	1.3%
David Carberry	100,000	353,000	0.3%
Richard Cunningham	—	1,082,875	0.6%
Donald W. DeGolyer	—	353,000	0.2%
Steve Hoffman(3)	20,022,566	—	11.6%
Douglas A. Michels(4)	110,000	348,833	0.3%
Frank L. Porfido(5)	10,000	206,048	0.1%
Dr. Gerald Sokol	5,865	353,000	0.2%
Timothy C. Tyson(6)	5,865	403,958	0.2%
All Tyme directors and executive officers as a group (twelve persons)(7),(8)	20,379,446	6,972,843	15.3%

(1) The address of each of the beneficial owners identified herein is 1 Pluckemin Way, Suite 103, Bedminster, NJ 07921.

(2) Includes 150 shares of Tyme common stock held indirectly by Mr. Biehl's spouse. Mr. Biehl also owns Currently Exercisable options to purchase 490,000 shares of Tyme common stock from each of Mr. Hoffman and Mr. Demurjian with an expiration date of March 2027. See footnote 3 hereto.

(3) Includes shares of Tyme common stock for which this holder possesses sole voting power, but which are subject to a Currently Exercisable (non-Tyme) option through which an executive officer, Mr. Biehl, may acquire 490,000 shares of Tyme common stock from Mr. Hoffman with an expiration date of March 2027. See footnote 2 hereto. Tyme and Mr. Hoffman also entered into a Voting Agreement dated March 24, 2022, pursuant to which Mr. Hoffman agreed to vote all shares of Tyme common stock beneficially owned by him in accordance with the Tyme's board of directors' recommendation with respect to any matter presented to the stockholders for a period of one year from the date of the agreement.

(4) Mr. Michels holds his Tyme common stock in a joint account with his spouse and, accordingly, shares voting and investment power over such shares of Tyme common stock.
(5) Frank Porfido joined Tyme as Chief Financial Officer on June 14, 2021.
(6) Mr. Tyson's spouse, as co-trustee of the Tyson Revocable Trust, shares voting and investment power over 5,865 shares of Tyme common stock held in a trust account.
(7) Shares of Tyme common stock owned by Mr. Hoffman subject to the option described in footnotes 2 and 3 are counted once as currently owned shares, and not double-counted as Currently Exercisable options for purposes of this calculation. As described in footnote 2, Mr. Biehl has another option through which he may acquire 490,000 shares of Tyme common stock from a non-affiliate Tyme stockholder with an expiration date of March 2027, which shares of Tyme common stock are included as Currently Exercisable options for purposes of this calculation.
(8) On July 3, 2022, each of the Tyme directors and officers, except Mr. Hoffman, entered into a Support Agreement with Syros and Tyme, in which each such director and executive officer agreed, to, among other things, vote all of the director or executive officer's shares of Tyme common stock owned as of the record date for the applicable stockholder meeting (i) in favor of the adoption of the proposals required for the merger, (ii) against any competing acquisition proposal, and (iii) against any proposal, action or agreement that would reasonably be expected to impede, interfere with, delay or postpone, prevent or otherwise impair the merger or the other transactions contemplated by the Merger Agreement.

The following table sets forth certain information regarding the beneficial ownership of Tyme common stock as of July 1, 2022 for each person known to Tyme who beneficially owns more than five percent of Tyme's outstanding common stock, the name and address of such beneficial owner and the percentage such shares comprise of the outstanding Tyme common stock, other than Mr. Hoffman, who is discussed in table directly above.

	Amount and Nature of Beneficial Ownership		
Name and Address of Beneficial Owner	Tyme Common Stock Owned	Options Exercisable Within 60 Days of Record Date	Percentage
Michael Demurjian(1) 157 Broad Street, Suite 304 Red Bank, NJ 07701	23,048,846	472,222	13.6%
Eagle Pharmaceuticals, Inc.(2) 50 Tice Boulevard, Suite 315 Woodcliff Lake, NJ 07677	10,000,000	—	5.8%
Tyme Technologies, Inc.(3) 1 Pluckemin Way, Suite 103 Bedminster, NJ 07921	43,071,412	472,222	25.2%

(1) Based on a Schedule 13G/A filed with the SEC on February 14, 2020 by Michael Demurjian, reflecting holdings as of January 7, 2020, Mr. Demurjian's Form 4 filed on June 28, 2021, as well as the Tyme's records subsequent those dates. Mr. Demurjian's ownership includes 490,000 shares of Tyme common stock for which this holder possesses sole voting power, but which are subject to a currently exercisable (non-Company) option through which Mr. Biehl may acquire such shares of Tyme common stock. As noted in footnote 7 to the table directly above, these shares of Tyme common stock are also reflected as Currently Exercisable options for purposes of the calculation of beneficial ownership of Tyme's directors and officers as a group. Additionally, on April 18, 2022, Tyme and Michael Demurjian entered into a Voting Agreement, pursuant to which Mr. Demurjian agreed to vote all shares of Tyme common stock beneficially owned by him in accordance with the Tyme's board of directors' recommendation with respect to any matter presented to Tyme's stockholders for a period of two years from the date of the agreement.
(2) Based on a Schedule 13G filed with the SEC on January 17, 2020, by Eagle reflecting holdings as of January 7, 2020. Tyme issued and sold these shares of Tyme common stock to Eagle pursuant to a

Securities Purchase Agreement, dated January 7, 2020. On July 3, 2022, Eagle entered into a Support Agreement with Syros and Tyme, in which it agreed, to, among other things, vote all of its shares of Tyme common stock that it owns as of the record date for the applicable stockholder meeting (i) in favor of the adoption of the proposals required for the merger, (ii) against any competing acquisition proposal, and (iii) against any proposal, action or agreement that would reasonably be expected to impede, interfere with, delay or postpone, prevent or otherwise impair the merger or the other transactions contemplated by the Merger Agreement.

(3) Consists of (i) 20,022,566 shares of common stock owned by Steve Hoffman and (ii) 23,048,846 shares of common stock and options to acquire 472,222 shares of common stock owned by Michael Demurjian. Each of Mr. Hoffman and Mr. Demurjian has entered into separate voting agreements with Tyme pursuant to which he has agreed to vote all shares of Tyme common stock beneficially owned by him in accordance with Tyme's board of directors' recommendation with respect to any matter presented to Tyme's stockholders. As a result of such voting agreement, Tyme may be deemed to have beneficial ownership of these shares. Tyme has no investment discretion over the shares beneficially owned by Mr. Hoffman or Mr. Demurjian and disclaims beneficial ownership of these shares.

PRINCIPAL STOCKHOLDERS OF THE COMBINED COMPANY

The following table sets forth information regarding the beneficial ownership of shares of Syros' common stock immediately after the closing of the PIPE Financing and the consummation of the merger by:

- each person or "group" (as such term is used in Section 13(d)(3) of the Exchange Act) known by Syros to be the beneficial owner of more than 5% of shares of Syros' common stock upon the closing of the PIPE Financing and the consummation of the merger;
- each person who will be an executive officer or director of the combined company upon the closing of the PIPE Financing and the consummation of the merger; and
- all executive officers and directors of the combined company as a group upon the closing of the PIPE Financing and the consummation of the merger.

Based on 62,989,020 shares of Syros common stock outstanding on June 30, 2022, and giving effect to the issuance of (i) 63,871,778 shares of Syros common stock (and, in lieu of shares of Syros common stock to certain investors, 74,267,400 Pre-Funded PIPE Warrants) and, in each case, accompanying PIPE Warrants to purchase an aggregate of up to 138,139,178 additional shares of Syros common stock (or Pre-Funded PIPE Warrants to purchase common stock in lieu thereof) in connection with the PIPE Financing, and (ii) an assumed 74,255,612 shares of Syros common stock to be issued in connection with the merger, based on an estimated exchange ratio of 0.4312, it is estimated that there will be 201,116,410 shares of Syros common stock issued and outstanding immediately following the closing of the PIPE Financing and the consummation of the merger. The following table does not reflect any adjustments to the merger consideration. If the actual facts are different from the foregoing assumptions, ownership figures in the combined company in the table that follows will be different.

The following table does not reflect beneficial ownership of any shares of Syros common stock issuable upon exercise of the accompanying PIPE Warrants issued in the PIPE Financing, as such securities are not exercisable within 60 days of June 30, 2022.

Unless otherwise indicated, Syros believes that all persons named in the table below have sole voting and investment power with respect to the voting securities beneficially owned by them.

Name of Beneficial Owner	Shares of Common Stock Beneficially Owned	+	Common Stock Underlying Options and Other Rights Acquirable Within 60 Days	=	Total Beneficial Ownership	
					Shares Beneficially Owned	Percentage of Shares Beneficially Owned
5% Stockholders						
Entities affiliated with Flagship Pioneering	9,938,494(1)		14,200,000(2)		24,138,494	11.21%
Entities affiliated with Avidity Partners	9,000,000(3)		12,200,000(4)		21,200,000	9.94%
Entities affiliated with Bain Capital Life Sciences, L.P.	10,824,061(5)		7,569,400(6)		18,393,461	8.81%
Deep Track Biotechnology Master Fund, Ltd.	—		15,950,000(7)		15,950,000	7.35%
Entities affiliated with Invus Public Equities, L.P.	14,128,297(8)		—		14,128,297	7.03%
Named Executive Officers and Directors						
Nancy Simonian, M.D.	852,723(9)		1,238,054		2,090,777	1.03%
Jason Haas	—		—		—	*
David A. Roth, M.D.	59,719		527,115		586,834	*
Srinivas Akkaraju, M.D., Ph.D.	8,814,509(10)		368,250(11)		9,182,759	4.56%
Mark J. Alles	10,000		66,110		76,110	*
Deborah Dunsire, M.D.	—		10,692		10,692	*
S. Gail Eckhardt, M.D.	—		39,860		39,860	*
Marsha H. Fanucci	—		104,666		104,666	*
Amir Nashat, Ph.D.	1,586,653(12)		90,000		1,676,653	*
Phillip A. Sharp, Ph.D.	266,666(13)		132,857		399,523	*
Peter Wirth	—		79,000		79,000	*
Richard A. Young, Ph.D.	321,711		90,000		411,711	*
All Current Executive Officers and Directors as a Group (15 persons)	12,002,600		3,480,190		15,482,790	7.57%

* Represents beneficial ownership of less than 1% of Syros' outstanding common stock.

(1) Includes 213,332 shares of common stock held by Flagship VentureLabs IV, LLC, or Flagship VentureLabs, 2,165,908 shares of common stock held by Flagship Ventures Fund IV, L.P., or Flagship Fund IV, and 559,254 shares of common stock held by Flagship Ventures Fund IV-Rx, L.P., or Flagship Fund IV-Rx" and together with Flagship VentureLabs and Flagship IV, the Flagship Funds, along with 7,000,000 shares of common stock to be issued in the PIPE Financing to Flagship Pioneering Fund VII, L.P. Flagship Fund IV is a member of Flagship VentureLabs and also serves as its manager. The general partner of each of Flagship Fund IV and Flagship Fund IV-Rx is Flagship Ventures Fund IV General Partner LLC, or Flagship Fund IV GP. Noubar B. Afeyan, Ph.D. and Edwin M. Kania, Jr. are the managers of Flagship Fund IV GP. While Mr. Kania is retired from Flagship Pioneering, Inc., or Pioneering, he continues to serve as a manager of Flagship Fund IV GP. Flagship Fund IV GP and each of these individuals may be deemed to share voting, investment and dispositive power with respect to all shares held by the Flagship Funds. Each of the foregoing persons disclaims beneficial ownership of the shares except to the extent of any pecuniary interest therein. The address of such stockholder is 55 Cambridge Parkway, Suite 800E, Cambridge, Massachusetts 02142. For information regarding the Flagship Funds, Syros and Tyme have relied on the Schedule 13D/A filed by the Flagship Funds with the SEC on August 21, 2017, the Form 13F filed by Pioneering with the SEC on February 13, 2020, and information provided to Syros and Tyme by representatives of Pioneering.

(2) Consists of shares of common stock issuable upon the exercise ofPre-Funded PIPE Warrants to be issued upon the completion of the PIPE Financing to Flagship Pioneering Fund VII, L.P.

(3) Consists of 3,319,700 shares of common stock issuable to Avidity Master Fund LP, 409,400 shares of common stock issuable to Avidity Master Fund LP, 305,600 shares of common stock issuable to Avidity Capital HL Sub Fund III LLC, and 4,965,300 shares of common stock issuable to Avidity Private Master Fund LP, in each case, upon the completion of the PIPE Financing.

(4) Consists of 4,500,000 shares of common stock issuable to Avidity Master Fund LP, 555,000 shares of common stock issuable to Avidity Master Fund LP, 414,200 shares of common stock issuable to Avidity Capital HL Sub Fund III LLC, and 6,730,800 shares of common stock issuable to Avidity Private Master Fund LP, in each case, upon the exercise of Pre-Funded PIPE Warrants to be issued upon the completion of the PIPE Financing.

(5) Bain Capital Life Sciences Fund II, L.P., or BCLS II, reports holding shared voting and dispositive power over 4,907,011 shares, and BCIP Life Sciences Associates, LP, or BCIPLS, and, together with BCLS II, the Bain Capital Life Science Entities, reports holding shared voting and dispositive power over 597,650 shares. In addition, BCLS II Equity Opportunities, LP will be issued 5,319,400 shares of common stock upon the completion of the PIPE Financing. Bain Capital Life Sciences Investors, LLC, or BCLSI, is the ultimate general partner of BCLS II and governs the investment strategy and decision-making process with respect to investments held by BCIPLS. As a result, BCLSI may be deemed to share voting and dispositive power with respect to the shares of common stock held by the Bain Capital Life Sciences Entities. The address of the Bain Capital Life Sciences Entities is c/o Bain Capital Life Sciences, LP, 200 Clarendon Street, Boston, MA 02116. For information regarding the Bain Capital Life Science Entities, Syros and Tyme have relied, without independent investigation, on the Schedule 13G/A filed by the Bain Capital Life Science Entities with the SEC on February 14, 2022.

(6) BCLS II owns warrants to purchase 1,114,286 shares of common stock (orpre-funded warrants in lieu thereof) and pre-funded warrants to purchase 891,429 shares of common stock, and BCIPLS owns warrants to purchase 135,714 shares of common stock (or pre-funded warrants in lieu thereof) and pre-funded warrants to purchase 108,571 shares of common stock, whichpre-funded warrants were issued in December 2020. In addition, BCLS II Equity Opportunities, LP will be issued Pre-Funded PIPE Warrants to purchase 5,319,400 shares of common stock upon the completion of the PIPE Financing. The Bain Capital Life Science Entities are prohibited from exercising such warrants and pre-funded warrants, if, as a result of such exercise, the Bain Capital Life Science Entities would beneficially own more than 9.99% of the total number of shares of common stock then issued and outstanding immediately after giving effect to the exercise. For information regarding the Bain Capital Life Science Entities, Syros and Tyme have relied, without independent investigation, on the Schedule 13G/A filed by the Bain Capital Life Science Entities with the SEC on February 14, 2022.

(7) Consists of shares of common stock issuable upon the exercise ofPre-Funded PIPE Warrants to be issued upon the completion of the PIPE Financing.

(8) Invus Public Equities, L.P., or Invus Public Equities, directly holds 3,500,000 shares of common stock. In addition, Invus Public Equities, L.P. will be issued 10,638,297 shares of common stock upon the completion of the PIPE Financing. Invus Public Equities Advisors, LLC, or Invus PE Advisors, as the general partner of Invus Public Equities, controls Invus Public Equities and, accordingly, may be deemed to beneficially own the shares held by Invus Public Equities. The Geneva branch of Artal International S.C.A, Artal International, as the managing member of Invus PE Advisors, controls Invus PE Advisors, and, accordingly, may be deemed to beneficially own the shares that Invus PE Advisors may be deemed to beneficially own. Artal International Management S.A., or Artal International Management, as the managing partner of Artal International, controls Artal International and, accordingly, may be deemed to beneficially own the shares that Artal International may be deemed to beneficially own. Artal Group S.A., or Artal Group, as the sole stockholder of Artal International Management, controls Artal International Management and, accordingly, may be deemed to beneficially own the shares that Artal International Management may be deemed to beneficially own. Westend S.A., or Westend, as the parent company of Artal Group, controls Artal Group and, accordingly, may be deemed to beneficially own the shares that Artal Group may be deemed to beneficially own. Stichting Administratiekabntoor Westland, Stichting, as the majority stockholder of

Westend, controls Westend and, accordingly, may be deemed to beneficially own the shares that Westend may be deemed to beneficially own. Mr. Amaury Wittouck, or Mr. Wittouck, as the sole member of the board of the Stichting, controls the Stichting and, accordingly, may be deemed to beneficially own the shares that the Stichting may be deemed to beneficially own. The address for Invus Public Equities and Invus PE Advisors is 750 Lexington Avenue, 30th Floor, New York, NY 10022. The address for Artal International, Artal International Management, Artal Group, Westend and Mr. Wittouck is Valley Park, 44, Rue de la Vallée, L-2661, Luxembourg. The address for Stichting is Claude Debussylaan, 46, 1082 MD Amsterdam, The Netherlands. For information regarding Invus Public Equities, Invus PE Advisors, Artal International, Artal International Management, Artal Group, Westend, Stichting, and Mr. Wittouck, Syros and Tyme have relied, without independent investigation, on the Schedule 13G filed by such parties with the SEC on February 11, 2022.

(9) Consists of (i) 692,723 shares of common stock held by Dr. Simonian, (ii) 80,000 shares of common stock held of record by the Douglas and Nancy Cole Family Trust f/b/o Bennett H. Cole, and (iii) 80,000 shares of common stock held of record by the Douglas and Nancy Cole Family Trust f/b/o William B. Cole.

(10) Consists of 1,899,616 shares owned by Samsara BioCapital, L.P., or Samsara LP, and 6,914,893 shares of common stock issuable to Samsara LP upon the completion of the PIPE Financing. The general partner of Samsara LP is Samsara BioCapital GP, LLC, or Samsara LLC. The managers of Samsara LLC are Srinivas Akkaraju and Michael Dybbs. These individuals may be deemed to have shared voting and investment power of the shares held by Samsara LP and may be deemed to beneficially own certain shares held by Samsara LP. Dr. Akkaraju disclaims beneficial ownership of these shares, except to the extent of his pecuniary interest therein.

(11) Includes warrants to purchase 289,250 shares of common stock that are owned by Samsara LP and are currently exercisable. Dr. Akkaraju disclaims beneficial ownership of such warrants and the shares of common stock underlying them, except to the extent of his pecuniary interest therein.

(12) Consists of 1,538,333 shares of common stock held by Polaris Partners VII, L.P. and 48,320 shares of common stock held by Polaris Entrepreneurs' Fund VII, L.P. The general partner of Polaris Partners VII, L.P. and Polaris Entrepreneurs' Fund VII, L.P. is Polaris Management Co. VII, L.L.C., or Polaris Management, and Polaris Management may be deemed to have sole voting and investment power over such shares. Polaris Management disclaims beneficial ownership of these shares, except to the extent of its pecuniary interest therein. Amir Nashat, a managing member of Polaris Management, may be deemed to have voting and investment power over such shares. The address of such stockholders is One Marina Park Drive, 10th Floor, Boston, MA 02210. For information regarding Polaris Partners VII, L.P. Syros and Tyme have relied, without independent investigation, on the Schedule 13D/A filed by Polaris Management with the SEC on February 14, 2019.

(13) Consists of (i) 146,666 shares of common stock held of record by Dr. Sharp, (ii) 40,000 shares of common stock held of record by Ann H. Sharp and Christine S. Carey, as Trustees of the Phillip A. Sharp 2008 Irrevocable Trust f/b/o Christine S. Carey, (iii) 40,000 shares of common stock held of record by Ann H. Sharp and Helena S. Gordon, as Trustees of the Phillip A. Sharp 2008 Irrevocable Trust f/b/o Helena H. Sharp, and (iv) 40,000 shares of common stock held of record by Ann H. Sharp and Sarah S. Brokaw, as Trustees of the Phillip A. Sharp 2008 Irrevocable Trust f/b/o Sara S. Brokaw.

LEGAL MATTERS

Wilmer Cutler Pickering Hale and Dorr LLP will pass upon the validity of Syros common stock offered by this joint proxy statement/prospectus.

EXPERTS

The consolidated financial statements of Syros Pharmaceuticals, Inc. at December 31, 2021 and 2020, and for each of the three years in the period ended December 31, 2021, included in this joint proxy statement/prospectus, have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their report appearing elsewhere herein, and are included in reliance upon such report given on the authority of such firm as experts in accounting and auditing.

The consolidated financial statements of Tyme Technologies, Inc. at March 31, 2022 and 2021, and for each of the two years in the period ended March 31, 2022, included in this joint proxy statement/prospectus, have been audited by Grant Thornton LLP, independent registered public accounting firm, as set forth in their report appearing elsewhere herein, and are included in reliance upon such report given on the authority of such firm as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

This joint proxy statement/prospectus incorporates documents by reference which are not presented in or delivered with this joint proxy statement/prospectus. Syros stockholders and Tyme stockholders should rely only on the information contained in this joint proxy statement/prospectus and in the documents that Syros and Tyme have incorporated by reference into this joint proxy statement/prospectus. Syros and Tyme have not authorized anyone to provide Syros stockholders or Tyme stockholders with information that is different from or in addition to the information contained in this document or incorporated by reference into this joint proxy statement/prospectus.

Syros and Tyme are subject to the informational requirements of the Exchange Act and in accordance therewith, files annual, quarterly and current reports, proxy statements and other information with the SEC electronically, and the SEC maintains a website that contains Syros' and Tyme's filings as well as reports, proxy and information statements, and other information issuers file electronically with the SEC at *www.sec.gov*. In addition, you may obtain free copies of the documents Syros files with the SEC, including the registration statement on Form S-4, of which this joint proxy statement/prospectus forms a part, by going to Syros' Internet website at www.Syros.com, and you may obtain free copies of the documents Tyme files with the SEC by going to Tyme's Internet website at www.tymeinc.com. The Internet website addresses of Syros and Tyme are provided as inactive textual references only. The information provided on the Internet websites of Syros and Tyme, other than copies of the documents that have been filed with the SEC, is not part of this joint proxy statement/prospectus and, therefore, is not incorporated herein by reference.

Syros has supplied all the information contained in this joint proxy statement/prospectus relating to Syros, and Tyme has supplied all information contained in this joint proxy statement/prospectus relating to Tyme.

You may request a copy of this joint proxy statement/prospectus or any of the documents incorporated by reference into this joint proxy statement/prospectus without charge. If you would like to request documents from Syros or Tyme, please send a request in writing or by telephone to either Syros or Tyme at the following addresses:

Syros Pharmaceuticals, Inc.
35 CambridgePark Drive, 4th Floor
Cambridge, Massachusetts 02140
Attention: Corporate Secretary
Telephone: (617) 744-1340

Tyme Technologies, Inc.
1 Pluckemin Way—Suite 103
Bedminster, New Jersey 07921
Attention: Corporate Secretary
Telephone: (212) 461-2315
Email: investorrelations@tymeinc.com

TRADEMARK NOTICE

"Syros" and Syros' logo™ are trademarks of Syros Pharmaceuticals, Inc. in the United States. Tyme Technologies, Inc.'s trademark portfolio consists of one domestic trademark: CMBT (cancer metabolism-based therapies). Other third-party logos and product/trade names are registered trademarks or trade names of their respective companies.

OTHER MATTERS

Delinquent Section 16(a) Reports

Section 16(a) of the Exchange Act requires Syros' and Tyme's executive officers, directors and persons who own more than 10% of Syros common stock and Tyme common stock, respectively, to file reports of ownership and reports of changes in ownership of common stock and other equity securities of Syros or Tyme, as applicable, with the SEC. Executive officers, directors and greater than 10% stockholders are required by SEC regulations to furnish Syros or Tyme, as applicable, with copies of all Section 16(a) forms they file.

To Syros' knowledge, based solely on a review of the copies of reports furnished to Syros, Syros believes that during the year ended December 31, 2021, Syros' executive officers, directors and greater than 10% stockholders complied with all Section 16(a) filing requirements.

Based solely on (i) Tyme's review of reports submitted to it during and with respect to the year ended March 31, 2022, filed with the SEC pursuant to Section 16(a) of the Exchange Act, including any amendment thereto and (ii) written representations of its directors, executive officers and certain beneficial owners of more than 10% of Tyme's common stock, Tyme believes that, with the following exceptions, all reports required to be filed under Section 16(a) of the Exchange Act, with respect to transactions in Tyme's equity securities through March 31, 2022, were filed on a timely basis, except for the initial statement of beneficial ownership of Dr. Van Tornout, who was Tyme's acting Chief Medical Officer during fiscal year 2022, but whose employment ended on June 23, 2022, upon his appointment on April 1, 2021 and three stock purchases by Dr. Van Tornout on April 5, 6, and 7, 2021 totaling 1,809 shares of Common Stock, all of which were reported on April 14, 2021, a stock purchase of 7,022 shares of Tyme common stock by Dr. Van Tornout on February 17, 2022 which was reported on February 22, 2022, and a sale of 9,380 shares of Tyme common stock by Michael Demurjian on November 22, 2021, which was reported on November 29, 2021.

More Information About Syros Stockholder Proposals

Stockholder Proposals Included in Proxy Statement

In order to be considered for inclusion in Syros' proxy statement and proxy card relating to Syros' 2023 annual meeting of stockholders, stockholder proposals must be received by Syros no later than December 22, 2022, which is 120 days prior to the first anniversary of the mailing date of Syros' definitive proxy statement in connection with its 2022 annual meeting of stockholders, unless the date of the 2023 annual meeting of stockholders is changed by more than 30 days from the anniversary of Syros' 2022 annual meeting, in which case, the deadline for such proposals will be a reasonable time before Syros begins to print and send its proxy materials. Upon receipt of any such proposal, Syros will determine whether or not to include such proposal in the proxy statement and proxy card in accordance with regulations governing the solicitation of proxies.

Stockholder Proposals Not Included in Proxy Statement

In addition, Syros' amended and restated by-laws establish an advance notice procedure for nominations for election to Syros' board of directors and other matters that stockholders wish to present for action at an annual meeting other than those to be included in Syros' proxy statement. In general, Syros must receive other proposals of stockholders (including director nominations) intended to be presented at the 2023 annual meeting of stockholders but not included in the proxy statement by March 3, 2023, but not before February 1, 2023, which is not less than 90 days nor more than 120 days prior to the anniversary date of the immediately preceding annual meeting. However, if the date of the annual meeting is more than 30 days before or more than 60 days after such anniversary date, notice must be received no earlier than the close of business 120 calendar days prior to such annual meeting and no later than the close of business on the later of 90 days prior to such annual meeting and 10 days following the day on which notice of the date of such annual meeting was mailed or public

announcement of the date of such annual meeting was first made. If the stockholder fails to give notice by these dates, then the persons named as proxies in the proxies solicited by the board of directors for the 2023 annual meeting of stockholders may exercise discretionary voting power regarding any such proposal. Stockholders are advised to review Syros' amended and restated by-laws which also specify requirements as to the form and content of a stockholder's notice.

Any proposals, notices or information about proposed director candidates should be sent to Syros Pharmaceuticals, Inc., Attention: Nominating and Corporate Governance Committee, 35 CambridgePark Drive, 4th Floor, Cambridge, Massachusetts 02140.

Stockholder Communication with the Syros Board

Syros' board of directors will give appropriate attention to written communications that are submitted by stockholders and will respond if and as appropriate. The chair of the board of directors is primarily responsible for monitoring communications from stockholders and for providing copies or summaries to the other directors as he considers appropriate.

Communications are forwarded to all directors if they relate to important substantive matters and include suggestions or comments that the chair of the board considers to be important for the directors to know. In general, communications relating to corporate governance and corporate strategy are more likely to be forwarded than communications relating to ordinary business affairs, personal grievances and matters as to which Syros receives repetitive or duplicative communications.

Stockholders who wish to send communications on any topic to Syros' board of directors should address such communications to Syros Pharmaceuticals, Inc., Attention: Board of Directors, 35 CambridgePark Drive, 4th Floor, Cambridge, Massachusetts 02140.

More Information About Tyme Stockholder Proposals

Stockholder Proposals Included in Proxy Statement

Because Tyme does not expect to hold an annual meeting of stockholders within 30 days of the anniversary of its 2021 annual meeting of stockholders, Tyme intends to provide notice, in a quarterly report on Form 10-Q or current report on Form 8-K, of the meeting date and record date for such meeting when those dates have been determined by Tyme's board of directors. In that notice, Tyme will also provide notice of the deadline for receipt of any stockholder proposals submitted pursuant to Rule 14a-8 under the Exchange Act for inclusion in Tyme's proxy materials for the next annual meeting of stockholders, which deadline will be a date determined to be a reasonable time before Tyme prints and mails its proxy materials. Any such stockholder proposal must be in writing, comply with the proxy rules of the SEC, and be sent to: Tyme Technologies, Inc., 1 Pluckemin Way, Suite 103, Bedminster, NJ 07921, Attention: Corporate Secretary.

When the meeting date and record date for the next annual meeting of stockholders have been determined by Tyme's board of directors, Tyme will also provide notice of the date by which proposals of stockholders made outside of Rule 14a-8 of the Exchange Act must be received by Tyme to be considered at such annual meeting. Any such proposal must also comply with Tyme's Amended and Restated By-laws, or Tyme's By-Laws, and other applicable laws. Tyme's By-Laws provide that, to bring a proposal other than the nomination of a director before an annual meeting of stockholders, a stockholder's notice of proposal must include: (i) a brief description of the business desired to be brought before the annual meeting and the reasons for conducting such business at the annual meeting, (ii) the text of the proposal or business (including the exact text of any resolutions proposed for consideration and, in the event that such business includes a proposal to amend the By-Laws, the exact text of the proposed amendment), (iii) a description of any material interest of such stockholder or such beneficial owner and the respective affiliates and associates of, or others acting in concert with, such stockholder or such

beneficial owner in such business, (iv) any other information relating to such stockholder and such beneficial owner, that would be required to be disclosed in a proxy statement or other filings required to be made in connection with solicitations of proxies for the proposal and pursuant to and in accordance with Regulation 14A of the Exchange Act and (v) the other information described in Article II, Section 9(b) of Tyme's By-Laws.

Tyme Director Nominations

When the meeting date and record date for the next annual meeting of stockholders have been determined by Tyme's board of directors, Tyme will also provide notice of the date by which stockholder nominations for election as director at such annual meeting of stockholders must be received. Any such nomination must also comply with Tyme's By-Laws and other applicable laws. Tyme's By-Laws provide that, for a nomination to be properly brought before an annual meeting, the Tyme stockholder's notice of nomination must include: (i) the name, age, business address and, if known, residence address of each proposed nominee, (ii) the principal occupation or employment of each such nominee, (iii) the class and number of shares of Tyme Common Stock that are, directly or indirectly, owned, beneficially or of record, by each nominee, (iv) a description of all direct and indirect compensation and other material monetary agreements, arrangements and understandings during the past three years, and any other material relationships between or among (x) the stockholder, the beneficial owner, if any, on whose behalf the nomination is being made and the respective affiliates of, or others acting in concert with, such stockholder and such beneficial owner, on the one hand, and (y) each proposed nominee, and his or her respective affiliates and associates, or others acting in concert with such nominee(s) on the other hand, including all information that would be required to be disclosed pursuant to Item 404 of Regulation S-K if the stockholder making the nomination and any beneficial owner on whose behalf the nomination is made or any affiliate or associate thereof or person acting in concert therewith were the registrant for purposes of such Item 404 and the proposed nominee were a director or executive officer of such registrant, (v) such other information concerning each nominee that is required to be disclosed in solicitations for proxies for election of directors pursuant to Regulation 14A under the Exchange Act or applicable law, (vi) the written consent of the nominee to serve as a director if elected, and (vii) the other information as specified in Article II, Section 10(b) of our By-Laws, including in regards of the proposing stockholder and the beneficial owner, if any, on whose behalf the nomination is made.

In addition to a stockholder's ability to nominate candidates to serve on the board, stockholders may recommend candidates to the Nominating and Corporate Governance Committee for consideration. The committee will consider recommendations from stockholders regarding director nominee candidates that are received in writing and accompanied by sufficient information to enable the committee to assess the candidate's qualifications, along with confirmation of the candidate's consent to serve as a director if elected. Such recommendations should be sent to our Corporate Secretary at our headquarters. Any recommendation received from a stockholder after March 31 of any year is not assured of being considered for nomination in that year.

Communications with the Tyme Board

Any proposals, notices or information about proposed director candidates should be sent to Tyme Technologies, Inc., 1 Pluckemin Way, Suite 103, Bedminster, NJ 07921, Attention: Corporate Secretary.

Tyme stockholders should understand, however, that if the merger is completed, Tyme will become a subsidiary of Syros upon the completion of the merger in accordance with the Merger Agreement, shares of Tyme common stock will be exchanged for shares of Syros common stock and these proposal and nominee processes will have no further impact.

Householding of Joint Proxy Statement/Prospectus

The SEC has adopted rules that permit companies and intermediaries (e.g., brokers) to satisfy the delivery requirements for Notices of Internet Availability of Proxy Materials or other meeting materials with respect to

two or more stockholders sharing the same address by delivering a single proxy materials or other meeting materials addressed to those stockholders. This process, which is commonly referred to as "householding," potentially means extra convenience for stockholders and cost savings for companies. Some brokers household proxy materials, delivering a single proxy statement or notice to multiple stockholders sharing an address unless contrary instructions have been received from the affected stockholders. Once you have received notice from your broker that they will be householding materials to your address, householding will continue until you are notified otherwise or until you revoke your consent. If, at any time, you no longer wish to participate in householding and would prefer to receive a separate proxy statement or notice, or if your household is receiving multiple copies of these documents and you wish to request that future deliveries be limited to a single copy, please notify your broker.

Requests for additional copies of this joint proxy statement/prospectus should be directed to, as applicable:

Syros Pharmaceuticals, Inc.
35 CambridgePark Drive, 4th Floor
Cambridge, Massachusetts 02140
Attention: Corporate Secretary
Telephone: (617) 744-1340

Tyme Technologies, Inc.
1 Pluckemin Way—Suite 103
Bedminster, New Jersey 07921
Attention: Corporate Secretary
Telephone: (212) 461-2315
Email: investorrelations@tymeinc.com

*****

INDEX TO FINANCIAL STATEMENTS

SYROS PHARMACEUTICALS, INC.

TYME TECHNOLOGIES, INC.

SYROS PHARMACEUTICALS, INC.
CONDENSED CONSOLIDATED BALANCE SHEETS
(in thousands, except share and per share data)
(unaudited)

	March 31, 2022	December 31, 2021
Assets		
Current assets:		
Cash and cash equivalents	$ 69,575	$ 92,302
Marketable securities	40,686	38,067
Contract assets	3,182	2,979
Prepaid expenses and other current assets	3,034	3,237
Total current assets	116,477	136,585
Property and equipment, net	12,554	12,844
Marketable securities—noncurrent	2,638	13,038
Other long-term assets	3,155	2,941
Restricted cash	3,086	3,086
Right-of-use asset—operating lease	13,900	14,104
Right-of-use assets—financing leases	271	337
Total assets	$ 152,081	$ 182,935
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 2,841	$ 3,692
Accrued expenses	13,249	15,624
Deferred revenue	7,773	10,181
Financing lease obligations, current portion	274	291
Operating lease obligation, current portion	1,789	1,720
Debt, current portion	1,667	—
Total current liabilities	27,593	31,508
Financing lease obligations, net of current portion	12	65
Operating lease obligation, net of current portion	22,378	22,858
Warrant liability	581	3,029
Debt, net of debt discount, long term	38,775	40,257
Commitments and contingencies (See Note 10)		
Stockholders' equity:		
Preferred stock, $0.001 par value; 10,000,000 shares authorized at March 31, 2022 and December 31, 2021; 0 shares issued and outstanding at March 31, 2022 and December 31, 2021	—	—
Common stock, $0.001 par value; 200,000,000 shares authorized at March 31, 2022 and December 31, 2021; 62,801,296 and 62,024,035 shares issued and outstanding at March 31, 2022 and December 31, 2021, respectively	61	61
Additional paid-in capital	551,679	548,815
Accumulated other comprehensive loss	(273)	(79)
Accumulated deficit	(488,725)	(463,579)
Total stockholders' equity	62,742	85,218
Total liabilities and stockholders' equity	$ 152,081	$ 182,935

See accompanying notes to unaudited condensed consolidated financial statements.

SYROS PHARMACEUTICALS, INC.
CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS
(in thousands, except share and per share data)
(unaudited)

	Three Months Ended March 31,	
	2022	2021
Revenue	$ 5,467	$ 4,827
Operating expenses:		
Research and development	25,171	20,029
General and administrative	6,949	5,739
Total operating expenses	32,120	25,768
Loss from operations	(26,653)	(20,941)
Interest income	35	10
Interest expense	(976)	(967)
Change in fair value of warrant liability	2,448	7,670
Net loss applicable to common stockholders	$ (25,146)	$ (14,228)
Net loss per share applicable to common stockholders—basic and diluted	$ (0.40)	$ (0.23)
Weighted-average number of common shares used in net loss per share applicable to common stockholders—basic and diluted	63,061,423	61,379,641

See accompanying notes to unaudited condensed consolidated financial statements.

SYROS PHARMACEUTICALS, INC.
CONDENSED CONSOLIDATED STATEMENTS OF COMPREHENSIVE LOSS
(in thousands)
(unaudited)

	Three Months Ended March 31,	
	2022	2021
Net loss	$(25,146)	$ (14,228)
Other comprehensive loss:		
Unrealized holding loss on marketable securities	(194)	—
Comprehensive loss	$(25,340)	$ (14,228)

See accompanying notes to unaudited condensed consolidated financial statements.

SYROS PHARMACEUTICALS, INC.
CONDENSED CONSOLIDATED STATEMENTS OF STOCKHOLDER'S EQUITY
For the three months ended March 31, 2022 and 2021
(in thousands, except share data)
(unaudited)

	Common Stock			Accumulated		
	Number of Shares	Par Value	Additional Paid-In Capital	Other Comprehensive Gain (Loss)	Accumulated Deficit	Stockholders' Equity
Balance at December 31, 2020	56,222,746	$ 56	$467,518	$ —	$ (377,021)	$ 90,553
Exercise of stock options	20,134	—	157	—	—	157
Vesting of restricted stock units	206,762	—	—	—	—	—
Stock-based compensation expense	—	—	2,930	—	—	2,930
Issuance of common stock at-the-market, net of issuance costs of $5,132	5,400,000	5	70,463	—	—	70,468
Net loss	—	—	—	—	(14,228)	(14,228)
Balance at March 31, 2021	61,849,642	$ 61	$541,068	$ —	$ (391,249)	$ 149,880
Balance at December 31, 2021	62,024,035	$ 61	$548,815	$ (79)	$ (463,579)	$ 85,218
Exercise of stock options	37,700	—	1	—	—	1
Vesting of restricted stock units	739,561	—	—	—	—	—
Stock-based compensation expense	—	—	2,863	—	—	2,863
Other comprehensive loss	—	—	—	(194)	—	(194)
Net loss	—	—	—	—	(25,146)	(25,146)
Balance at March 31, 2022	62,801,296	$ 61	$551,679	$ (273)	$ (488,725)	$ 62,742

SYROS PHARMACEUTICALS, INC.
CONDENSED CONSOLIDATED STATEMENTS OF CASH FLOWS
(in thousands)
(unaudited)

	Three Months Ended March 31,	
	2022	2021
Operating activities		
Net loss	$(25,146)	$ (14,228)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	681	666
Amortization of right-of-use asset	66	65
Stock-based compensation expense	2,863	2,930
Change in fair value of warrant liability	(2,448)	(7,670)
Net amortization of premiums and discounts on marketable securities	76	—
Amortization of debt-discount and accretion of deferred debt costs	185	167
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	203	329
Accounts receivable	—	7
Contract assets	(203)	(298)
Other long-term assets	(338)	(27)
Accounts payable	(969)	63
Accrued expenses	(2,372)	(1,680)
Deferred revenue	(2,408)	(2,134)
Operating lease asset and liabilities	(207)	(180)
Net cash used in operating activities	(30,017)	(21,990)
Investing activities		
Purchases of property and equipment	(128)	(262)
Maturities of marketable securities	7,511	—
Net cash (used in) provided by investing activities	7,383	(262)
Financing activities		
Payments on financing lease obligations	(70)	(64)
Proceeds from issuance of common stock through employee benefit plans	—	157
Proceeds from the issuance of common stock through exercise of option	1	—
Proceeds from issuance of common stock and warrants in public offerings, net of issuance costs	—	70,353
Payment of issuance costs related to out of period offering	(24)	(36)
Net cash (used in) provided by financing activities	(93)	70,410
Net (decrease) increase in cash, cash equivalents and restricted cash	(22,727)	48,158
Cash, cash equivalents and restricted cash (See reconciliation in Note 6)		
Beginning of period	95,388	177,070
End of period	$ 72,661	$225,228
Supplemental disclosure of cash flow information:		
Cash paid for interest	$ 783	$ 789
Non-cash investing and financing activities:		
Property and equipment received but unpaid as of period end	$ 165	$ —
Offering costs incurred but unpaid as of period end	$ 10	$ 26

See accompanying notes to unaudited condensed consolidated financial statements.

1. Nature of Business

Syros Pharmaceuticals, Inc. (the "Company"), a Delaware corporation formed in November 2011, is a biopharmaceutical company seeking to redefine the power of small molecules to control the expression of genes.

The Company is subject to a number of risks similar to those of other early stage companies, including dependence on key individuals; risks inherent in the development and commercialization of medicines to treat human disease; competition from other companies, many of which are larger and better capitalized; risks relating to obtaining and maintaining necessary intellectual property protection; and the need to obtain adequate additional financing to fund the development of its product candidates and discovery activities. If the Company is unable to raise capital when needed or on favorable terms, it would be forced to delay, reduce, eliminate or out-license certain of its research and development programs or future commercialization rights to its product candidates.

The Company has incurred significant net operating losses in every year since its inception. It expects to continue to incur significant and increasing net operating losses for at least the next several years. The Company's net losses were $86.6 million, $84.0 million and $75.4 million for the years ended December 31, 2021, 2020 and 2019, respectively. As of March 31, 2022, the Company had an accumulated deficit of $488.7 million. The Company has not generated any revenues from product sales, has not completed the development of any product candidate and may never have a product candidate approved for commercialization. The Company has financed its operations to date primarily through a credit facility, the sale of equity securities and through license and collaboration agreements. The Company has devoted substantially all of its financial resources and efforts to research and development and general and administrative activities to support such research and development. The Company's net losses may fluctuate significantly from quarter to quarter and year to year. Net losses and negative cash flows have had, and will continue to have, an adverse effect on the Company's stockholders' equity and working capital.

Under ASC Topic 205-40, *Presentation of Financial Statements—Going Concern*, management is required at each reporting period to evaluate whether there are conditions and events, considered in the aggregate, that raise substantial doubt about an entity's ability to continue as a going concern within one year after the date that the financial statements are issued. This evaluation initially does not take into consideration the potential mitigating effect of management's plans that have not been fully implemented as of the date the financial statements are issued. When substantial doubt exists, management evaluates whether the mitigating effect of its plans sufficiently alleviates the substantial doubt about the Company's ability to continue as a going concern. The mitigating effect of management's plans, however, is only considered if both (i) it is probable that the plans will be effectively implemented within one year after the date that the financial statements are issued and (ii) it is probable that the plans, when implemented, will mitigate the relevant conditions or events that raise substantial doubt about the entity's ability to continue as a going concern within one year after the date that the financial statements are issued. Generally, to be considered probable of being effectively implemented, the plans must have been approved by the Company's board of directors before the date that the financial statements are issued.

Successful completion of the Company's development program and, ultimately, the attainment of profitable operations are dependent upon future events, including obtaining adequate financing to support the Company's cost structure and operating plan. Management's plans to alleviate its financing requirements include, among other things, pursuing one or more of the following steps to raise additional capital, none of which can be guaranteed or are entirely within the Company's control:

- raise funding through the sale of the Company's common or preferred stock;

- raise funding through debt financing; and
- establish collaborations with potential partners to advance the Company's product pipeline.

Based on its current operating plan, the Company's management believes that its cash, cash equivalents and marketable securities of $112.9 million as of March 31, 2022 will allow the Company to meet its liquidity requirements into the second quarter of 2023. The Company's history of significant losses, its negative cash flows from operations, its limited liquidity resources currently on hand, and its dependence on its ability to obtain additional financing to fund its operations after the current resources are exhausted, about which there can be no certainty, have resulted in management's assessment that there is substantial doubt about the Company's ability to continue as a going concern for a period of at least twelve months from the issuance date of this Quarterly Report on Form 10-Q. The accompanying consolidated financial statements have been prepared on a going concern basis, which contemplates the realization of assets and the satisfaction of liabilities in the normal course of business, and do not include any adjustments that may result from the outcome of this uncertainty.

If the Company is unable to raise capital when needed or on acceptable terms, or if it is unable to procure collaboration arrangements to advance its programs, the Company would be forced to discontinue some of its operations or develop and implement a plan to further extend payables, reduce overhead or scale back its current operating plan until sufficient additional capital is raised to support further operations. There can be no assurance that such a plan would be successful.

2. Summary of Significant Accounting Policies

Basis of Presentation

The Company's consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States ("U.S. GAAP"). Any reference in these notes to applicable guidance is meant to refer to the authoritative U.S. GAAP as found in the Accounting Standards Codification ("ASC") and Accounting Standards Updates ("ASU") of the Financial Accounting Standards Board ("FASB").

The unaudited interim condensed consolidated financial statements have been prepared on the same basis as the audited financial statements. In the opinion of the Company's management, the accompanying unaudited interim condensed consolidated financial statements contain all adjustments that are necessary to present fairly the Company's financial position as of March 31, 2022, the results of its operations, statements of cash flows and statements of stockholders' equity for the three months ended March 31, 2022 and 2021. Such adjustments are of a normal and recurring nature. The results for the three months ended March 31, 2022 are not necessarily indicative of the results for the year ending December 31, 2022, or for any future period.

Principles of Consolidation

The accompanying condensed consolidated financial statements include the accounts of Syros Pharmaceuticals, Inc. and its wholly owned subsidiaries, Syros Securities Corporation, a Massachusetts corporation formed by the Company in December 2014 to exclusively engage in buying, selling and holding securities on its own behalf, and Syros Pharmaceuticals (Ireland) Limited, an Irish limited liability company formed by the Company in January 2019. All intercompany transactions and balances have been eliminated in consolidation.

Use of Estimates

The preparation of financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts in the financial statements and accompanying notes. Management considers many factors in selecting appropriate financial accounting policies and in developing the estimates and assumptions that are used in the preparation of the financial statements. Management must apply

significant judgment in this process. In addition, other factors may affect estimates, which include, but are not limited to, expected business and operational changes, sensitivity and volatility associated with the assumptions used in developing estimates and whether historical trends are expected to be representative of future trends. Management's estimation process may yield a range of potentially reasonable estimates and management must select an amount that falls within that range of reasonable estimates. On an ongoing basis, the Company's management evaluates its estimates, which include, but are not limited to, estimates related to revenue recognition, warrant liability, stock-based compensation expense, accrued expenses, income taxes and the evaluation of the existence of conditions and events that raise substantial doubt regarding the Company's ability to continue as a going concern. Actual results may differ from those estimates or assumptions.

Segment Information

Operating segments are identified as components of an enterprise about which separate discrete financial information is available for evaluation by the chief operating decision maker, or decision-making group, in making decisions on how to allocate resources and assess performance. The Company's chief operating decision maker is its chief executive officer. The Company and the chief operating decision maker view the Company's operations and manage its business in one operating segment. The Company operates only in the United States.

Cash and Cash Equivalents

The Company considers all highly liquid instruments that have original maturities of three months or less when acquired to be cash equivalents. Cash equivalents, which consist of money market funds that invest in U.S. Treasury obligations, as well as overnight repurchase agreements and corporate debt securities, are stated at fair value. The Company maintains its bank accounts at one major financial institution.

Off-Balance Sheet Risk and Concentrations of Credit Risk

The Company has no financial instruments with off-balance sheet risk, such as foreign exchange contracts, option contracts, or other foreign hedging arrangements. Financial instruments that potentially subject the Company to concentrations of credit risk primarily consist of cash equivalents and marketable securities. Under its investment policy, the Company limits amounts invested in such securities by credit rating, maturity, industry group, investment type and issuer, except for securities issued by the U.S. government. The Company is not exposed to any significant concentrations of credit risk from these financial instruments. The goals of the Company's investment policy, in order of priority, are safety and preservation of principal and liquidity of investments sufficient to meet cash flow requirements.

Fair Value of Financial Instruments

ASC 820, *Fair Value Measurement* ("ASC 820"), established a fair value hierarchy for instruments measured at fair value that distinguishes between assumptions based on market data (observable inputs) and the Company's own assumptions (unobservable inputs). Observable inputs are those that market participants would use in pricing the asset or liability based on market data obtained from sources independent of the Company. Unobservable inputs are those that reflect the Company's assumption about the inputs that market participants would use in pricing the asset or liability. These are developed based on the best information available under the circumstances.

ASC 820 identified fair value as the exchange price, or exit price, representing the amount that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants. As a basis for considering market participant assumptions in fair value measurements, ASC 820 established a three-tier fair value hierarchy that distinguishes between the following:

Level 1—Quoted market prices (unadjusted) in active markets for identical assets or liabilities.

Level 2—Inputs other than quoted prices included within Level 1 that are either directly or indirectly observable, such as quoted market prices, interest rates and yield curves.

Level 3—Unobservable inputs developed using estimates or assumptions developed by the Company, which reflect those that a market participant would use.

To the extent that the valuation is based on models or inputs that are less observable or unobservable in the market, the determination of fair value requires more judgment. Accordingly, the degree of judgment exercised by the Company in determining fair value is greatest for instruments categorized as Level 3. A financial instrument's level within the fair value hierarchy is based on the lowest level of any input that is significant to the fair value measurement.

The carrying amounts reflected in the condensed consolidated balance sheets for cash and cash equivalents, prepaid expenses, other current assets, restricted cash, accounts payable, accrued expenses and deferred revenue approximate their respective fair values due to their short-term nature.

Property and Equipment

Property and equipment consists of laboratory equipment, computer equipment, furniture and fixtures and leasehold improvements, all of which are stated at cost, less accumulated depreciation. Expenditures for maintenance and repairs that do not improve or extend the lives of the respective assets are recorded to expense as incurred. Major betterments are capitalized as additions to property and equipment. Depreciation and amortization are recognized over the estimated useful lives of the assets using the straight-line method.

Construction-in-progress is stated at cost, which relates to the cost of leasehold improvements not yet placed into service. No depreciation expense is recorded on construction-in-progress until such time as the relevant assets are completed and put into use.

Impairment of Long-Lived Assets

The Company continually evaluates long-lived assets for potential impairment when events or changes in circumstances indicate the carrying value of the assets may not be recoverable. Recoverability is measured by comparing the book values of the assets to the expected future net undiscounted cash flows that the assets are expected to generate. If such assets are considered to be impaired, the impairment to be recognized is measured by the amount by which the book values of the assets exceed their fair value. The Company has not recognized any impairment losses from inception through March 31, 2022.

Other Long-Term Assets

Other long-term assets primarily consisted of advance payments made to the contract research organizations responsible for conducting the Company's tamibarotene and SY-5609 clinical trials.

Revenue Recognition

To date the Company's only revenue has consisted of collaboration and license revenue. The Company has not generated any revenue from product sales and does not expect to generate any revenue from product sales for the foreseeable future.

The Company recognizes revenue in accordance with ASC 606, *Revenue from Contracts with Customers* ("ASC 606"). ASC 606 applies to all contracts with customers, except for contracts that are within the scope of other standards, such as leases, insurance, collaboration arrangements and financial instruments. Under ASC 606, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that

reflects the consideration the entity expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that an entity determines are within the scope of ASC 606, the entity performs the following five steps:

(i) identify the contract(s) with a customer;

(ii) identify the performance obligations in the contract;

(iii) determine the transaction price;

(iv) allocate the transaction price to the performance obligations in the contract; and

(v) recognize revenue when (or as) the entity satisfies a performance obligation.

The Company only applies the five-step model to contracts when it is probable that the Company will collect the consideration it is entitled to in exchange for the goods or services it transfers to the customer. If a contract is determined to be within the scope of ASC 606 at inception, the Company assesses the goods or services promised within such contract, determines which of those goods and services are performance obligations, and assesses whether each promised good or service is distinct. The Company then recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied.

If the Company performs by transferring goods or services to a customer before the customer pays consideration or before payment is due, the Company records a contract asset, excluding any amounts presented as accounts receivable. The Company includes unbilled accounts receivable as contract assets on its consolidated balance sheets. The Company records accounts receivable for amounts billed to the customer for which the Company has an unconditional right to consideration. The Company assesses contract assets and accounts receivable for impairment and, to date, no impairment losses have been recorded.

From time to time, the Company may enter into agreements that are within the scope of ASC 606. The terms of these arrangements typically include payment to the Company of one or more of the following: non-refundable, up-front license fees or prepaid research and development services; development, regulatory and commercial milestone payments; and royalties on net sales of licensed products. Each of these payments results in license and collaboration revenues, except for revenues from royalties on net sales of licensed products, which will be classified as royalty revenues.

The Company analyzes its collaboration arrangements to assess whether they are within the scope of ASC 808,*Collaborative Arrangements* (“ASC 808”), to determine whether such arrangements involve joint operating activities performed by parties that are both active participants in the activities and exposed to significant risks and rewards dependent on the commercial success of such activities. This assessment is performed throughout the life of the arrangement based on changes in the responsibilities of all parties in the arrangement. For collaboration arrangements within the scope of ASC 808 that contain multiple elements, the Company first determines which elements of the collaboration are deemed to be within the scope of ASC 808 and those that are more reflective of a vendor-customer relationship and therefore within the scope of ASC 606. For elements of collaboration arrangements that are accounted for pursuant to ASC 808, an appropriate recognition method is determined and applied consistently, generally by analogy to ASC 606. For those elements of the arrangement that are accounted for pursuant to ASC 606, the Company applies the five-step model described above.

Research and Development

Expenditures relating to research and development are expensed in the period incurred. Research and development expenses consist of both internal and external costs associated with the development of the Company’s gene control platform and product candidates. Research and development costs include salaries and benefits, materials and supplies, external research, preclinical and clinical development expenses, stock-based compensation expense and facilities costs. Facilities costs primarily include the allocation of rent, utilities, depreciation and amortization.

In certain circumstances, the Company is required to make non-refundable advance payments to vendors for goods or services that will be received in the future for use in research and development activities. In such circumstances, the non-refundable advance payments are deferred and capitalized, even when there is no alternative future use for the research and development, until related goods or services are provided.

The Company records accruals for estimated ongoing research costs. When evaluating the adequacy of the accrued liabilities, the Company analyzes progress of the work being performed, including the phase or completion of the event, invoices received and costs. Significant judgements and estimates may be made in determining the accrued balances at the end of any reporting period. Actual results could differ from the Company's estimates.

The Company may in-license the rights to develop and commercialize product candidates. For each in-license transaction the Company evaluates whether it has acquired processes or activities along with inputs that would be sufficient to constitute a "business" as defined under U.S. GAAP. A "business" as defined under U.S. GAAP consists of inputs and processes applied to those inputs that have the ability to create outputs. Although businesses usually have outputs, outputs are not required for an integrated set of activities to qualify as a business. When the Company determines that it has not acquired sufficient processes or activities to constitute a business, any up-front payments, as well as milestone payments, are immediately expensed as acquired research and development in the period in which they are incurred.

Warrants

The Company accounts for issued warrants either as a liability or equity in accordance with ASC 480-10, *Accounting for Certain Financial Instruments with Characteristics of both Liabilities and Equity* ("ASC 480-10") or ASC 815-40, *Accounting for Derivative Financial Instruments Indexed to, and Potentially Settled in, a Company's Own Stock* ("ASC 815-40"). Under ASC 480-10, warrants are considered a liability if they are mandatorily redeemable and they require settlement in cash, other assets, or a variable number of shares. If warrants do not meet liability classification under ASC 480-10, the Company considers the requirements of ASC 815-40 to determine whether the warrants should be classified as a liability or as equity. Under ASC 815-40, contracts that may require settlement for cash are liabilities, regardless of the probability of the occurrence of the triggering event. Liability-classified warrants are measured at fair value on the issuance date and at the end of each reporting period. Any change in the fair value of the warrants after the issuance date is recorded in the consolidated statements of operations as a gain or loss. If warrants do not require liability classification under ASC 815-40, in order to conclude warrants should be classified as equity, the Company assesses whether the warrants are indexed to its common stock and whether the warrants are classified as equity under ASC 815-40 or other applicable GAAP standard. Equity-classified warrants are accounted for at fair value on the issuance date with no changes in fair value recognized after the issuance date.

Stock-Based Compensation Expense

The Company accounts for its stock-based compensation awards in accordance with ASC 718, *Compensation—Stock Compensation* ("ASC 718"). ASC 718 requires all stock-based payments to employees and directors, including grants of restricted stock units and stock option awards, to be recognized as expense in the consolidated statements of operations based on their grant date fair values. Consistent with the grants for employees and directors, grants of restricted stock units and stock option awards to other service providers, referred to as non-employees, are measured based on the grant-date fair value of the award and expensed in the Company's condensed consolidated statement of operations over the vesting period. The Company estimates the fair value of stock options granted using the Black-Scholes option-pricing model. Prior to June 30, 2016, the Company was a private company and, therefore, lacks Company-specific historical and implied volatility information. As a result, the Company determines its expected volatility by using a blend of its historical experience and a weighted average of selected peer companies. The expected term of the Company's stock options has been determined utilizing the "simplified" method for awards that qualify as "plain-vanilla"

options. The expected term of stock options to non-employees can be determined using either the contractual term of the option award or the "simplified" method. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the time of grant of the award for time periods approximately equal to the expected term of the award. Expected dividend yield is based on the fact that the Company has never paid cash dividends and does not expect to pay any cash dividends in the foreseeable future. The Company uses the value of its common stock to determine the fair value of restricted stock awards.

The Company expenses the fair value of its stock-based awards to employees and non-employees on a straight-line basis over the associated service period, which is generally the vesting period. The Company accounts for forfeitures as they occur instead of estimating forfeitures at the time of grant. Ultimately, the actual expense recognized over the vesting period will be for only those options that vest.

Compensation expense for discounted purchases under the employee stock purchase plan is measured using the Black-Scholes model to compute the fair value of the lookback provision plus the purchase discount and is recognized as compensation expense over the offering period.

For stock-based awards that contain performance-based milestones, the Company records stock-based compensation expense in accordance with the accelerated attribution model. Management evaluates when the achievement of a performance-based milestone is probable based on the expected satisfaction of the performance conditions as of the reporting date.

Income Taxes

The Company accounts for uncertain tax positions using a more-likely-than-not threshold for recognizing and resolving uncertain tax positions. The evaluation of uncertain tax positions is based on factors including, but not limited to, changes in the law, the measurement of tax positions taken or expected to be taken in tax returns, the effective settlement of matters subject to audit, new audit activity, and changes in facts or circumstances related to a tax position.

Net Loss per Share

Basic net earnings per share applicable to common stockholders is calculated by dividing net earnings applicable to common stockholders by the weighted average shares outstanding during the period, without consideration for common stock equivalents. Diluted net earnings per share applicable to common stockholders is calculated by adjusting the weighted average shares outstanding for the dilutive effect of common stock equivalents outstanding for the period, determined using the treasury-stock method and the if-converted method. For purposes of the calculation of dilutive net loss per share applicable to common stockholders, stock options, unvested restricted stock units, and warrants are considered to be common stock equivalents but are excluded from the calculation of diluted net loss per share applicable to common stockholders, as their effect would be anti-dilutive; therefore, basic and diluted net loss per share applicable to common stockholders were the same for all periods presented.

As of March 31, 2022, 1,000,000 Pre-Funded Warrants to purchase common stock, issued in connection with the December 2020 private placement (refer to Note 10) were included in the basic and diluted net loss per share calculation.

The following common stock equivalents were excluded from the calculation of diluted net loss per share applicable to common stockholders for the periods indicated because including them would have had an anti-dilutive effect:

	As of March 31,	
	2022	2021
Stock options	7,527,152	6,504,401
Unvested restricted stock units	4,539,729	2,070,150
Warrants*	4,990,156	4,990,156
Total	17,057,037	13,564,707

* As of March 31, 2022 and 2021, this is comprised of 2,117,094 warrants to purchase common stock issued in connection with the Company's April 2019 financing (refer to Note 10), 27,548 warrants to purchase common stock issued in connection with the execution of the Company's loan agreement in February 2020 (refer to Note 7), 17,389 warrants to purchase common stock issued in connection with the second draw on this loan agreement in December 2020 (refer to Note 7), and 2,828,125 warrants to purchase common stock issued in connection with the private placement in December 2020 (refer to Note 10).

Recent Accounting Pronouncements

In June 2016, the FASB issued ASU 2016-13, *Financial Instruments-Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments* ("ASU 2016-13"), which requires the measurement and recognition of expected credit losses for financial assets held at amortized cost. ASU 2016-13 replaces the existing incurred loss impairment model with an expected loss model that requires the use of forward-looking information to calculate credit loss estimates. It also eliminates the concept of other-than-temporary impairment and requires credit losses on available-for-sale debt securities to be recorded through an allowance for credit losses instead of as a reduction in the amortized cost basis of the securities. As a smaller reporting company, ASU 2016-13 will become effective for the Company for fiscal years beginning after December 15, 2022, and early adoption is permitted. The Company is currently evaluating this new standard and does not anticipate that it will have a material impact on its consolidated financial statements and related disclosures.

Recently Adopted Accounting Pronouncements

In August 2020, the FASB issued ASU No. 2020-06, *Debt—Debt with Conversion and Other Options (Subtopic 470-20) and Derivatives and Hedging—Contracts in Entity's Own Equity (Subtopic 815-40): Accounting for Convertible Instruments and Contracts in an Entity's Own Equity*("ASU 2020-06"). The amendments in ASU 2020-06 simplify the accounting for certain financial instruments with characteristics of liabilities and equity, including convertible instruments and contracts in an entity's own equity. The standard is effective for public companies for fiscal years, and interim periods within those fiscal years, beginning after December 15, 2021. The Company has adopted on a modified retrospective basis the new standard effective January 1, 2022, and it did not have a material impact on its condensed consolidated financial statements and related disclosures.

3. Collaboration and Research Arrangements

Collaboration with Global Blood Therapeutics

On December 17, 2019, the Company entered into a license and collaboration agreement (the "GBT Collaboration Agreement") with Global Blood Therapeutics, Inc. ("GBT"), pursuant to which the parties agreed to a research collaboration to discover novel targets that induce fetal hemoglobin in order to develop new small molecule treatments for sickle cell disease and beta thalassemia. The research term (the "Research Term") is for an initial period of three years and can be extended for up to two additional one-year terms upon mutual agreement.

Pursuant to the terms of the GBT Collaboration Agreement, GBT paid the Company an upfront payment of $20.0 million. GBT also agreed to reimburse the Company for full-time employee and out-of-pocket costs and expenses incurred by the Company in accordance with the agreed-upon research budget, which is anticipated to total approximately $40.0 million over the initial Research Term.

The Company granted to GBT an option (the "Option") to obtain an exclusive, worldwide license, with the right to sublicense, under relevant intellectual property rights and know-how of the Company arising from the collaboration to develop, manufacture and commercialize any compounds or products resulting from the collaboration. GBT may exercise the Option at any time during the period (i) commencing on the earlier of (a) the date of GBT's designation of the first product candidate to enter investigational new drug application-enabling studies, or (b) if no such candidate is designated as of the expiration of the Research Term, the date of expiration of the Research Term, and (ii) ending on the 180th day after the date of expiration or earlier termination of the Research Term. GBT's exercise of the Option will be subject to any required filings with the applicable antitrust authority as required by the antitrust laws and satisfaction of any applicable antitrust conditions.

Should GBT exercise its Option, the Company could receive up to $315.0 million in option exercise, development, regulatory, commercialization and sales-based milestones per product candidate and product resulting from the collaboration.

The Company will also be entitled to receive, subject to certain reductions,tiered mid-to-high single digit royalties as percentages of calendar year net sales on any product.

Either party may terminate the GBT Collaboration Agreement for the other party's uncured material breach or insolvency, and in certain other specified circumstances, subject to specified notice and cure periods. GBT may unilaterally terminate the GBT Collaboration Agreement in its entirety, for any or no reason, upon nine-months' prior written notice to the Company if such notice is delivered during the Research Term, or 90 days' prior written notice to the Company if such notice is delivered after the expiration or termination of the Research Term.

GBT Collaboration Revenue

The Company analyzed the GBT Collaboration Agreement and concluded that it represents a contract with a customer within the scope of ASC 606.

The Company identified a single performance obligation, which includes a (i) non-exclusive research license that GBT will have access to during the initial Research Term and (ii) research and development services provided during the initial Research Term. The GBT Collaboration Agreement includes the Option. The Option does not provide a material right to GBT that it would receive without entering into the GBT Collaboration Agreement, principally because the Option exercise fee is at least equal to the standalone selling price for the underlying goods. The non-exclusive research license is not distinct as GBT cannot benefit from the license without the research and development services that are separately identifiable in the contract. The non-exclusive research license only allows GBT to evaluate the candidate compounds developed under the research plan or to conduct work allocated to it during the Research Term. GBT cannot extract any benefit from the non-exclusive research license without the research and development services performed by the Company, including the provision of data package information. As such, these two promises are inputs to a combined output (the delivery of data package allowing GBT to make an Option exercise decision) and are bundled into a single performance obligation (the non-exclusive research license and research and development service performance obligation).

At inception, the total transaction price was determined to be approximately $60.0 million, which consisted of a $20.0 million upfront non-refundable and non-creditable technology access fee and approximately $40.0 million in reimbursable costs for employee and external research and development expenses. The GBT

Collaboration Agreement also provides for development and regulatory milestones which are only payable subsequent to the exercise of the Option, and therefore are excluded from the transaction price at inception. The Company will re-evaluate the transaction price at the end of each reporting period and as uncertain events are resolved or other changes in circumstances occur. As of December 31, 2021, the Company reduced the transaction price from the initial estimate of $60.0 million to $54.2 million. The reduction of the transaction price was driven by a lower actual cost reimbursement and 2022 reimbursable cost budget approved by the Company and GBT.

During the three months ended March 31, 2022, there was no change in the total transaction price, which remained at approximately $54.2 million.

ASC 606 requires an entity to recognize revenue only when it satisfies a performance obligation by transferring a promised good or service to a customer. A good or service is considered to be transferred when the customer obtains control. As the non-exclusive research license and research and development services represent one performance obligation, the Company has determined that it will satisfy its performance obligation over a period of time as services are performed and GBT receives the benefit of the services, as the overall purpose of the arrangement is for the Company to perform the services. The Company will recognize revenue associated with the performance obligation as the research and development services are provided using an input method, according to the costs incurred as related to the research and development activities and the costs expected to be incurred in the future to satisfy the performance obligation. The transfer of control occurs during this time and is the best measure of progress towards satisfying the performance obligation.

During the three months ended March 31, 2022 and 2021, the Company recognized revenue of $5.1 million and $4.0 million, respectively, under the GBT Collaboration Agreement. As of March 31, 2022, the Company had deferred revenue outstanding under the GBT Collaboration Agreement of approximately $6.9 million, all of which is classified as deferred revenue, current portion on the Company's condensed consolidated balance sheets.

Agreements with Incyte Corporation

In January 2018, the Company and Incyte entered into a Target Discovery, Research Collaboration and Option Agreement (the "Incyte Collaboration Agreement"). The Incyte Collaboration Agreement was amended in November 2019. Under the Incyte Collaboration Agreement, the Company is using its proprietary gene control platform to identify novel therapeutic targets with a focus on myeloproliferative neoplasms, and Incyte has received options to obtain exclusive worldwide rights to intellectual property resulting from the collaboration for the development and commercialization of therapeutic products directed to up to seven validated targets. For each option exercised by Incyte, Incyte will have the exclusive worldwide right to use the licensed intellectual property to develop and commercialize therapeutic products that modulate the target as to which the option was exercised. Under the terms of the Incyte Collaboration Agreement, Incyte paid the Company $10.0 million in up-front consideration, consisting of $2.5 million in cash and $7.5 million in pre-paid research funding (the "Prepaid Research Amount"). The Company's activities under the Incyte Collaboration Agreement are subject to a joint research plan and, subject to certain exceptions, Incyte is responsible for funding the Company's activities under the research plan, including amounts in excess of the Prepaid Research Amount.

In January 2018, the Company also entered into a Stock Purchase Agreement with Incyte (the "Stock Purchase Agreement") whereby, for an aggregate purchase price of $10.0 million, Incyte purchased 793,021 shares of the Company's common stock at $12.61 per share. Under the terms of the Stock Purchase Agreement, the shares were purchased at a 30% premium over the volume-weighted sale price of the shares of the Company's common stock over the 15-trading day period immediately preceding the date of the Stock Purchase Agreement.

Incyte Collaboration Revenue

The Company analyzed the Incyte Collaboration Agreement and concluded that it represents a contract with a customer within the scope of ASC 606.

The Company identified a single performance obligation which includes (i) a research license that Incyte retains as long as there remains an unexercised option (the "Research License"), and (ii) research and development services provided during the research term. The Incyte Collaboration Agreement includes options to (x) obtain additional time to exercise the license options for certain targets designated as definitive validation targets, and (y) obtain license rights to each validated target, both of which were not considered by the Company's management to be material rights, and therefore not performance obligations, at inception.

At inception, the total transaction price was determined to be $12.3 million and was subsequently increased to $12.8 million following a November 2019 amendment. As of March 31, 2022, the total transaction price is $12.8 million, consisting of a $2.5 million upfront non-refundable and non-creditable payment, the $7.5 million Prepaid Research Amount, $2.3 million in premium paid on the equity investment made pursuant the Stock Purchase Agreement, and $0.5 million of additional consideration. The Company accounted for the contract amendment as a modification as if it were part of the existing contract as the remaining goods and services are not distinct, and therefore form part of a single performance obligation that was partially satisfied at the date of the amendment. This additional consideration is recognized on a percent complete basis as work is performed.

The Incyte Collaboration Agreement also provides for development and regulatory milestones that are only payable subsequent to the exercise of an option and were therefore excluded from the transaction price at inception. The Company re-evaluates the transaction price at the end of each reporting period and as uncertain events are resolved or other changes in circumstances occur.

The Company recognizes revenue associated with the performance obligation as the research and development services are provided using an input method, according to the costs incurred as related to the research and development activities and the costs expected to be incurred in the future to satisfy the performance obligation. The transfer of control occurs during this time and is the best measure of progress towards satisfying the performance obligation.

During the three months ended March 31, 2022 and 2021, the Company recognized revenue of $0.4 million and $0.8 million, respectively, under the Incyte Collaboration Agreement. As of March 31, 2022, the Company had deferred revenue outstanding under the Incyte Collaboration Agreement of approximately $0.8 million, all of which is classified as deferred revenue, current portion on the Company's condensed consolidated balance sheets.

The following table presents the changes in accounts receivable, contract assets and liabilities for the three months ended March 31, 2022 (in thousands):

	Balance at December 31, 2021	Additions	Deductions	Balance at March 31, 2022
Accounts receivable and contract assets:				
Billed receivables from collaboration partners	$ —	$ 2,857	$ (2,857)	$ —
Unbilled receivables from collaboration partners	2,979	3,181	(2,978)	3,182
Total accounts receivable and contract assets	$ 2,979	$ 6,038	$ (5,835)	$ 3,182
Contract liabilities:				
Deferred revenue—Incyte	$ 1,268	$ —	$ (421)	$ 847
Deferred revenue—GBT	8,913	—	(1,987)	6,926
Total contract liabilities	$ 10,181	$ —	$ (2,408)	$ 7,773

4. Cash, Cash Equivalents and Marketable Securities

Cash equivalents are highly liquid investments that are readily convertible into cash with original maturities of three months or less when purchased. Marketable securities consist of securities with original maturities greater than 90 days when purchased. The Company classifies these marketable securities as available-for-sale and records them at fair value in the accompanying condensed consolidated balance sheets. Unrealized gains or losses are included in accumulated other comprehensive loss. Premiums or discounts from par value are amortized to interest income over the life of the underlying security.

Cash, cash equivalents and marketable securities consisted of the following at March 31, 2022 and December 31, 2021 (in thousands):

March 31, 2022	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Cash and cash equivalents:				
Cash and money market funds	$ 69,575	$ —	$ —	$ 69,575
Marketable securities:				
Corporate debt securities—due in one year or less	28,915	—	(111)	28,804
US Treasury obligation—due in one year or less	12,000	—	(118)	11,882
Corporate debt securities—due in more than one year to five years	2,682	—	(44)	2,638
Total	$ 113,172	$ —	$ (273)	$112,899

December 31, 2021	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Cash and cash equivalents:				
Cash and money market funds	$ 92,302	$ —	$ —	$ 92,302
Marketable securities:				
Corporate debt securities—due in one year or less	30,100	—	(12)	30,088
US Treasury obligation—due in one year or less	8,000	—	(21)	7,979
Corporate debt securities—due in more than one year to five years	9,085	—	(33)	9,052
US Treasury obligation—due in more than one year to five years	3,999	—	(13)	3,986
Total	$ 143,486	$ —	$ (79)	$143,407

Although available to be sold to meet operating needs or otherwise, securities are generally held through maturity. The cost of securities sold is determined based on the specific identification method for purposes of recording realized gains and losses. During the three months ended March 31, 2022 and 2021, there were no realized gains or losses on sales of investments, and no investments were adjusted for other-than-temporary declines in fair value.

As of March 31, 2022, marketable securities with maturities of one year or less when purchased are presented in current assets and those with maturities of more than one year are presented in the noncurrent assets in the accompanying condensed consolidated balance sheet.

At March 31, 2022, the Company held ten securities that were in an unrealized loss position. The aggregate fair value of securities held by the Company in an unrealized loss position for less than twelve months as of March 31, 2022 was $27.4 million. There were no securities held by the Company in an unrealized loss position for more than twelve months as of March 31, 2022. The Company has the intent and ability to hold such securities until recovery. The Company determined that there was no material change in the credit risk of the above marketable securities. As a result, the Company determined it did not hold any marketable securities with an other-than temporary impairment as of March 31, 2022.

5. Fair Value Measurements

Assets and liabilities measured at fair value on a recurring basis as of March 31, 2022 and December 31, 2021 were as follows (in thousands):

Description	March 31, 2022	Active Markets (Level 1)	Observable Inputs (Level 2)	Unobservable Inputs (Level 3)
Assets:				
Cash	$ 59,769	$59,769	—	$ —
Money market funds	9,806	9,806	—	—
Corporate debt securities—due in one year or less	28,804	—	28,804	—
US Treasury obligation—due in one year or less	11,882	11,882	—	—
Corporate debt securities—due in more than one year to five years	2,638	—	2,638	—
Total	$ 112,899	$81,457	$ 31,442	$ —
Liabilities:				
Warrant liability	$ 581	$ —	$ —	$ 581
Total	$ 581	$ —	$ —	$ 581

Description	December 31, 2021	Active Markets (Level 1)	Observable Inputs (Level 2)	Unobservable Inputs (Level 3)
Assets:				
Cash	$ 57,213	$ 57,213	$ —	$ —
Money market funds	35,089	35,089	—	—
Corporate debt securities—due in one year or less	30,088	—	30,088	—
US Treasury obligation—due in one year or less	7,979	7,979	—	—
US Treasury obligation—due in more than one year to five years	3,986	3,986	—	—
Corporate debt securities—due in more than one year to five years	9,052	—	9,052	—
Total	$ 143,407	$104,267	$ 39,140	$ —
Liabilities:				
Warrant liability	$ 3,029	$ —	$ —	$ 3,029
Total	$ 3,029	$ —	$ —	$ 3,029

Assumptions Used in Determining Fair Value of Warrants

The Company issued warrants to purchase an aggregate of up to 2,828,125 shares of common stock in connection with a private placement on December 8, 2020 (see Note 10) (the "Warrants"). In the event of certain fundamental transactions involving the Company, the Warrant holders may require the Company to make a payment based on a Black-Scholes valuation, using specified inputs; therefore, the Warrants were accounted for as liabilities. The Company recorded the fair value of the Warrants upon issuance using the Black-Scholes valuation model and is required to revalue the Warrants at each reporting date with any changes in fair value recorded on our statement of operations. The valuation of the Warrants is considered under Level 3 of the fair value hierarchy and influenced by the fair value of the underlying common stock of the Company.

A summary of the Black Scholes pricing model assumptions used to record the fair value of the Warrants is as follows:

	March 31, 2022	December 31, 2021
Stock price	$ 1.19	$ 3.26
Risk-free interest rate	2.44%	1.11%
Dividend yield	—	—
Expected life (in years)	3.69	3.94
Expected volatility	85.49%	81.14%

Changes in Level 3 Liabilities Measured at Fair Value on a Recurring Basis

The following table reflects the change in the Company's Level 3 Warrant liability for the three months ended March 31, 2022 and the year ended December 31, 2021 (in thousands):

	March 31, 2022	December 31, 2021
Fair value of warrant liability as of beginning of the period	$ 3,029	$ 19,711
Change in fair value	(2,448)	(16,682)
Fair value of warrant liability as of end of the period	$ 581	$ 3,029

6. Restricted Cash

At March 31, 2022 and December 31, 2021, the Company had $3.1 million in restricted cash, which was classified as long-term on the Company's condensed consolidated balance sheets, and all of which was attributable to the HQ Lease (See Note 9).

In connection with the execution of the HQ Lease, the Company was required to provide the landlord with a letter of credit in the amount of $3.1 million that will expire 95 days after expiration or early termination of the HQ Lease. The Company will have the right, under certain conditions, to reduce the amount of the letter of credit to $2.1 million in October 2023.

The following table provides a reconciliation of cash, cash equivalents, and restricted cash reported within the condensed consolidated balance sheets that sum to the total of the amounts shown in the Company's condensed consolidated statement of cash flows as of March 31, 2022, and December 31, 2021 (in thousands):

	March 31, 2022	December 31, 2021
Cash and cash equivalents	$ 69,575	$ 92,302
Restricted cash, net of current portion	3,086	3,086
Total cash, cash equivalents and restricted cash	$ 72,661	$ 95,388

7. Oxford Finance Loan Agreement

On February 12, 2020, the Company entered into a Loan and Security Agreement (the "Loan Agreement") with Oxford Finance LLC (the "Lender"). Pursuant to the Loan Agreement, a term loan of up to an aggregate principal amount of $60.0 million is available to the Company. A first tranche term loan for $20.0 million was funded on February 12, 2020, and a second tranche term loan for $20.0 million was funded on December 23, 2020. The remaining $20.0 million is still available under the Loan Agreement, at the sole discretion of the Lender.

The term loan bears interest at an annual rate equal to the greater of (i) 7.75% and (ii) the sum of 5.98% and the greater of (A) one-month LIBOR or (B) 1.77%. The Loan Agreement provides for interest-only payments until March 1, 2023, and repayment of the aggregate outstanding principal balance of the term loan in monthly installments starting on March 1, 2023 and continuing through February 1, 2025 (the "Maturity Date"). The Company paid a facility fee of $0.1 million upon the funding of the first tranche, paid a facility fee of $75,000 upon funding of the second tranche and must pay a $50,000 facility fee if and when the third loan tranche is funded. The Company will be required to make a final payment fee of 5.00% of the amount of the term loan drawn payable on the earlier of (i) the prepayment of the term loan or (ii) the Maturity Date. At the Company's option, the Company may elect to prepay the loans subject to a prepayment fee equal to the following percentage of the principal amount being prepaid: 2% if an advance is prepaid during the first 12 months following the applicable advance date, 1% if an advance is prepaid after 12 months but prior to 24 months following the applicable advance date, and 0.5% if an advance is prepaid any time after 24 months following the applicable advance date but prior to the Maturity Date.

In connection with the Loan Agreement, the Company granted the Lender a security interest in all of the Company's personal property now owned or hereafter acquired, excluding intellectual property (but including the right to payments and proceeds of intellectual property), and a negative pledge on intellectual property. The Loan Agreement also contains certain events of default, representations, warranties and non-financial covenants of the Company.

In connection with the funding of the first tranche in February 2020, the Company issued the Lender warrants to purchase 27,548 shares of the Company's common stock at an exercise price per share of $7.26. In connection with the funding of the second tranche in December 2020, the Company issued the Lender warrants to purchase 17,389 shares of the Company's common stock at an exercise price of $11.50 per share (collectively, the "Oxford Warrants"). The Oxford Warrants are exercisable within five years from their respective dates of issuance.

The Oxford Warrants are classified as a component of permanent equity because they are freestanding financial instruments that are legally detachable and separately exercisable from the shares of common stock with which they were issued, are immediately exercisable, do not embody an obligation for the Company to repurchase its shares, and permit the holders to receive a fixed number of shares of common stock upon exercise. In addition, the Oxford Warrants do not provide any guarantee of value or return. The Company valued the Oxford Warrants at issuance using the Black-Scholes option pricing model and determined the fair value of the Oxford Warrants to be $0.1 million for the first tranche and $0.2 million for the second tranche. The key inputs to the valuation model included an average volatility of 75.43% for the first tranche and 82.41% for the second tranche, and an expected term of 5.0 years for both tranches.

The Company has the following minimum aggregate future loan payments as of March 31, 2022 (in thousands):

Nine months ending December 31, 2022	$ —
Year ending December 31, 2023	16,666
Year ending December 31, 2024	20,000
Year ending December 31, 2025	3,334
Total minimum payments	$40,000
Less unamortized debt discount	(410)
Plus accumulated accretion of final fees	852
Total carrying value of debt	40,442
Less current portion	(1,667)
Long-term debt, net of current portion	$38,775

For the three months ended March 31, 2022 and 2021, interest expense related to the Loan Agreement was approximately $1.0 million and $0.9 million, respectively. For the three months ended March 31, 2022, the current portion of debt is $1.7 million and the long-term portion of debt is $38.8 million as classified on the Company's condensed consolidated balance sheets as of March 31, 2022.

8. Accrued Expenses

Accrued expenses consisted of the following as of March 31, 2022 and December 31, 2021 (in thousands):

	March 31, 2022	December 31, 2021
External research and preclinical development	8,521	$ 8,274
Employee compensation and benefits	3,180	6,344
Professional fees	1,495	953
Facilities and other	53	53
Accrued expenses	$ 13,249	$ 15,624

9. Commitments and Contingencies

Operating Lease

On January 8, 2019, the Company entered into a lease (the "HQ Lease") with respect to approximately 52,859 square feet of space in Cambridge, Massachusetts for a lease term commencing in January 2019 and ending in February 2030. The Company has the option to extend the lease term for one additional ten-year period. The HQ Lease has escalating rent payments and the Company records rent expense on a straight-line basis over the term of the HQ Lease, including any rent-free periods.

In connection with the execution of the HQ Lease, the Company was required to provide the landlord with a letter of credit in the amount of $3.1 million (See Note 6).The Company determined that, for purposes of applying the lease accounting guidance codified in ASU No. 2016-02, *Leases (Topic 842) (*"ASC 842"), the commencement date of the HQ Lease occurred on May 1, 2019. The Company recorded a right-of-use asset and lease liability of $15.8 million using an incremental borrowing rate of 9.3%, net of tenant allowances expected to be received of $9.3 million, on the May 1, 2019 lease commencement date. The Company is amortizing the tenant allowance to offset rent expenses over the term of the HQ Lease starting at the lease commencement date on a straight-line basis. On the Company's condensed consolidated balance sheets, the Company classified $1.8 million of the lease liability as short-term and $22.4 million of the lease liability as long-term as of March 31, 2022.

The Company elected the practical expedient provided under ASC 842 and therefore combined all lease and non-lease components when determining the right-of-use asset and lease liability for the HQ Lease.

Financing Lease

In March 2019, the Company entered into an equipment lease agreement (the "Equipment Lease") that has a 48-month term. At the end of the term, the Company has the right to return the leased equipment, extend the lease, or buy the equipment at the then-current fair market value of the equipment. The Company accounted for the Equipment Lease as a financing lease under ASC 842 and recorded a financing lease right-of-use asset and a corresponding financing lease liability of approximately $1.0 million at the time the Equipment Lease was executed.

The following is a maturity analysis of the annual undiscounted cash flows reconciled to the carrying value of the operating and financing lease liabilities as of March 31, 2022 (in thousands):

	Operating	Financing
Nine months ending December 31, 2022	$ 2,956	$ 234
Year ending December 31, 2023	4,049	66
Year ending December 31, 2024	4,166	—
Year ending December 31, 2025	4,287	—
Year ending December 31, 2026 and beyond	19,256	—
Total minimum lease payments	34,714	300
Less imputed interest	(10,547)	(14)
Total lease liability	$ 24,167	$ 286

The following table outlines the total lease cost for the Company's operating and financing leases as well as weighted average information for these leases as of March 31, 2022 (in thousands):

	Three Months Ended March 31, 2022
Lease cost:	
Operating lease cost	$ 772
Financing lease cost:	
Amortization of right-of-use asset	$ 66
Interest on lease liabilities	7
Total financing lease cost	$ 73
Cash paid for amounts included in the measurement of liabilities:	
Operating cash flows from operating lease	$ 979
Operating cash flows from financing lease	$ 78

	Three Months Ended March 31, 2022
Other information:	
Weighted-average remaining lease term (in years)—operating lease	7.92
Weighted-average discount rate—operating lease	9.30%
Weighted-average remaining lease term (in years)—financing lease	1.07
Weighted-average discount rate—financing lease	9.47%

Following the adoption of ASC 842, the Company has aright-of-use asset and lease liability that results in recording a temporary tax difference. This temporary tax difference is the result of recognizing a right-of-use asset and related lease liability while such asset and liability have no corresponding tax basis.

Asset Purchase Agreement

Orsenix, LLC

On December 4, 2020, the Company entered into an asset purchase agreement (the "Asset Purchase Agreement") with Orsenix, LLC ("Orsenix"), pursuant to which the Company acquired Orsenix's assets related

to a novel oral form of arsenic trioxide, which the Company refers to as SY-2101. Under the terms of the Asset Purchase Agreement, the Company is required to pay to Orsenix:

- an upfront fee of $12.0 million, which was paid with cash on hand upon the closing of the transaction;
- single-digit million milestone payments related to the development of SY-2101 in indications other than APL;
- $6.0 million following the achievement of a regulatory milestone related to the development of SY-2101 in APL; and
- up to $10.0 million upon the achievement of certain commercial milestones with respect to SY-2101.

The Company's obligation to pay the commercial milestone payments expires following the tenth anniversary of the first commercial sale of SY-2101. The Asset Purchase Agreement requires the Company to use commercially reasonable efforts to develop and commercialize SY-2101 for APL in the United States during such period, and to use commercially reasonable efforts to dose the first patient in a Phase 3 clinical trial of SY-2101 on or before the third anniversary of the closing of the transaction; however, the Company retains sole discretion to operate the acquired assets as it determines. The assets acquired from Orsenix do not meet the definition of a business under ASC 805 "*Business Combinations"* ("ASC 805") because substantially all of the fair value of the assets acquired is concentrated in a single identifiable asset, the rights to SY-2101. Furthermore, as the acquired asset does not include a substantive process, the asset does not meet the minimum requirements to be considered a business under ASC 805. As SY-2101 does not have an alternative future use, the Company recorded the $12.0 million upfront cash payment as research and development expense on the date of acquisition in December 2020. The Company will expense any future milestone payments made prior to the time an alternative future use for SY-2101 has been established. Once an alternative future use for SY-2101 has been established, the Company will capitalize milestone payments as an addition to the carrying value of SY-2101.

License Agreement

TMRC Co. Ltd.

In September 2015, the Company entered into an exclusive license agreement with TMRC Co. Ltd. ("TMRC") to develop and commercialize tamibarotene in North America and Europe for the treatment of cancer. This agreement was amended and restated in April 2016, and further amended in January 2021 to expand the territory under which the Company is licensed to include Central and South America, Australia, Israel, and Russia.

In exchange for this license, the Company agreed to a non-refundable upfront payment of $1.0 million, for which $0.5 million was paid in September 2015 upon execution of the agreement, and the remaining $0.5 million was paid in May 2016. Under the agreement, the Company is also obligated to make payments upon the successful achievement of clinical and regulatory milestones totaling approximately $13.0 million per indication, defined as a distinct tumor type. The Company paid $1.0 million to TMRC for a development milestone achieved upon the successful dosing of the first patient in its Phase 2 clinical trial of tamibarotene in 2016. In May 2021, the Company paid $2.0 million to TMRC for a development milestone achieved upon the successful dosing of the first patient in its Phase 3 clinical trial of tamibarotene in MDS patients. In September 2021, the Company paid $1.0 million to TMRC for a development milestone achieved upon the successful dosing of the first patient in its Phase 2 clinical trial of tamibarotene in AML patients. In addition, the Company is obligated to pay TMRC a single-digit percentage royalty, on a country-by-country and product-by-product basis, on net product sales of tamibarotene using know-how and patents licensed from TMRC in North America and Europe for a defined royalty term.

The Company also entered into a supply management agreement with TMRC under which the Company agreed to pay TMRC a fee for each kilogram of tamibarotene that is produced. The Company did not incur any fees under this supply management agreement during the three months ended March 31, 2022 and 2021.

10. Stockholders' equity

Issuance of Securities through an Underwritten Public Offering

On January 22, 2021, the Company issued and sold an aggregate of 5,400,000 shares of its common stock in an underwritten public offering at a public offering price of $14.00 per share, resulting in gross proceeds of $75.6 million before deducting underwriting discounts and commissions and other transaction expenses of approximately $5.1 million.

Issuance of Securities through a Private Placement

On December 8, 2020, the Company issued in a private placement 10,312,500 shares of common stock, and, in lieu of shares of common stock, pre-funded warrants (the "Pre-Funded Warrants") to purchase an aggregate of 1,000,000 shares of common stock, and, in each case, accompanying Warrants to purchase an aggregate of up to 2,828,125 additional shares of common stock (or Pre-Funded Warrants to purchase common stock in lieu thereof) at a price of $8.00 per share and accompanying Warrant (or $7.99 per Pre-Funded Warrant and accompanying Warrant). The private placement resulted in aggregate gross proceeds of $90.5 million, before $0.4 million of transaction costs.

In the event of certain fundamental transactions involving the Company, the holders of Warrants may require the Company to make a payment based on a Black-Scholes valuation, using specified inputs. The holders of Pre-Funded Warrants do not have similar rights. Therefore, the Company accounted for the Warrants as liabilities, while the Pre-Funded Warrants met the permanent equity criteria classification. The Pre-Funded Warrants are classified as a component of permanent equity because they are freestanding financial instruments that are legally detachable and separately exercisable from the shares of common stock with which they were issued, are immediately exercisable, do not embody an obligation for the Company to repurchase its shares, and permit the holders to receive a fixed number of shares of common stock upon exercise. In addition, the Pre-Funded Warrants do not provide any guarantee of value or return. The initial fair value of the Warrants at issuance was $19.3 million, determined using the Black-Scholes valuation model. The Company remeasured the Warrants' fair value at March 31, 2022 and December 31, 2021 as $0.6 million and $3.0 million, respectively. The change in fair value of $2.4 million was recorded in the condensed statement of operations for the three months ended March 31, 2022.

Convertible Preferred Stock and 2019 Warrants

On April 9, 2019, the Company completed two concurrent underwritten public offerings of its equity securities. In the first public offering, the Company sold 8,667,333 shares of its common stock and accompanying Class A warrants (the "2019 Warrants") to purchase 1,951,844 shares of the Company's common stock at a combined price to the public of $7.50 per common share and accompanying 2019 Warrant. In the second public offering, the Company sold 666 shares of its Series A convertible preferred stock (the "Series A Preferred Stock") and accompanying 2019 Warrants to purchase 166,500 shares of the Company's common stock at a combined public offering price of $7,500 per share and accompanying 2019 Warrant. The offerings resulted in aggregate gross proceeds to the Company of $70.0 million, before underwriting discounts and commissions and offering expenses payable by the Company of approximately $5.0 million.

In November 2019, all 666 shares of Series A Preferred Stock were converted by the holder into 666,000 shares of common stock. As of March 31, 2022, there were no shares of Series A Preferred Stock outstanding.

Each 2019 Warrant has an exercise price per share of common stock of $8.625, subject to adjustment in certain circumstances, and will expire on October 10, 2022. Each 2019 Warrant is immediately exercisable, provided that the holder is prohibited, subject to certain exceptions, from exercising the 2019 Warrant for shares of the Company's common stock to the extent that immediately prior to or after giving effect to such exercise, the holder, together with its affiliates and other attribution parties, would own more than 4.99% of the total

number of shares of the Company's common stock then issued and outstanding. This percentage may be changed at the holders' election to a higher or lower percentage upon 61 days' notice to the Company.

The Company evaluated the Series A Preferred Stock and 2019 Warrants for liability or equity classification in accordance with the provisions of ASC 480, *Distinguishing Liabilities from Equity*, and determined that equity treatment was appropriate because neither the Series A Preferred Stock nor the 2019 Warrants met the definition of liability instruments.

The Series A Preferred Stock was not mandatorily redeemable and did not embody an obligation to buy back the shares outside of the Company's control in a manner that could require the transfer of assets. Additionally, the Company determined that the Series A Preferred Stock would be recorded as permanent equity, not temporary equity, given that the holders of equally and more subordinated equity would be entitled to receive the same form of consideration upon the occurrence of the event that gives rise to the redemption or events of redemption that are within the control of the Company.

Additionally, as the effective conversion price of the Series A Preferred Stock of $6.57 was below the fair value of the Company's common stock on the date of issuance of $7.50, the Company determined that the Series A Preferred Stock included a beneficial conversion feature. The Company calculated the beneficial conversion feature to be approximately $0.6 million, which was recorded as a discount to the Series A Preferred Stock at the time of issuance.

The 2019 Warrants are classified as a component of permanent equity because they are freestanding financial instruments that are legally detachable and separately exercisable from the shares of common stock with which they were issued, are immediately exercisable, do not embody an obligation for the Company to repurchase its shares, and permit the holders to receive a fixed number of shares of common stock upon exercise. In addition, the 2019 Warrants do not provide any guarantee of value or return. The Company valued the 2019 Warrants at issuance using the Black-Scholes option pricing model and determined the fair value of the 2019 Warrants to purchase 2,118,344 shares of the Company's common stock was $9.0 million. The key inputs to the valuation model included an average volatility of 86.06% and an expected term of 3.5 years.

As of March 31, 2022, the 2019 Warrants to purchase 2,117,094 shares of common stock are outstanding and remain unexercised.

11. Stock-Based Payments

2016 Stock Incentive Plan

The 2016 Stock Incentive Plan (the "2016 Plan") was adopted by the board of directors on December 15, 2015, approved by the stockholders on June 17, 2016, and became effective on July 6, 2016 upon the closing of the Company's initial public offering ("IPO"). The 2016 Plan replaced the 2012 Equity Incentive Plan (the "2012 Plan"). Any options or awards outstanding under the 2012 Plan remained outstanding and effective. Under the 2016 Plan, the Company may grant incentive stock options, non-statutory stock options, stock appreciation rights, restricted stock, restricted stock units and other stock-based awards. The number of shares of the Company's common stock reserved for issuance under the 2016 Plan automatically increases on the first day of each calendar year, through the 2025 calendar year, in an amount equal to the least of (i) 1,600,000 shares of common stock, (ii) 4.0% of the outstanding shares of common stock as of such date, or (iii) such lesser amount as specified by the board of directors. This number is subject to adjustment in the event of a stock split, stock dividend or other change in the Company's capitalization. For the calendar year beginning January 1, 2022, the number of shares reserved for issuance under the 2016 Plan was increased by 1,600,000 shares. At March 31, 2022, 428,219 shares remained available for future issuance under the 2016 Plan. Under the 2016 Plan, stock options may not be granted at less than fair value on the date of grant.

2016 Employee Stock Purchase Plan

The 2016 Employee Stock Purchase Plan (the "2016 ESPP") was adopted by the board of directors on December 15, 2015, approved by the stockholders on June 17, 2016, and became effective on July 6, 2016 upon the closing of the IPO. The number of shares of the Company's common stock reserved for issuance under the 2016 ESPP automatically increases on the first day of each calendar year through the 2025 calendar year, in an amount equal to the least of (i) 1,173,333 shares of the Company's common stock, (ii) 1.0% of the total number of shares of the Company's common stock outstanding on the first day of the applicable year, and (iii) an amount determined by the Company's board of directors. For the calendar year beginning January 1, 2022, the number of shares reserved for issuance under the 2016 ESPP was increased by 620,241 shares. At March 31, 2022, 2,857,306 shares remained available for future issuance under the 2016 ESPP.

Inducement Grants

During the year ended December 31, 2021, the Company granted non-statutory stock options to purchase an aggregate of 1,110,000 shares of the Company's common stock. These stock options were granted outside of the 2016 Plan as an inducement material to the applicable employee's acceptance of employment with the Company in accordance with Nasdaq Listing Rule 5635(c)(4).These stock options will vest over a four-year period, with 25% of the shares underlying each option award vesting on the one-year anniversary of the applicable employee's employment commencement date and the remaining 75% of the shares underlying each award vesting monthly thereafter for three-years. Vesting of each option is subject to such employee's continued service with the Company through the applicable vesting dates.

2022 Inducement Stock Incentive Plan

On January 25, 2022, the Company's board of directors adopted the 2022 Inducement Stock Incentive Plan (the "2022 Plan"), pursuant to which the Company may grant non-statutory stock options, stock appreciation rights, restricted stock, restricted stock units and other stock-based awards with respect to an aggregate of 1,000,000 shares of common stock. Awards under the 2022 Plan may only be granted to persons who (i) were not previously an employee or director of the Company or (ii) are commencing employment with the Company following a bona fide period of non-employment, in either case as an inducement material to the individual's entering into employment with the Company and in accordance with the requirements of Nasdaq Stock Market Rule 5635(c)(4).

Stock Options

Terms of stock option agreements, including vesting requirements, are determined by the board of directors, subject to the provisions of the 2016 Plan. Stock option awards granted by the Company generally vest over four years, with 25% vesting on the first anniversary of the vesting commencement date and 75% vesting ratably, on a monthly basis, over the remaining three years. Such awards have a contractual term of ten years from the grant date.

The Company has granted certain stock options to management for which vesting accelerates upon the achievement of performance-based criteria. Milestone events are specific to the Company's corporate goals, including but not limited to certain clinical development milestones for the Company's product candidates and the Company's ability to execute on its corporate development and financing strategies. Stock-based compensation expense associated with these performance-based stock options is recognized based on the accelerated attribution model. Management evaluates when the achievement of a performance-based milestone is probable based on the expected satisfaction of the performance conditions as of the reporting date. Notwithstanding any vesting in accordance with the achievement of performance-based milestones, such awards vest in full on the sixth anniversary of the vesting commencement date. As of December 31, 2020, all performance-based milestones related to these stock options were achieved. The Company did not record any additional stock-based compensation expense related to the achievement of performance-based milestones during the three months ended March 31, 2022 and 2021

The Company has granted options to purchase 75,000 shares of common stock to an advisor that vest solely upon the achievement of performance-based criteria. As of March 31, 2022, none of these performance-based criteria had been achieved. As of March 31, 2022, there was $0.3 million of unrecognized compensation cost related to this option, with a remaining contractual period of 4.5 years.

A summary of the status of stock options as of December 31, 2021 and March 31, 2022 and changes during the three months ended March 31, 2022 is presented below:

	Shares	Weighted Average Exercise Price	Remaining Contractual Life (in years)	Aggregate Intrinsic Value (in thousands)
Outstanding at December 31, 2021	6,657,268	$ 8.27	7.2	$ 494
Granted	951,300	1.59		
Exercised	(37,700)	0.04		
Cancelled	(43,716)	9.93		
Outstanding at March 31, 2022	7,527,152	$ 7.45	6.9	$ 26
Exercisable at March 31, 2022	4,081,501	$ 9.01	5.4	$ 26

The intrinsic value of stock options exercised during the three months ended March 31, 2022 and 2021 was $0.1 million and $0.1 million, respectively.

As of March 31, 2022, there was $12.1 million of total unrecognized compensation cost related tonon-vested stock options granted to employees, which is expected to be recognized over a weighted-average period of 3.1 years.

Restricted Stock Units

From time to time, upon approval by the Company's board of directors, certain employees have been granted restricted stock units with time-based vesting criteria. The majority of these restricted stock units vest annually over a four-year term with 25% vesting on each anniversary of the grant date. Restricted stock units granted to the Company's executive officers vest in full three-years from the date of grant. The fair value of restricted stock units is calculated based on the closing sale price of the Company's common stock on the date of grant.

A summary of the status of restricted stock units as of December 31, 2021 and March 31, 2022 and changes during the three months ended March 31, 2022 is presented below:

	Shares	Weighted Average Grant Date Fair Value
Outstanding at December 31, 2021	2,687,487	$ 6.52
Granted	2,768,128	1.58
Vested	(739,561)	7.32
Forfeited	(176,325)	6.76
Outstanding at March 31, 2022	4,539,729	$ 3.37

As of March 31, 2022, there was $13.9 million of unrecognized stock-based compensation expense related to outstanding restricted stock units, with an expected recognition period of 2.9 years.

Stock-based Compensation Expense

The fair value of each stock option granted was estimated on the date of grant using the Black-Scholes option-pricing model based on the following weighted-average assumptions:

	Three Months Ended March 31,	
	2022	2021
Weighted-average risk-free interest rate	1.98%	0.78%
Expected dividend yield	— %	— %
Expected option term (in years)	6.07	6.08
Volatility	80.70%	82.10%

The weighted-average grant date fair value per share of options granted in the three months ended March 31, 2022 and 2021 was $1.11 and $7.89, respectively.

The following table summarizes the stock-based compensation expense for stock options and restricted stock units granted to employees and non-employees recorded in the Company's condensed consolidated statements of operations:

	Three Months Ended March 31,	
	2022	2021
Research and development	$1,395	$1,323
General and administrative	1,468	1,607
Total stock-based compensation expense	$2,863	$2,930

Due to an operating loss, the Company does not record tax benefits associated withstock-based compensation or option exercises. Tax benefits will be recorded when realized.

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Syros Pharmaceuticals, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Syros Pharmaceuticals, Inc. (the Company) as of December 31, 2021 and 2020, the related consolidated statements of operations, comprehensive loss, convertible preferred stock and stockholders' equity and cash flows for each of the three years in the period ended December 31, 2021, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2021 and 2020, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2021, in conformity with US generally accepted accounting principles.

The Company's Ability to Continue as a Going Concern

The accompanying consolidated financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 1 to the consolidated financial statements, the Company has suffered recurring losses from operations and has stated that substantial doubt exists about the Company's ability to continue as a going concern. Management's evaluation of the events and conditions and management's plans regarding these matters are also described in Note 1. The consolidated financial statements do not include any adjustments that might result from the outcome of this uncertainty.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

Critical Audit Matter

The critical audit matter communicated below is a matter arising from the current period audit of the financial statements that was communicated or required to be communicated to the audit committee and that: (1) relates to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging,

subjective or complex judgments. The communication of the critical audit matter does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing separate opinions on the critical audit matter or on the accounts or disclosures to which it relates.

Collaboration revenue recognition

Description of the Matter	As of December 31, 2021, the Company's revenue totaled $23.5 million. Additionally, the Company's deferred revenue totaled $10.2 million, all of which was current. As discussed in Note 3 to the consolidated financial statements, the Company recognizes revenue associated with each performance obligation as the research and development services are provided measured based on the ratio of costs incurred to date to the total estimated costs at completion. Determining the estimated costs at completion is especially challenging because it requires the Company to forecast costs associated with internal employee efforts, materials costs, and third-party contract costs, as well as the assumed timing and duration of these activities. Due to uncertainties attributed to such factors, auditing the amount of revenue recognized from collaboration agreements involved especially challenging, subjective and complex judgments.
How We Addressed the Matter in Our Audit	To test the amount of revenue recognized in the current period from collaboration agreements and the balance of deferred revenue, we performed audit procedures that included, among others, reviewing minutes of meetings held with collaboration partners for any changes to key assumptions used. We obtained and inspected the agreements, amendments, and change orders to test the existence of customer arrangements and understand the scope and pricing of the related projects. We also evaluated management's estimates of total costs expected to be incurred and the estimated timeframe over which costs are to be incurred by making direct inquiries of the Company's research and development personnel overseeing the projects, comparing cost estimates to costs previously incurred for similar activities, inspecting evidence of actual costs incurred and by performing analytical procedures. We recalculated the revenue recognized for the period based on the ratio of costs incurred to estimated total costs at completion of the research and development services and the transaction price.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2014.

Boston, Massachusetts
March 15, 2022

SYROS PHARMACEUTICALS, INC.
CONSOLIDATED BALANCE SHEETS
(in thousands, except share and per share data)

	December 31, 2021	December 31, 2020
Assets		
Current assets:		
Cash and cash equivalents	$ 92,302	$ 173,984
Marketable securities	38,067	—
Accounts receivable	—	7
Contract assets	2,979	2,324
Prepaid expenses and other current assets	3,237	2,242
Total current assets	136,585	178,557
Property and equipment, net	12,844	14,213
Marketable securities – noncurrent	13,038	—
Other long-term assets	2,941	1,966
Restricted cash	3,086	3,086
Right-of-use asset – operating lease	14,104	14,831
Right-of-use assets – financing leases	337	597
Total assets	$ 182,935	$ 213,250
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 3,692	$ 3,603
Accrued expenses	15,624	11,084
Deferred revenue, current portion	10,181	12,209
Financing lease obligations, current portion	291	265
Operating lease obligation, current portion	1,720	1,463
Total current liabilities	31,508	28,624
Deferred revenue, net of current portion	—	9,877
Financing lease obligations, net of current portion	65	356
Operating lease obligation, net of current portion	22,858	24,578
Warrant liability	3,029	19,711
Debt, net of debt discount, long term	40,257	39,551
Commitments and contingencies (See Note 10)		
Stockholders' equity:		
Preferred stock, $0.001 par value; 10,000,000 shares authorized at December 31, 2021 and December 31, 2020; 0 shares issued and outstanding at December 31, 2021 and December 31, 2020	—	—
Common stock, $0.001 par value; 200,000,000 shares authorized at December 31, 2021 and December 31, 2020; 62,024,035 and 56,222,746 shares issued and outstanding at December 31, 2021 and December 31, 2020, respectively	61	56
Additional paid-in capital	548,815	467,518
Accumulated other comprehensive loss	(79)	—
Accumulated deficit	(463,579)	(377,021)
Total stockholders' equity	85,218	90,553
Total liabilities and stockholders' equity	$ 182,935	$ 213,250

See accompanying notes to consolidated financial statements.

SYROS PHARMACEUTICALS, INC.
CONSOLIDATED STATEMENTS OF OPERATIONS
(in thousands, except share and per share data)

	Year Ended December 31,		
	2021	2020	2019
Revenue	$ 23,488	$ 15,093	$ 1,982
Operating expenses:			
Research and development	99,872	76,065	58,245
General and administrative	23,036	21,325	21,478
Total operating expenses	122,908	97,390	79,723
Loss from operations	(99,420)	(82,297)	(77,741)
Interest income	87	426	2,375
Interest expense	(3,907)	(1,792)	(72)
Change in fair value of warrant liability	16,682	(375)	—
Net loss applicable to common stockholders	$ (86,558)	$ (84,038)	$ (75,438)
Net loss per share applicable to common stockholders – basic and diluted	$ (1.38)	$ (1.82)	$ (1.88)
Weighted-average number of common shares used in net loss per share applicable to common stockholders – basic and diluted	62,534,978	46,051,617	40,222,182

See accompanying notes to consolidated financial statements.

SYROS PHARMACEUTICALS, INC.
CONSOLIDATED STATEMENTS OF COMPREHENSIVE LOSS
(in thousands)

	Year Ended December 31,		
	2021	2020	2019
Net loss	$ (86,558)	$ (84,038)	$ (75,438)
Other comprehensive (loss) gain:			
Unrealized holding (loss) gain on marketable securities	(79)	(24)	27
Comprehensive loss	$ (86,637)	$ (84,062)	$ (75,411)

See accompanying notes to consolidated financial statements.

SYROS PHARMACEUTICALS, INC.
CONSOLIDATED STATEMENTS OF CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY
(in thousands except share data)

	Common Stock		Series A Convertible Preferred Stock		Additional Paid-In Capital	Accumulated Other Comprehensive (Loss) Gain	Accumulated Deficit	Stockholders' Equity
	Number of Shares	Par Value	Number of Shares	Par Value				
Balance at December 31, 2018	33,765,864	$ 34	—	$ —	$ 296,100	$ (3)	$ (217,545)	$ 78,586
Exercise of stock options	60,181	—	—	—	211	—	—	211
Issuance of common stock and accompanying warrants in underwritten public offering, net of issuance costs of $4,600	8,667,333	9	—	—	60,350	—	—	60,359
Issuance of preferred stock and accompanying warrants in underwritten public offering, net of issuance costs of $400	—	—	666	—	4,638	—	—	4,638
Conversion of preferred stock (1,000 to 1 conversion ratio)	666,000	—	(666)	—	—	—	—	—
Issuance of common stock at-the-market, net of issuance cost	180,787	—	—	—	799	—	—	799
Issuance of shares under Employee Stock Purchase Plan	27,386	—	—	—	161	—	—	161
Exercise of warrants	250	—	—	—	2	—	—	2
Stock-based compensation expense	—	—	—	—	9,839	—	—	9,839
Other comprehensive gain	—	—	—	—	—	27	—	27
Net loss	—	—	—	—	—	—	(75,438)	(75,438)
Balance at December 31, 2019	43,367,801	$ 43	—	$ —	$ 372,100	$ 24	$ (292,983)	$ 79,184
Exercise of stock options	170,723	—	—	—	1,076	—	—	1,076
Vesting of restricted stock units	109,362	—	—	—	—	—	—	—
Issuance of shares under Employee Stock Purchase Plan	59,550	—	—	—	433	—	—	433
Issuance of common stock at-the-market, net of issuance costs of $411	2,201,810	2	—	—	11,917	—	—	11,919
Issuance of common stock and accompanying Pre-funded warrants at private placement, net of issuance costs of $401	10,312,500	11	—	—	70,742	—	—	70,753
Issuance of warrants related to entering into debt arrangement	—	—	—	—	302	—	—	302
Exercise of warrants	1,000	—	—	—	9	—	—	9
Stock-based compensation expense	—	—	—	—	10,939	—	—	10,939
Other comprehensive loss	—	—	—	—	—	(24)	—	(24)
Net loss	—	—	—	—	—	—	(84,038)	(84,038)
Balance at December 31, 2020	56,222,746	$ 56	—	$ —	$ 467,518	$ —	$ (377,021)	$ 90,553
Exercise of stock options	20,134	—	—	—	157	—	—	157
Vesting of restricted stock units	286,837	—	—	—	—	—	—	—
Issuance of shares under Employee Stock Purchase Plan	94,318	—	—	—	323	—	—	323
Issuance of common stock in underwritten public offering, net of issuance costs of $5,132	5,400,000	5	—	—	70,463	—	—	70,468
Stock-based compensation expense	—	—	—	—	10,354	—	—	10,354
Other comprehensive loss	—	—	—	—	—	(79)	—	(79)
Net loss	—	—	—	—	—	—	(86,558)	(86,558)
Balance at December 31, 2021	62,024,035	$ 61	—	$ —	$ 548,815	$ (79)	$ (463,579)	$ 85,218

See accompanying notes to consolidated financial statements

SYROS PHARMACEUTICALS, INC.
CONSOLIDATED STATEMENTS OF CASH FLOWS
(in thousands)

	Year Ended December 31,		
	2021	**2020**	**2019**
Operating activities			
Net loss	$ (86,558)	$ (84,038)	$ (75,438)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	2,758	2,774	2,521
Amortization of right-of-use asset	260	261	201
Loss on disposal of fixed assets	—	—	(181)
Stock-based compensation expense	10,354	10,939	9,839
Change in fair value of warrant liability	(16,682)	375	—
Net amortization of premiums and discounts on marketable securities	224	(49)	(949)
Amortization of debt-discount and accretion of deferred debt costs	706	287	—
Changes in operating assets and liabilities:	—	—	—
Prepaid expenses and other current assets	(995)	309	(783)
Accounts receivable	7	19,993	(20,158)
Contract assets	(655)	(2,166)	—
Other long-term assets	(1,196)	(1,269)	—
Accounts payable	48	(1,057)	1,493
Accrued expenses	4,830	593	(3,576)
Deferred revenue	(11,905)	(6,292)	18,176
Proceeds for tenant improvement incentive from landlord	—	2,035	7,237
Operating lease asset and liabilities	(736)	(59)	1,365
Net cash used in operating activities	(99,540)	(57,364)	(60,253)
Investing activities			
Purchases of property and equipment	(1,245)	(3,336)	(12,638)
Proceeds from the disposition of property and equipment	—	—	110
Purchases of marketable securities	(51,408)	—	(108,206)
Maturities of marketable securities	—	50,000	109,000
Net cash (used in) provided by investing activities	(52,653)	46,664	(11,734)
Financing activities			
Payments on financing lease obligations	(265)	(241)	(205)
Proceeds from issuance of common stock through employee benefit plans	157	1,076	211
Proceeds from the issuance of common stock through employee stock purchase plan	323	433	161
Proceeds from the issuance of common stock through exercise of warrants	—	—	2
Proceeds from issuance of common stock through at-the-market sales agreement, net of issuance costs	—	11,896	824
Proceeds from term loan, net of issuance costs	—	39,619	—
Proceeds from issuance of common stock and accompanying warrants and pre-funded warrants in private placement, net of issuance costs	—	90,377	—
Proceeds from issuance of common stock and warrants in public offerings, net of issuance costs	70,337	—	60,359
Proceeds from issuance of convertible preferred stock and accompanying warrants in public offering, net of issuance costs	—	—	4,638
Payment of issuance costs related to out of period offering	(41)	(207)	—
Net cash provided by financing activities	70,511	142,953	65,990
Net (decrease) increase in cash, cash equivalents and restricted cash	(81,682)	132,253	(5,997)
Cash, cash equivalents and restricted cash (See reconciliation in Note 6)			
Beginning of period	177,070	44,817	50,814
End of period	$ 95,388	$177,070	$ 44,817
Supplemental disclosure of cash flow information:			
Cash paid for interest	$ 3,191	$ 1,505	$ 72
Cash paid for tax	$ —	$ 7	$ 29
Non-cash investing and financing activities:			
Property and equipment received but unpaid as of period end	$ 26	$ 6	$ 1,565
Asset acquired under operating lease	$ —	$ —	$ 16,240
Assets acquired under financing lease	$ —	$ —	$ 1,059
Deferred debt financing costs incurred but unpaid as of period end	$ 24	$ 5	$ 58
Offering costs incurred but unpaid as of period end	$ 10	$ 298	$ 23

See accompanying notes to consolidated financial statements.

1. Nature of Business

Syros Pharmaceuticals, Inc. (the "Company"), a Delaware corporation formed in November 2011, is a biopharmaceutical company seeking to redefine the power of small molecules to control the expression of genes.

The Company is subject to a number of risks similar to those of other early stage companies, including dependence on key individuals; risks inherent in the development and commercialization of medicines to treat human disease; competition from other companies, many of which are larger and better capitalized; risks relating to obtaining and maintaining necessary intellectual property protection; and the need to obtain adequate additional financing to fund the development of its product candidates and discovery activities. If the Company is unable to raise capital when needed or on favorable terms, it would be forced to delay, reduce, eliminate or out-license certain of its research and development programs or future commercialization rights to its product candidates.

In January 2021, the Company issued and sold an aggregate of 5,400,000 shares of the Company's common stock in an underwritten public offering at a public offering price of $14.00 per share, resulting in gross proceeds of $75.6 million before deducting underwriting discounts and commissions and other transaction expenses of approximately $5.1 million.

On December 8, 2020, through a private placement, the Company issued 10,312,500 shares of the Company's common stock, par value $0.001 per share, and, in lieu of such shares of common stock, pre-funded warrants (the "Pre-Funded Warrants") to purchase an aggregate of 1,000,000 shares of common stock, and, in each case, accompanying warrants (the "Warrants") to purchase an aggregate of up to 2,828,125 additional shares of common stock (or Pre-Funded Warrants to purchase common stock in lieu thereof) at a price of $8.00 per share and accompanying Warrant (or $7.99 per Pre-Funded Warrant and accompanying Warrant). The private placement resulted in gross proceeds of $90.5 million, before $0.4 million of transaction costs.

On December 4, 2020, the Company entered into an asset purchase agreement (the "Asset Purchase Agreement") with Orsenix, LLC ("Orsenix"), pursuant to which the Company acquired all of Orsenix's assets related to a novel oral form of arsenic trioxide, which the Company refers to as SY-2101 (the "Product"). Under the terms of the Asset Purchase Agreement, the Company was required to pay to Orsenix an upfront fee of $12.0 million, which was paid with cash on hand upon the closing of the transaction. In addition the Company is required to pay single-digit million dollar milestone payments related to the development of the Product in indications other than APL; $6.0 million following the achievement of a regulatory milestone related to the development of the Product in APL; and up to $10.0 million upon the achievement of certain commercial milestones with respect to the Product.

In April 2019, the Company completed two concurrent underwritten public offerings of the Company's equity securities, which together resulted in gross proceeds to the Company of $70.0 million, before underwriting discounts and commissions and offering expenses of approximately $5.0 million. In one of the public offerings, the Company sold 8,667,333 shares of its common stock and accompanying Class A warrants (the "2019 Warrants") to purchase 1,951,844 shares of the Company's common stock, at a combined price to the public of $7.50 per common share and accompanying 2019 Warrant. In the other public offering, the Company sold 666 shares of its Series A convertible preferred stock (the "Series A Stock"), and accompanying 2019 Warrants to purchase 166,500 shares of the Company's common stock, at a combined public offering price of $7,500 per share and accompanying 2019 Warrant. Each 2019 Warrant is immediately exercisable at an exercise price of $8.625 per share, subject to adjustment in certain circumstances, and will expire on October 10, 2022. During November 2019, the Company issued and sold an aggregate of 180,787 shares of its common stock to the public pursuant to its at-the-market sales facility, resulting in aggregate gross proceeds of $0.9 million.

The Company has incurred significant annual net operating losses in every year since its inception. It expects to continue to incur significant and increasing net operating losses for at least the next several years. The Company's net losses were $86.6 million, $84.0 million and $75.4 million for the years ended December 31, 2021, 2020 and 2019, respectively. As of December 31, 2021, the Company had an accumulated deficit of $463.6 million. The Company has not generated any revenues from product sales, has not completed the development of any product candidate and may never have a product candidate approved for commercialization. The Company has financed its operations to date primarily through a credit facility, the sale of equity securities and through license and collaboration agreements. The Company has devoted substantially all of its financial resources and efforts to research and development and general and administrative expense to support such research and development. The Company's net losses may fluctuate significantly from quarter to quarter and year to year. Net losses and negative cash flows have had, and will continue to have, an adverse effect on the Company's stockholders' equity and working capital.

Under ASC Topic 205-40, *Presentation of Financial Statements - Going Concern*, management is required at each reporting period to evaluate whether there are conditions and events, considered in the aggregate, that raise substantial doubt about an entity's ability to continue as a going concern within one year after the date that the financial statements are issued. This evaluation initially does not take into consideration the potential mitigating effect of management's plans that have not been fully implemented as of the date the financial statements are issued. When substantial doubt exists, management evaluates whether the mitigating effect of its plans sufficiently alleviates the substantial doubt about the Company's ability to continue as a going concern. The mitigating effect of management's plans, however, is only considered if both (i) it is probable that the plans will be effectively implemented within one year after the date that the financial statements are issued and (ii) it is probable that the plans, when implemented, will mitigate the relevant conditions or events that raise substantial doubt about the entity's ability to continue as a going concern within one year after the date that the financial statements are issued. Generally, to be considered probable of being effectively implemented, the plans must have been approved by the Company's board of directors before the date that the financial statements are issued.

Successful completion of the Company's development program and, ultimately, the attainment of profitable operations are dependent upon future events, including obtaining adequate financing to support the Company's cost structure and operating plan. Management's plans to alleviate its financing requirements include, among other things, pursuing one or more of the following steps to raise additional capital, none of which can be guaranteed or are entirely within the Company's control:

- raise funding through the sale of the Company's common or preferred stock;
- raise funding through debt financing; and
- establish collaborations with potential partners to advance the Company's product pipeline.

Based on the Company's current operating plan, its cash, cash equivalents and marketable securities of $143.4 million as of December 31, 2021 will allow the Company to meet its liquidity requirements into the first quarter of 2023. The Company's history of significant losses, its negative cash flows from operations, its limited liquidity resources currently on hand, and its dependence on its ability to obtain additional financing to fund its operations after the current resources are exhausted, about which there can be no certainty, have resulted in management's assessment that there is substantial doubt about the Company's ability to continue as a going concern for a period of at least twelve months from the issuance date of this Annual Report on Form 10-K. The accompanying consolidated financial statements have been prepared on a going concern basis, which contemplates the realization of assets and the satisfaction of liabilities in the normal course of business, and do not include any adjustments that may result from the outcome of this uncertainty.

If the Company is unable to raise capital when needed or on acceptable terms, or if it is unable to procure collaboration arrangements to advance its programs, the Company would be forced to discontinue some of its operations or develop and implement a plan to further extend payables, reduce overhead or scale back its current operating plan until sufficient additional capital is raised to support further operations. There can be no assurance that such a plan would be successful.

2. Summary of Significant Accounting Policies

Basis of Presentation

The Company's consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States ("U.S. GAAP"). Any reference in these notes to applicable guidance is meant to refer to the authoritative U.S. GAAP as found in the Accounting Standards Codification ("ASC") and Accounting Standards Updates ("ASU") of the Financial Accounting Standards Board ("FASB").

Principles of Consolidation

The accompanying consolidated financial statements include the accounts of Syros Pharmaceuticals, Inc. and its wholly owned subsidiaries, Syros Securities Corporation, a Massachusetts corporation formed by the Company in December 2014 to exclusively engage in buying, selling and holding securities on its own behalf, and Syros Pharmaceuticals (Ireland) Limited, an Irish limited liability company formed by the Company in January 2019. All intercompany transactions and balances have been eliminated in consolidation.

Use of Estimates

The preparation of financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts in the financial statements and accompanying notes. Management considers many factors in selecting appropriate financial accounting policies and in developing the estimates and assumptions that are used in the preparation of the financial statements. Management must apply significant judgment in this process. In addition, other factors may affect estimates, which include, but are not limited to, expected business and operational changes, sensitivity and volatility associated with the assumptions used in developing estimates and whether historical trends are expected to be representative of future trends. Management's estimation process often may yield a range of potentially reasonable estimates and management must select an amount that falls within that range of reasonable estimates. On an ongoing basis, the Company's management evaluates its estimates, which include, but are not limited to, estimates related to revenue recognition, warrant liability, stock-based compensation expense, accrued expenses, income taxes and the evaluation of the existence of conditions and events that raise substantial doubt regarding the Company's ability to continue as a going concern. Actual results may differ from those estimates or assumptions.

Segment Information

Operating segments are identified as components of an enterprise about which separate discrete financial information is available for evaluation by the chief operating decision maker, or decision-making group, in making decisions on how to allocate resources and assess performance. The Company's chief operating decision maker is the Chief Executive Officer. The Company and the chief operating decision maker view the Company's operations and manage its business in one operating segment. The Company operates only in the United States.

Cash and Cash Equivalents

The Company considers all highly liquid instruments that have original maturities of three months or less when acquired to be cash equivalents. Cash equivalents, which consist of money market funds that invest in U.S.

Treasury obligations, as well as overnight repurchase agreements, are stated at fair value. The Company maintains its bank accounts at one major financial institution.

Off-Balance Sheet Risk and Concentrations of Credit Risk

The Company has no financial instruments with off-balance sheet risk, such as foreign exchange contracts, option contracts, or other foreign hedging arrangements. Financial instruments that potentially subject the Company to concentrations of credit risk primarily consist of cash equivalents and marketable securities. Under its investment policy, the Company limits amounts invested in such securities by credit rating, maturity, industry group, investment type and issuer, except for securities issued by the U.S. government. The Company is not exposed to any significant concentrations of credit risk from these financial instruments. The goals of the Company's investment policy, in order of priority, are safety and preservation of principal and liquidity of investments sufficient to meet cash flow requirements.

Fair Value of Financial Instruments

ASC 820, *Fair Value Measurement* ("ASC 820"), established a fair value hierarchy for instruments measured at fair value that distinguishes between assumptions based on market data (observable inputs) and the Company's own assumptions (unobservable inputs). Observable inputs are inputs that market participants would use in pricing the asset or liability based on market data obtained from sources independent of the Company. Unobservable inputs are inputs that reflect the Company's assumption about the inputs that market participants would use in pricing the asset or liability. These are developed based on the best information available under the circumstances.

ASC 820 identified fair value as the exchange price, or exit price, representing the amount that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants. As a basis for considering market participant assumptions in fair value measurements, ASC 820 established a three-tier fair value hierarchy that distinguishes between the following:

Level 1—Quoted market prices (unadjusted) in active markets for identical assets or liabilities.

Level 2—Inputs other than quoted prices included within Level 1 that are either directly or indirectly observable, such as quoted market prices, interest rates and yield curves.

Level 3—Unobservable inputs developed using estimates or assumptions developed by the Company, which reflect those that a market participant would use.

To the extent that the valuation is based on models or inputs that are less observable or unobservable in the market, the determination of fair value requires more judgment. Accordingly, the degree of judgment exercised by the Company in determining fair value is greatest for instruments categorized as Level 3. A financial instrument's level within the fair value hierarchy is based on the lowest level of any input that is significant to the fair value measurement.

The carrying amounts reflected in the consolidated balance sheets for cash and cash equivalents, prepaid expenses, other current assets, restricted cash, accounts payable, accrued expenses, deferred revenue, and financing and operating lease liabilities approximate their respective fair values due to their short-term nature.

Property and Equipment

Property and equipment consists of laboratory equipment, computer equipment, furniture and fixtures and leasehold improvements, all of which are stated at cost, less accumulated depreciation. Expenditures for

maintenance and repairs that do not improve or extend the lives of the respective assets are recorded to expense as incurred. Major betterments are capitalized as additions to property and equipment. Depreciation and amortization are recognized over the estimated useful lives of the assets using the straight-line method.

Construction-in-progress is stated at cost, which relates to the cost of leasehold improvements not yet placed into service. No depreciation expense is recorded on construction-in-progress until such time as the relevant assets are completed and put into use.

Impairment of Long-Lived Assets

The Company continually evaluates long-lived assets for potential impairment when events or changes in circumstances indicate the carrying value of the assets may not be recoverable. Recoverability is measured by comparing the book values of the assets to the expected future net undiscounted cash flows that the assets are expected to generate. If such assets are considered to be impaired, the impairment to be recognized is measured by the amount by which the book values of the assets exceed their fair value. The Company has not recognized any impairment losses from inception through December 31, 2021.

Other Long-Term Assets

As of December 31, 2021 and 2020, other long-term assets primarily consisted of advance payments made to the contract research organizations responsible for conducting the Company's tamibarotene and SY-5609 clinical trials.

Revenue Recognition

To date the Company's only revenue has consisted of collaboration and license revenue. The Company has not generated any revenue from product sales and does not expect to generate any revenue from product sales for the foreseeable future. For the year ended December 31, 2021, the Company recognized approximately $23.5 million of revenue, $19.4 million of which was related to the Company's collaboration with Global Blood Therapeutics, Inc. ("GBT"), and $4.1 million of which was related to the Company's target discovery collaboration with Incyte Corporation ("Incyte"). For the year ended December 31, 2020 the Company recognized $15.1 million of revenue, $11.7 million of which was related to the Company's collaboration with GBT, and $3.4 million of which was related to the Company's target discovery collaboration with Incyte. For the year ended December 31, 2019, the Company recognized $2.0 million of revenue, all of which was attributable to the target discovery collaboration with Incyte.

The Company recognizes revenue in accordance with ASC 606, *Revenue from Contracts with Customers* ("ASC 606"). ASC 606 applies to all contracts with customers, except for contracts that are within the scope of other standards, such as leases, insurance, collaboration arrangements and financial instruments. Under ASC 606, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration the entity expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that an entity determines are within the scope of ASC 606, the entity performs the following five steps:

(i) identify the contract(s) with a customer;

(ii) identify the performance obligations in the contract;

(iii) determine the transaction price;

(iv) allocate the transaction price to the performance obligations in the contract; and

(v) recognize revenue when (or as) the entity satisfies a performance obligation.

The Company only applies the five-step model to contracts when it is probable that the entity will collect the consideration it is entitled to in exchange for the goods or services it transfers to the customer. If a contract is determined to be within the scope of ASC 606 at inception, the Company assesses the goods or services promised within such contract, determines which of those goods and services are performance obligations, and assesses whether each promised good or service is distinct. The Company then recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied.

If the Company performs by transferring goods or services to a customer before the customer pays consideration or before payment is due, the Company records a contract asset, excluding any amounts presented as accounts receivable. The Company includes contract assets as unbilled accounts receivable on its consolidated balance sheets. The Company records accounts receivable for amounts billed to the customer for which the Company has an unconditional right to consideration. The Company assesses contract assets and accounts receivable for impairment and, to date, no impairment losses have been recorded.

From time to time, the Company may enter into agreements that are within the scope of ASC 606. The terms of these arrangements typically include payment to the Company of one or more of the following: non-refundable, up-front license fees or prepaid research and development services; development, regulatory and commercial milestone payments; and royalties on net sales of licensed products. Each of these payments results in license and collaboration revenues, except for revenues from royalties on net sales of licensed products, which will be classified as royalty revenues.

The Company analyzes its collaboration arrangements to assess whether they are within the scope of ASC 808,*Collaborative Arrangements* ("ASC 808"), to determine whether such arrangements involve joint operating activities performed by parties that are both active participants in the activities and exposed to significant risks and rewards dependent on the commercial success of such activities. This assessment is performed throughout the life of the arrangement based on changes in the responsibilities of all parties in the arrangement. For collaboration arrangements within the scope of ASC 808 that contain multiple elements, the Company first determines which elements of the collaboration are deemed to be within the scope of ASC 808 and those that are more reflective of a vendor-customer relationship and therefore within the scope of ASC 606. For elements of collaboration arrangements that are accounted for pursuant to ASC 808, an appropriate recognition method is determined and applied consistently, generally by analogy to ASC 606. For those elements of the arrangement that are accounted for pursuant to ASC 606, the Company applies the five-step model described above.

Research and Development

Expenditures relating to research and development are expensed in the period incurred. Research and development expenses consist of both internal and external costs associated with the development of the Company's gene control platform and product candidates. Research and development costs include salaries and benefits, materials and supplies, external research, preclinical and clinical development expenses, stock-based compensation expense and facilities costs. Facilities costs primarily include the allocation of rent, utilities, depreciation and amortization.

In certain circumstances, the Company is required to make nonrefundable advance payments to vendors for goods or services that will be received in the future for use in research and development activities. In such circumstances, the nonrefundable advance payments are deferred and capitalized, even when there is no alternative future use for the research and development, until related goods or services are provided.

The Company records accruals for estimated ongoing research costs. When evaluating the adequacy of the accrued liabilities, the Company analyzes progress of the work being performed, including the phase or

completion of the event, invoices received and costs. Significant judgements and estimates may be made in determining the accrued balances at the end of any reporting period. Actual results could differ from the Company's estimates.

The Company may in-license the rights to develop and commercialize product candidates. For each in-license transaction the Company evaluates whether it has acquired processes or activities along with inputs that would be sufficient to constitute a "business" as defined under U.S. GAAP. A "business" as defined under U.S. GAAP consists of inputs and processes applied to those inputs that have the ability to create outputs. Although businesses usually have outputs, outputs are not required for an integrated set of activities to qualify as a business. When the Company determines that it has not acquired sufficient processes or activities to constitute a business, any up-front payments, as well as milestone payments, are immediately expensed as acquired research and development in the period in which they are incurred.

Warrants

The Company accounts for issued warrants as either liability or equity in accordance with ASC 480-10, *Accounting for Certain Financial Instruments with Characteristics of both Liabilities and Equity* ("ASC 480-10") or ASC 815-40, *Accounting for Derivative Financial Instruments Indexed to, and Potentially Settled in, a Company's Own Stock* ("ASC 815-40"). Under ASC 480-10, warrants are considered liability if they are mandatorily redeemable and they require settlement in cash or other assets, or a variable number of shares. If warrants do not meet liability classification under ASC 480-10, the Company considers the requirements of ASC 815-40 to determine whether the warrants should be classified as liability or equity. Under ASC 815-40, contracts that may require settlement for cash are liabilities, regardless of the probability of the occurrence of the triggering event. Liability classified warrants are measured at fair value on the issuance date and at the end of each reporting period. Any change in the fair value of the warrants after the issuance date is recorded in the consolidated statements of operations as a gain or loss. If warrants do not require liability classification under ASC 815-40, in order to conclude warrants should be classified as equity, the Company assesses whether the warrants are indexed to its common stock and whether the warrants are classified as equity under ASC 815-40 or other applicable GAAP. Equity classified warrants are accounted for at fair value on the issuance date with no changes in fair value recognized after the issuance date.

Stock-Based Compensation Expense

The Company accounts for its stock-based compensation awards in accordance with ASC 718, *Compensation—Stock Compensation* ("ASC 718"). ASC 718 requires all stock-based payments to employees and directors, including grants of restricted stock units and stock option awards, to be recognized as expense in the consolidated statements of operations based on their grant date fair values. Effective January 1, 2019, grants of restricted stock units and stock option awards to other service providers, referred to as non-employees, are measured based on the grant-date fair value of the award and expensed in the Company's consolidated statement of operations over the vesting period. Through December 31, 2018, grants of restricted stock unit and stock option awards to non-employees were required to be recognized as expense in the consolidated statements of operations based on their vesting date fair values. The Company estimates the fair value of stock options granted using the Black-Scholes option-pricing model. Prior to June 30, 2016, the Company was a private company and, therefore, lacks Company-specific historical and implied volatility information. As a result, the Company estimates its expected stock volatility based on a combination of its historical volatility and that of a publicly traded set of peer companies. The Company expects to continue to do so until such time as it has adequate historical data regarding the volatility of its own traded stock price. The expected term of the Company's stock options has been determined utilizing the "simplified" method for awards that qualify as "plain-vanilla" options. Through December 31, 2018, the expected term of stock options granted to non-employees was equal to the contractual term of the option award. Effective January 1, 2019, the expected term of stock options to

non-employees can be determined using either the contractual term of the option award or the "simplified" method. The Company elected to continue to use the contractual term in determining the expected term of the stock option. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the time of grant of the award for time periods approximately equal to the expected term of the award. Expected dividend yield is based on the fact that the Company has never paid cash dividends and does not expect to pay any cash dividends in the foreseeable future. The Company uses the value of its common stock to determine the fair value of restricted stock awards.

The Company expenses the fair value of its stock-based awards to employees and non-employees on a straight-line basis over the associated service period, which is generally the vesting period. The Company accounts for forfeitures as they occur instead of estimating forfeitures at the time of grant. Ultimately, the actual expense recognized over the vesting period will be for only those options that vest.

Compensation expense for discounted purchases under the employee stock purchase plan is measured using the Black-Scholes model to compute the fair value of the lookback provision plus the purchase discount and is recognized as compensation expense over the offering period.

For stock-based awards that contain performance-based milestones, the Company records stock-based compensation expense in accordance with the accelerated attribution model. Management evaluates when the achievement of a performance-based milestone is probable based on the expected satisfaction of the performance conditions as of the reporting date. For certain of the performance-based awards, notwithstanding any vesting in accordance with the achievement of performance-based milestones, such awards vest in full on the sixth anniversary of the vesting commencement date. Compensation expense for such awards is recognized over the six-year vesting period unless management determines that the achievement of any performance-based milestones is probable, in which case expense is accelerated. Compensation expense related to these awards were all recognized as of December 31, 2020 as the performance-based milestones were achieved.

Income Taxes

The Company accounts for uncertain tax positions using a more-likely-than-not threshold for recognizing and resolving uncertain tax positions. The evaluation of uncertain tax positions is based on factors including, but not limited to, changes in the law, the measurement of tax positions taken or expected to be taken in tax returns, the effective settlement of matters subject to audit, new audit activity, and changes in facts or circumstances related to a tax position.

Net Loss per Share

Basic net earnings per share applicable to common stockholders is calculated by dividing net earnings applicable to common stockholders by the weighted average shares outstanding during the period, without consideration for common stock equivalents. Diluted net earnings per share applicable to common stockholders is calculated by adjusting the weighted average shares outstanding for the dilutive effect of common stock equivalents outstanding for the period, determined using the treasury-stock method and the if-converted method. For purposes of the calculation of dilutive net loss per share applicable to common stockholders, stock options, unvested restricted stock units, and warrants are considered to be common stock equivalents but are excluded from the calculation of diluted net loss per share applicable to common stockholders, as their effect would be anti-dilutive; therefore, basic and diluted net loss per share applicable to common stockholders were the same for all periods presented.

As of December 31, 2021 and 2020, 1,000,000 Pre-Funded Warrants to purchase common stock, issued in connection with the December 2020 private placement (refer to Note 11), were included in the basic and diluted net loss per share calculation.

The following common stock equivalents were excluded from the calculation of diluted net loss per share applicable to common stockholders for the periods indicated because including them would have had an anti-dilutive effect:

	As of December 31,		
	2021	2020	2019
Stock options	6,657,268	5,468,605	4,618,421
Unvested restricted stock units	2,687,487	1,734,383	1,116,358
Warrants*	4,990,156	4,990,156	2,118,094
Total	14,334,911	12,193,144	7,852,873

* As of December 31, 2021 and 2020, this is comprised of 2,117,094 2019 Warrants to purchase common stock issued in connection with the Company's April 2019 financing (refer to Note 11), 27,548 warrants to purchase common stock issued in connection with the execution and first draw of the Loan Agreement in February 2020 (refer to Note 7), 17,389 warrants to purchase common stock issued in connection with the second draw on the Loan Agreement in December 2020 (refer to Note 7), and 2,828,125 warrants to purchase common stock issued in connection with the private placement in December 2020 (refer to Note 11). As of December 31, 2019, this was comprised solely of 2,118,094 2019 Warrants to purchase common stock issued in connection with the Company's April 2019 financing.

The weighted average number of common shares used in net loss per share applicable to common stockholders on a basic and diluted basis were 62,534,978, 46,051,617 and 40,222,182 shares for the years ended December 31, 2021, 2020 and 2019, respectively.

Recent Accounting Pronouncements

In August 2020, the FASB issued ASU No. 2020-06, *Debt—Debt with Conversion and Other Options (Subtopic 470-20) and Derivatives and Hedging—Contracts in Entity's Own Equity (Subtopic 815-40): Accounting for Convertible Instruments and Contracts in an Entity's Own Equity* ("ASU 2020-06"). The amendments in ASU 2020-06 simplify the accounting for certain financial instruments with characteristics of liabilities and equity, including convertible instruments and contracts on an entity's own equity. The standard is effective for public companies for fiscal years, and interim periods within those fiscal years, beginning after December 15, 2021. Early adoption is permitted. The Company is currently evaluating this new standard and does not anticipate that it will have a material impact on its consolidated financial statements and related disclosures.

In June 2016, the FASB issued ASU 2016-13, *Financial Instruments-Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments* ("ASU 2016-13"), which requires the measurement and recognition of expected credit losses for financial assets held at amortized cost. ASU 2016-13 replaces the existing incurred loss impairment model with an expected loss model that requires the use of forward-looking information to calculate credit loss estimates. It also eliminates the concept of other-than-temporary impairment and requires credit losses on available-for-sale debt securities to be recorded through an allowance for credit losses instead of as a reduction in the amortized cost basis of the securities. As a smaller reporting company, ASU 2016-13 will become effective for the Company for fiscal years beginning after December 15, 2022, and

early adoption is permitted. The Company is currently evaluating this new standard and does not anticipate that it will have a material impact on its consolidated financial statements and related disclosures.

Recently Adopted Accounting Pronouncements

In December 2019, the FASB issued ASU2019-12, *Income Taxes (Topic 740)* ("ASU 2019-12"), which simplifies the accounting for income taxes. The Company adopted ASU 2019-12 effective January 1, 2021, and the adoption of the new standard did not have a significant impact on the Company's consolidated financial statements.

3. Collaboration and Research Arrangements

Collaboration with Global Blood Therapeutics

On December 17, 2019, the Company entered into a license and collaboration agreement (the "GBT Collaboration Agreement") with Global Blood Therapeutics, Inc. ("GBT"), pursuant to which the parties agreed to a research collaboration to discover novel targets that induce fetal hemoglobin in order to develop new small molecule treatments for sickle cell disease and beta thalassemia. The research term (the "Research Term") is for an initial period of three years and can be extended for up to two (2) additional one-year terms upon mutual agreement.

Pursuant to the terms of the GBT Collaboration Agreement, GBT agreed to pay the Company an upfront payment of $20.0 million, which was collected in January 2020. GBT also agreed to reimburse the Company for full-time employee and out-of-pocket costs and expenses incurred by the Company in accordance with the agreed-upon research budget, which is anticipated to total approximately $40.0 million over the initial Research Term.

The Company granted to GBT an option (the "Option") to obtain an exclusive, worldwide license, with the right to sublicense, under relevant intellectual property rights and know-how of the Company arising from the collaboration to develop, manufacture and commercialize any compounds or products resulting from the collaboration. GBT may exercise the Option at any time during the period (i) commencing on the earlier of (a) the date of GBT's designation of the first product candidate to enter into investigational new drug application-enabling studies, or (b) if no such candidate is designated as of the expiration of the Research Term, the date of expiration of the Research Term, and (ii) ending on the 180th day after the date of expiration or earlier termination of the Research Term. GBT's exercise of the Option will be subject to any required filings with the applicable antitrust authority as required by the antitrust laws and satisfaction of any applicable antitrust conditions.

Should GBT exercise its Option, the Company could receive up to $315.0 million in option exercise, development, regulatory, commercialization and sales-based milestones per product candidate and product resulting from the collaboration.

The Company will also be entitled to receive, subject to certain reductions,tiered mid-to-high single digit royalties as percentages of calendar year net sales on any product.

Either party may terminate the GBT Collaboration Agreement for the other party's uncured material breach or insolvency, and in certain other specified circumstances, subject to specified notice and cure periods. GBT may unilaterally terminate the GBT Collaboration Agreement in its entirety, for any or no reason, upon nine-months' prior written notice to the Company if such notice is delivered during the Research Term, or 90 days' prior written notice to the Company if such notice is delivered after the expiration or termination of the Research Term.

GBT Collaboration Revenue

The Company analyzed the GBT Collaboration Agreement and concluded that it represents a contract with a customer within the scope of ASC 606.

The Company has identified a single performance obligation, which includes a(i) non-exclusive research license that GBT will have access to during the initial Research Term and (ii) research and development services provided during the initial Research Term. The GBT Collaboration Agreement includes the Option. The Option does not provide a material right to GBT that it would receive without entering into the GBT Collaboration Agreement, principally because the Option exercise fee is at least equal to the standalone selling price for the underlying goods. The non-exclusive research license is not distinct as GBT cannot benefit from the license without the research and development services that are separately identifiable in the contract. The non-exclusive research license only allows GBT to evaluate the candidate compounds developed under the research plan or to conduct work allocated to it during the Research Term. GBT cannot extract any benefit from the non-exclusive research license without the research and development services performed by the Company, including the provision of data package information. As such, these two promises are inputs to a combined output (the delivery of data package allowing GBT to make an Option exercise decision) and are bundled into a single performance obligation (the non-exclusive research license and research and development service performance obligation).

At inception, the total transaction price was determined to be approximately $60.0 million, which consisted of a $20.0 million upfront non-refundable and non-creditable technology access fee and approximately $40.0 million in reimbursable costs for employee and external research and development expenses. The GBT Collaboration Agreement also provides for development and regulatory milestones which are only payable subsequent to the exercise of the Option, and therefore are excluded from transaction price at inception. The Company will re-evaluate the transaction price at the end of each reporting period and as uncertain events are resolved or other changes in circumstances occur. As of December 31, 2021, the Company reduced the transaction price from the initial estimate of $60.0 million to $54.2 million. The reduction of the transaction price was driven by a lower actual cost reimbursement and 2022 reimbursable cost budget approved by the Company and GBT.

ASC 606 requires an entity to recognize revenue only when it satisfies a performance obligation by transferring a promised good or service to a customer. A good or service is considered to be transferred when the customer obtains control. As the non-exclusive research license and research and development services represent one performance obligation, the Company has determined that it will satisfy its performance obligation over a period of time as services are performed and GBT receives the benefit of the services, as the overall purpose of the arrangement is for the Company to perform the services. The Company will recognize revenue associated with the performance obligation as the research and development services are provided using an input method, according to the costs incurred as related to the research and development activities and the costs expected to be incurred in the future to satisfy the performance obligation. The transfer of control occurs during this time and is the best measure of progress towards satisfying the performance obligation.

The Company had no account receivable balance as of December 31, 2021 and 2020. The Company had contract asset balances of $3.0 million and $2.3 million as of December 31, 2021 and 2020, respectively. As of December 31, 2021, the Company had deferred revenue related to the GBT Collaboration Agreement of $9.0 million, all of which was classified as deferred revenue, current portion on the Company's consolidated balance sheet. As of December 31, 2020, the Company had deferred revenue of $16.7 million, of which $8.4 million and $8.3 million was classified as deferred revenue, current portion and deferred revenue, net of current portion, respectively, on the Company's consolidated balance sheet. The Company recognized revenue under the GBT Collaboration Agreement of $19.4 million and $11.7 million, respectively, during the years ended December 31, 2021 and 2020.

Agreements with Incyte Corporation

In January 2018, the Company and Incyte entered into a Target Discovery, Research Collaboration and Option Agreement (the "Incyte Collaboration Agreement"). The Incyte Collaboration Agreement was amended in November 2019. Under the Incyte Collaboration Agreement, the Company is using its proprietary gene control platform to identify novel therapeutic targets with a focus on myeloproliferative neoplasms, and Incyte has received options to obtain exclusive worldwide rights to intellectual property resulting from the collaboration for the development and commercialization of therapeutic products directed to up to seven validated targets. For each option exercised by Incyte, Incyte will have the exclusive worldwide right to use the licensed intellectual property to develop and commercialize therapeutic products that modulate the target as to which the option was exercised. Under the terms of the Collaboration Agreement, Incyte paid the Company $10.0 million in up-front consideration, consisting of $2.5 million in cash and $7.5 million in pre-paid research funding (the "Prepaid Research Amount"). The Company's activities under the Collaboration Agreement are subject to a joint research plan and, subject to certain exceptions, Incyte is responsible for funding the Company's activities under the research plan, including amounts in excess of the Prepaid Research Amount.

In January 2018, the Company also entered into a Stock Purchase Agreement with Incyte (the "Stock Purchase Agreement") whereby, for an aggregate purchase price of $10.0 million, Incyte purchased 793,021 shares of the Company's common stock at $12.61 per share. Under the terms of the Stock Purchase Agreement, the shares were purchased at a 30% premium over the volume-weighted sale price of the shares of the Company's common stock over the 15-trading day period immediately preceding the date of the Stock Purchase Agreement.

Incyte Collaboration Revenue

The Company analyzed the Incyte Collaboration Agreement and concluded that it represents a contract with a customer within the scope of ASC 606.

The Company identified a single performance obligation which includes (i) a research license that Incyte retains as long as there remains an unexercised option (the "Research License") and (ii) research and development services provided during the research term. The Incyte Collaboration Agreement includes options to (x) obtain additional time to exercise the license options for certain targets designated as definitive validation targets and (y) obtain license rights to each validated target, both of which were not considered by the Company's management to be material rights, and therefore not performance obligations, at inception.

At inception, the total transaction price was determined to be $12.3 million. Following a November 2019 amendment, the total transaction price is now $12.8 million, consisting of a $2.5 million upfront non-refundable and non-creditable payment, the $7.5 million Prepaid Research Amount and $2.3 million in premium paid on the equity investment made pursuant the Stock Purchase Agreement and $0.5 million of additional consideration. The Company accounted for the contract amendment as a modification as if it were part of the existing contract as the remaining goods and services are not distinct, and therefore form part of a single performance obligation that was partially satisfied at the date of the amendment.

The Incyte Collaboration Agreement also provides for development and regulatory milestones that are only payable subsequent to the exercise of an option and were therefore excluded from transaction price at inception. The Company re-evaluates the transaction price at the end of each reporting period and as uncertain events are resolved or other changes in circumstances occur.

The Company recognizes revenue associated with the performance obligation as the research and development services are provided using an input method, according to the costs incurred as related to the

research and development activities and the costs expected to be incurred in the future to satisfy the performance obligation. The transfer of control occurs during this time and is the best measure of progress towards satisfying the performance obligation.

During the years ended December 31, 2021, 2020 and 2019, the Company recognized $4.1 million, $3.4 million and $2.0 million of revenue, respectively, under the Incyte Collaboration Agreement. As of December 31, 2021, the Company has deferred revenue outstanding under the Incyte Collaboration Agreement of approximately $1.3 million, all of which was classified as deferred revenue, current portion on the Company's consolidated balance sheets.

The following table presents the changes in contract assets and liabilities for the year ended December 31, 2021 (in thousands):

	Balance at December 31, 2020	Additions	Deductions	Balance at December 31, 2021
Accounts receivable and contract assets:				
Billed receivables from collaboration partners	$ 7	$ 10,931	$ (10,938)	$ —
Unbilled receivables from collaboration partners	2,324	11,410	(10,755)	2,979
Total accounts receivable and contract assets	$ 2,331	$ 22,341	$ (21,693)	$ 2,979
Contract liabilities:				
Deferred revenue – Incyte	$ 5,365	$ —	$ (4,097)	$ 1,268
Deferred revenue – GBT	16,721	174	(7,982)	8,913
Total contract liabilities	$ 22,086	$ 174	$ (12,079)	$ 10,181

The change in deferred revenue is due to the timing of the payments and the recognition of revenue related to the Company's collaboration agreements during the period.

4. Cash, Cash Equivalents and Marketable Securities

Cash equivalents are highly liquid investments that are readily convertible into cash with original maturities of three months or less when purchased. Marketable securities consist of securities with original maturities greater than 90 days when purchased. The Company classifies these marketable securities as available-for-sale and records them at fair value in the accompanying consolidated balance sheets. Unrealized gains or losses are included in accumulated other comprehensive loss. Premiums or discounts from par value are amortized to other income over the life of the underlying security.

Cash, cash equivalents and marketable securities, available-for-sale, consisted of the following at December 31, 2021 and December 31, 2020 (in thousands):

December 31, 2021	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Cash and cash equivalents:				
Cash and money market funds	$ 92,302	$ —	$ —	$ 92,302
Marketable securities:				
Corporate debt securities – due in one year or less	30,100	—	(12)	30,088
US Treasury obligation – due in one year or less	8,000	—	(21)	7,979
Corporate debt securities – due in more than one year to five years	9,085	—	(33)	9,052
US Treasury obligation – due in more than one year to five years	3,999	—	(13)	3,986
Total	$143,486	$ —	$ (79)	$143,407

December 31, 2020	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Cash and cash equivalents:				
Cash and money market funds	$173,984	$ —	$ —	$173,984
Total	$173,984	$ —	$ —	$173,984

Although available to be sold to meet operating needs or otherwise, securities are generally held through maturity. The cost of securities sold is determined based on the specific identification method for purposes of recording realized gains and losses. During the years ended December 31, 2021, 2020 and 2019, there were no realized gains or losses on sales of investments, and no investments were adjusted for other than temporary declines in fair value.

As of December 31, 2021, marketable securities with maturities of one year or less when purchased are presented in current assets and those with maturities of more than one year are presented in the noncurrent assets in the accompanying condensed consolidated balance sheet. There were no marketable securities held as of December 31, 2020.

As of December 31, 2021, the Company held eleven securities that were in an unrealized loss position. The aggregate fair value of securities held by the Company in an unrealized loss position for less than twelve months as of December 31, 2021 was $30.1 million. There were no securities held by the Company in an unrealized loss position for more than twelve months as of December 31, 2021. The Company has the intent and ability to hold such securities until recovery. The Company determined that there was no material change in the credit risk of the above marketable securities during the year ended December 31, 2021. As a result, the Company determined it did not hold any marketable securities with an other than temporary impairment as of December 31, 2021.

5. Fair Value Measurements

Assets and liabilities measured at fair value on a recurring basis as of December 31, 2021 and 2020 were as follows (in thousands):

Description	December 31, 2021	Active Markets (Level 1)	Observable Inputs (Level 2)	Unobservable Inputs (Level 3)
Assets:				
Cash	$ 57,213	$ 57,213	$ —	$ —
Money market funds	35,089	35,089	—	—
Corporate debt securities – due in one year or less	30,088	—	30,088	—
US Treasury obligation – due in one year or less	7,979	7,979	—	—
US Treasury obligation – due in more than one year to five years	3,986	3,986	—	—
Corporate debt securities – due in more than one year to five years	9,052	—	9,052	—
Total	$ 143,407	$104,267	$ 39,140	$ —
Liabilities:				
Warrant liability	$ 3,029	$ —	$ —	$ 3,029
Total	$ 3,029	$ —	$ —	$ 3,029

Description	December 31, 2020	Active Markets (Level 1)	Observable Inputs (Level 2)	Unobservable Inputs (Level 3)
Assets:				
Cash	$ 47,579	$ 47,579	$ —	$ —
Money market funds	126,405	126,405	—	—
Total	$ 173,984	$173,984	$ —	$ —
Liabilities:				
Warrant liability	$ 19,711	$ —	$ —	$ 19,711
Total	$ 19,711	$ —	$ —	$ 19,711

Assumptions Used in Determining Fair Value of Warrants

The Company issued Warrants in connection with private placement on December 8, 2020 (see Note 11). In the event of certain fundamental transactions involving the Company, the Warrant holders may require the Company to make a payment based on a Black-Scholes valuation, using specified inputs; therefore, these Warrants were accounted as liabilities. The Company recorded the fair value of the Warrants upon issuance using the Black-Scholes valuation model and is required to revalue the Warrants at each reporting date with any changes in fair value recorded on our statement of operations. The valuation of the Warrants is considered under Level 3 of the fair value hierarchy and influenced by the fair value of the underlying common stock of the Company.

A summary of the Black Scholes pricing model assumptions used to record the fair value of the warrants is as follows:

	December 31, 2021	December 31, 2020
Stock price	$ 3.26	$ 10.85
Risk-free interest rate	1.11%	0.35%
Dividend yield	—	—
Expected life (in years)	3.94	4.94
Expected volatility	81.14%	82.66%

Changes in Level 3 Liabilities Measured at Fair Value on a Recurring Basis

The following table reflects the change in the Company's Level 3 Warrant liability for the years ended December 31, 2021 and December 31, 2020 (in thousands):

	December 31, 2021	December 31, 2020
Fair value of warrant liability as of beginning of year	$ 19,711	$ 19,336
Change in fair value	(16,682)	375
Fair value of warrant liability as of end of year	$ 3,029	$ 19,711

6. Restricted Cash

As of December 31, 2021, the Company had $3.1 million in restricted cash, which was classified as long-term on the Company's consolidated balance sheets. The restricted cash pertained to the $3.1 million letter of credit issued by the Company in connection with the 2019 Lease (See Note 10). The letter of credit will expire 95 days after expiration or early termination of the 2019 Lease. The Company will have the right, under certain conditions, to reduce the amount of the letter of credit to $2.1 million in October 2023.

The following table provides a reconciliation of cash, cash equivalents, and restricted cash reported within the consolidated balance sheets that sum to the total of the amounts shown in the consolidated statement of cash flows as of December 31, 2021, 2020, 2019 and 2018 (in thousands):

	December 31,			
	2021	2020	2019	2018
Cash and cash equivalents	$92,302	$173,984	$41,441	$49,886
Restricted cash, current portion	—	—	290	638
Restricted cash, net of current portion	3,086	3,086	3,086	290
Total cash, cash equivalents and restricted cash	$95,388	$177,070	$44,817	$50,814

7. Oxford Finance Loan Agreement

On February 12, 2020, the Company entered into a Loan and Security Agreement (the "Loan Agreement") with Oxford Finance LLC (the "Lender"). Pursuant to the Loan Agreement, a term loan of up to an aggregate principal amount of $60.0 million is available to the Company. A $20.0 million term loan (first tranche) was funded on February 12, 2020, and another $20.0 million term loan (second tranche) was funded on December 23, 2020. As of December 31, 2021, the final $20.0 million tranche remained available under the Loan Agreement, at the sole discretion of the Lender.

The term loan bears interest at an annual rate equal to the greater of (i) 7.75% and (ii) the sum of 5.98% and the greater of (A) one-month LIBOR or (B) 1.77%. The Loan Agreement provides for interest-only payments until March 1, 2023, and repayment of the aggregate outstanding principal balance of the term loan in monthly installments starting on March 1, 2023 and continuing through February 1, 2025 (the "Maturity Date"). The Company paid a facility fee of $0.1 million upon the issuance of the first tranche, paid a facility fee of $75,000 upon the issuance of the second tranche, and must pay a $50,000 facility fee if and when the third tranche is issued. The Company is required to make a final payment equal to 5.00% of the amount of the term loan drawn payable on the earlier of (i) the prepayment of the term loan or (ii) the Maturity Date. At the Company's option, the Company may elect to prepay the loans subject to a prepayment fee equal to the following percentage of the principal amount being prepaid: 2% if an advance is prepaid during the first 12 months following the applicable advance date, 1% if an advance is prepaid after 12 months but prior to 24 months following the applicable advance date, and 0.5% if an advance is prepaid any time after 24 months following the applicable advance date but prior to the Maturity Date.

In connection with the Loan Agreement, the Company granted the Lender a security interest in all of the Company's personal property now owned or hereafter acquired, excluding intellectual property (but including the right to payments and proceeds of intellectual property), and a negative pledge on intellectual property. The Loan Agreement also contains certain events of default, representations, warranties and non-financial covenants of the Company.

In connection with the issuance of the first tranche, the Company issued the Lender warrants to purchase 27,548 shares of the Company's common stock at an exercise price per share of $7.26 in February 2020. In connection with the issuance of the second tranche, the Company issued the Lender warrants to purchase 17,389 shares of the Company's common stock at an exercise price of $11.50 per share in December 2020 (collectively, the "Oxford Warrants"). The Oxford Warrants are exercisable within five years from the respective dates of issuance.

The Oxford Warrants are classified as a component of permanent equity because they are freestanding financial instruments that are legally detachable and separately exercisable from the shares of common stock with which they were issued, are immediately exercisable, do not embody an obligation for the Company to repurchase its shares, and permit the holders to receive a fixed number of shares of common stock upon exercise. In addition, the Oxford Warrants do not provide any guarantee of value or return. The Company valued the Oxford Warrants at issuance using the Black-Scholes option pricing model and determined the fair value of the Oxford Warrants to be $0.1 million for the first tranche and $0.2 million for the second tranche. The key inputs to the valuation model included an average volatility of 75.43% for the first tranche and 82.41% for the second tranche, and an expected term of 5.0 years for both tranches.

The Company has the following minimum aggregate future loan payments as of December 31, 2021 (in thousands):

Year ending December 31, 2022	$ —
Year ending December 31, 2023	16,666
Year ending December 31, 2024	20,000
Year ending December 31, 2025	3,334
Total minimum payments	$40,000
Less unamortized debt discount	(459)
Plus accumulated accretion of final fees	716
Less current portion	—
Long-term debt, net of current portion	$40,257

For the year ended December 31, 2021, interest expense related to the Loan Agreement was approximately $3.9 million. The total carrying value of debt is classified as long-term on the Company's consolidated balance sheets as of December 31, 2021. The carrying value of the outstanding debt facility approximates its fair value, considering that it bears interest that is similar to prevailing market rates. The debt facility fair value is determined based on the Level 2 fair value hierarchy.

8. Property and Equipment

Property and Equipment consist of the following as of December 31, 2021 and 2020 (in thousands):

	Estimated useful life (in years)	December 31, 2021	December 31, 2020
Construction-in-process	—	$ —	$ 6
Laboratory equipment	5	7,989	7,028
Computer equipment	3	1,979	1,841
Furniture and fixtures	4	1,075	897
Leasehold improvements	*	11,657	11,657
		$ 22,700	$ 21,429
Less: Accumulated depreciation		(9,856)	(7,216)
Total property and equipment, net		$ 12,844	$ 14,213

* Leasehold improvements are depreciated over the shorter of the life of the asset and the term of the lease at 8.2 years and 9.3 years as of December 31, 2021 and 2020, respectively. The Company moved into its corporate headquarters in November 2019 and the 2019 Lease term ends in February 2030.

Depreciation expense, including depreciation expense for two immaterial capital leases, for the years ended December 31, 2021, 2020 and 2019 was $2.8 million, $2.8 million and $2.5 million, respectively.

9. Accrued Expenses

Accrued expenses consist of the following as of December 31, 2021 and 2020 (in thousands):

	December 31, 2021	December 31, 2020
External research and preclinical development	$ 8,274	$ 4,702
Employee compensation and benefits	6,344	5,715
Professional fees	953	602
Facilities and other	53	65
Accrued expenses	$ 15,624	$ 11,084

10. Commitments and Contingencies

Operating Leases

On January 8, 2019, the Company entered into a lease (the "2019 Lease") with respect to approximately 52,859 square feet of space in Cambridge, Massachusetts for a lease term commencing in January 2019 and

ending in February 2030. The Company has the option to extend the lease term for one additional ten (10) year period. The 2019 Lease has escalating rent payments and the Company records rent expense on a straight-line basis over the term of the 2019 Lease, including any rent-free periods. The 2019 Lease includes certain lease incentives in the form of tenant allowances. The 2019 Lease also includes an abatement period in which the Company was not required to remit monthly rent payments until March 2020.

In connection with the execution of the 2019 Lease, the Company was required to provide the landlord with a letter of credit in the amount of $3.1 million (See Note 6).

The Company determined that, for purposes of applying ASC 842, the commencement date of the 2019 Lease occurred on May 1, 2019. The Company recorded a right-of-use asset and lease liability of $15.8 million using an incremental borrowing rate of 9.3%, net of tenant allowances expected to be received of $9.3 million, on the May 1, 2019 lease commencement date. The Company is amortizing the tenant allowance to offset rent expenses over the term of the 2019 Lease starting at the lease commencement date on a straight-line basis. On the Company's consolidated balance sheets, the Company classified $1.7 million and $1.4 million of the lease liability as short-term and $22.9 million and $24.6 million of the lease liability as long-term as of December 31, 2021 and 2020, respectively.

The Company elected the practical expedient provided under ASC 842 and therefore has combined all lease andnon-lease components when determining the right-of-use asset and lease liability for the 2019 Lease.

Financing Lease

In 2019, the Company entered into equipment lease agreements that have a48-month term. At the end of the term of these leases, the Company has the right to return the leased equipment, extend the leases, or buy the equipment at the then-current fair market value of the equipment. The Company accounted for these equipment lease agreements as financing leases under ASC 842 and recorded an aggregate financing lease right-of-use assets and a corresponding financing lease liabilities of approximately $1.0 million at the time of executing these leases.

The following is a maturity analysis of the annual undiscounted cash flows reconciled to the carrying value of the operating and financing lease liabilities as of December 31, 2021 (in thousands):

	Operating	Financing
Year ending December 31, 2022	$ 3,935	$ 313
Year ending December 31, 2023	4,049	66
Year ending December 31, 2024	4,166	—
Year ending December 31, 2025	4,287	—
Year ending December 31, 2026 and beyond	19,256	—
Total minimum lease payments	35,693	379
Less imputed interest	(11,115)	(23)
Total lease liability	$ 24,578	$ 356

The following table outlines the total lease cost for the Company's operating and financing leases as well as weighted average information for these leases as of December 31, 2021 (in thousands):

	Year Ended December 31, 2021
Lease cost:	
Operating lease cost	$ 2,958
Financing lease cost:	
Amortization of right-of-use asset	$ 260
Interest on lease liabilities	48
Total financing lease cost	$ 308
Cash paid for amounts included in the measurement of liabilities:	
Operating cash flows from operating lease	$ 3,823
Operating cash flows from financing lease	$ 312

Other information:	Year Ended December 31, 2021
Weighted-average remaining lease term (in years) – operating lease	8.17
Weighted-average discount rate – operating lease	9.30
Weighted-average remaining lease term (in years) – financing lease	1.26
Weighted-average discount rate – financing lease	9.47

Prior to the adoption of ASC 842 effective January 1, 2019, the Company accounted for its leases under the guidance of ASC 840 as either operating with the liability recorded to the balance sheet based on escalating rent payments or capital and recorded to fixed assets and amortized over the term of the lease.

Asset Purchase Agreement

Orsenix, LLC

On December 4, 2020, the Company entered into an asset purchase agreement (the "Asset Purchase Agreement") with Orsenix, LLC ("Orsenix"), pursuant to which the Company acquired all of Orsenix's assets related to a novel oral form of arsenic trioxide, which the Company refers to as SY-2101. Under the terms of the Asset Purchase Agreement, the Company is required to pay to Orsenix:

- an upfront fee of $12.0 million, which was paid with cash on hand upon the closing of the transaction;
- single-digit million milestone payments related to the development of SY-2101 in indications other than APL;
- $6.0 million following the achievement of a regulatory milestone related to the development of SY-2101 in APL; and
- up to $10.0 million upon the achievement of certain commercial milestones with respect to SY-2101.

The Company's obligation to pay the commercial milestone payments expires following the tenth anniversary of the first commercial sale of SY-2101. The Asset Purchase Agreement requires the Company to use commercially reasonable efforts to develop and commercialize SY-2101 for APL in the United States during

such period, and to use commercially reasonable efforts to dose the first patient in a Phase 3 clinical trial of SY-2101 on or before the third anniversary of the closing of the transaction; however, the Company retains sole discretion to operate the acquired assets as it determines. The assets acquired from Orsenix do not meet the definition of a business under ASC *Business Combinations* (or ASC 805) because substantially all of the fair value of the assets acquired is concentrated in a single identifiable asset, the rights to SY-2101. Furthermore, as the acquired asset does not include a substantive process, the asset does not meet the minimum requirements to be considered a business under ASC 805. As SY-2101 does not have an alternative future use, the Company recorded the $12.0 million upfront cash payment as research and development expense on the date of acquisition in December 2020. The Company will expense any future milestone payments made prior to the time an alternative future use for SY-2101 has been established. Once an alternative future use for SY-2101 has been established, the Company will capitalize milestone payments as an addition to the carrying value ofSY-2101.

License Agreement

TMRC Co. Ltd.

In September 2015, the Company entered into an exclusive license agreement with TMRC Co. Ltd. ("TMRC") to develop and commercialize tamibarotene in North America and Europe for the treatment of cancer. This agreement was amended and restated in April 2016, and further amended in January 2021 to expand the territory under which we are licensed to include Central and South America, Australia, Israel, and Russia.

In exchange for this license, the Company agreed to a non-refundable upfront payment of $1.0 million, for which $0.5 million was paid in September 2015 upon execution of the agreement, and the remaining $0.5 million was paid in May 2016. Under the agreement, the Company is also obligated to make payments upon the successful achievement of clinical and regulatory milestones totaling approximately $13.0 million per indication, defined as a distinct tumor type. The Company paid $1.0 million to TMRC for a development milestone achieved upon the successful dosing of the first patient in its Phase 2 clinical trial of tamibarotene in 2016. In May 2021, the Company paid $2.0 million to TMRC for a development milestone achieved upon the successful dosing of the first patient in its Phase 3 clinical trial of tamibarotene in MDS patients. In September 2021, the Company paid $1.0 million to TMRC for a development milestone achieved upon the successful dosing of the first patient in its Phase 2 clinical trial of tamibarotene in AML patients. In addition, the Company is obligated to pay TMRC a single-digit percentage royalty, on a country-by-country and product-by-product basis, on net product sales of tamibarotene using know-how and patents licensed from TMRC in North America and Europe for a defined royalty term.

The Company also entered into a supply management agreement with TMRC under which the Company agreed to pay TMRC a fee for each kilogram of tamibarotene that is produced. The Company incurred fees of $0.6 million and $0.9 million under this supply management agreement during the years ended December 31, 2021 and 2020, respectively. No payments were made under the supply management agreement during the year ended December 31, 2019.

Litigation

The Company is not party to any litigation and does not have contingency reserves established for any litigation liabilities as of December 31, 2021 or December 31, 2020.

11. Stockholders' equity

Issuance of Securities through an Underwritten Public Offering

On January 22, 2021, the Company issued and sold an aggregate of 5,400,000 shares of its common stock in an underwritten public offering at a public offering price of $14.00 per share, resulting in gross proceeds of $75.6 million before deducting underwriting discounts and commissions and other transaction expenses of approximately $5.1 million.

Issuance of Securities through a Private Placement

On December 8, 2020, through a private placement, the Company issued 10,312,500 shares of common stock, and, in lieu of shares of common stock, Pre-Funded Warrants to purchase an aggregate of 1,000,000 shares of common stock, and, in each case, accompanying Warrants to purchase an aggregate of up to 2,828,125 additional shares of common stock (or Pre-Funded Warrants to purchase common stock in lieu thereof) at a price of $8.00 per share and accompanying Warrant (or $7.99 per Pre-Funded Warrant and accompanying Warrant). The private placement resulted in aggregate gross proceeds of $90.5 million, before $0.4 million of transaction costs.

In the event of certain fundamental transactions involving the Company, the holders of Warrants may require the Company to make a payment based on a Black-Scholes valuation, using specified inputs. The holders of Pre-Funded Warrants do not have similar rights. Therefore, the Company accounted for the Warrants as liabilities, while the Pre-Funded Warrants met the permanent equity criteria classification. The Pre-Funded Warrants are classified as a component of permanent equity because they are freestanding financial instruments that are legally detachable and separately exercisable from the shares of common stock with which they were issued, are immediately exercisable, do not embody an obligation for the Company to repurchase its shares, and permit the holders to receive a fixed number of shares of common stock upon exercise. In addition, the Pre-Funded Warrants do not provide any guarantee of value or return. The initial fair value of the Warrants at issuance was $19.3 million, determined using the Black-Scholes valuation model. The Company remeasured the Warrant's fair value at December 31, 2021 and 2020 as $3.0 million and $19.7 million, respectively. The change in fair value of $16.7 million (loss) and $0.4 million (gain) was recorded in our statement of operations for the years ended December 31, 2021 and 2020, respectively.

Convertible Preferred Stock and 2019 Warrants

On April 9, 2019, the Company completed two concurrent underwritten public offerings of its equity securities. In the first public offering, the Company sold 8,667,333 shares of its common stock and accompanying 2019 Warrants to purchase 1,951,844 shares of the Company's common stock, at a combined price to the public of $7.50 per common share and accompanying 2019 Warrant. In the second public offering, the Company sold 666 shares of its Series A Preferred Stock, and accompanying 2019 Warrants to purchase 166,500 shares of the Company's common stock, at a combined public offering price of $7,500 per share and accompanying 2019 Warrant. The offerings resulted in aggregate gross proceeds to the Company of $70.0 million, before underwriting discounts and commissions and offering expenses payable by the Company of approximately $5.0 million.

In November 2019, all 666 shares of Series A Preferred Stock were converted to 666,000 shares of common stock. As of December 31, 2021, there were no shares of our Series A Preferred Stock outstanding.

Each 2019 Warrant has an exercise price per share of common stock of $8.625, subject to adjustment in certain circumstances, and will expire on October 10, 2022. Each 2019 Warrant is immediately exercisable,

provided that the holder is prohibited, subject to certain exceptions, from exercising the 2019 Warrant for shares of the Company's common stock to the extent that immediately prior to or after giving effect to such exercise, the holder, together with its affiliates and other attribution parties, would own more than 4.99% of the total number of shares of the Company's common stock then issued and outstanding. This percentage may be changed at the holders' election to a higher or lower percentage upon 61 days' notice to the Company.

The Company evaluated the Series A Preferred Stock and 2019 Warrants for liability or equity classification in accordance with the provisions of ASC 480, *Distinguishing Liabilities from Equity*, and determined that equity treatment was appropriate because neither the Series A Preferred Stock nor the 2019 Warrants met the definition of liability instruments.

The Series A Preferred Stock was not mandatorily redeemable and did not embody an obligation to buy back the shares outside of the Company's control in a manner that could require the transfer of assets. Additionally, the Company determined that the Series A Preferred Stock would be recorded as permanent equity, not temporary equity, given that the holders of equally and more subordinated equity would be entitled to receive the same form of consideration upon the occurrence of the event that gives rise to the redemption or events of redemption that are within the control of the Company.

Additionally, as the effective conversion price of the Series A Preferred Stock of $6.57 was below the fair value of the Company's common stock on the date of issuance of $7.50, the Company determined that the Series A Preferred Stock included a beneficial conversion feature. The Company calculated the beneficial conversion feature to be approximately $0.6 million, which was recorded as a discount to the Series A Preferred Stock at the time of issuance.

The 2019 Warrants are classified as a component of permanent equity because they are freestanding financial instruments that are legally detachable and separately exercisable from the shares of common stock with which they were issued, are immediately exercisable, do not embody an obligation for the Company to repurchase its shares, and permit the holders to receive a fixed number of shares of common stock upon exercise. In addition, the 2019 Warrants do not provide any guarantee of value or return. The Company valued the 2019 Warrants at issuance using the Black-Scholes option pricing model and determined the fair value of the 2019 Warrants to purchase 2,118,344 shares of the Company's common stock at $9.0 million. The key inputs to the valuation model included an average volatility of 86.06% and an expected term of 3.5 years.

As of December 31, 2021, 2019 Warrants to purchase 2,117,094 shares of common stock are outstanding and remain unexercised.

12. Stock-Based Payments

2016 Stock Incentive Plan

The 2016 Stock Incentive Plan (the "2016 Plan") was adopted by the board of directors on December 15, 2015, approved by the stockholders on June 17, 2016, and became effective on July 6, 2016 upon the closing of the Company's initial public offering ("IPO"). The 2016 Plan replaced the 2012 Equity Incentive Plan (the "2012 Plan"). Any options or awards outstanding under the 2012 Plan remained outstanding and effective. Under the 2016 Plan, the Company may grant incentive stock options, non-statutory stock options, stock appreciation rights, restricted stock, restricted stock units and other stock-based awards. The number of shares of the Company's common stock reserved for issuance under the 2016 Plan automatically increases on the first day of each calendar year, through the 2025 calendar year, in an amount equal to the least of (i) 1,600,000 shares of common stock, (ii) 4.0% of the outstanding shares of common stock as of such date, or (iii) such lesser amount

as specified by the board of directors. This number is subject to adjustment in the event of a stock split, stock dividend or other change in the Company's capitalization. For the calendar year beginning January 1, 2021, the number of shares reserved for issuance under the 2016 Plan was increased by 1,600,000 shares. At December 31, 2021, 2,238,206 shares remained available for future issuance under the 2016 Plan. Under the 2016 Plan, stock options may not be granted at less than fair value on the date of grant.

2016 Employee Stock Purchase Plan

The 2016 Employee Stock Purchase Plan (the "2016 ESPP") was adopted by the board of directors on December 15, 2015, approved by the stockholders on June 17, 2016, and became effective on July 6, 2016 upon the closing of the IPO. The number of shares of the Company's common stock reserved for issuance under the 2016 ESPP automatically increases on the first day of each calendar year through the 2025 calendar year, in an amount equal to the least of (i) 1,173,333 shares of the Company's common stock, (ii) 1.0% of the total number of shares of the Company's common stock outstanding on the first day of the applicable year, and (iii) an amount determined by the Company's board of directors. For the calendar year beginning January 1, 2021, the number of shares reserved for issuance under the 2016 ESPP was increased by 562,227 shares. At December 31, 2021, 2,237,065 shares remained available for future issuance under the 2016 ESPP.

Inducement Grants

During the year ended December 31, 2021, the Company granted non-statutory stock options to purchase an aggregate of 1,110,000 shares of the Company's common stock. These stock options were granted outside of the 2016 Plan as an inducement material to the applicable employee's acceptance of employment with the Company in accordance with Nasdaq Listing Rule 5635(c)(4).These stock options will vest over a four-year period, with 25% of the shares underlying each option award vesting on the one-year anniversary of the applicable employee's employment commencement date and the remaining 75% of the shares underlying each award vesting monthly thereafter for three-years. Vesting of each option is subject to such employee's continued service with the Company through the applicable vesting dates.

Stock Options

Terms of stock option agreements, including vesting requirements, are determined by the board of directors, subject to the provisions of the 2016 Plan. Stock option awards granted by the Company generally vest over four years, with 25% vesting on the first anniversary of the vesting commencement date and 75% vesting ratably, on a monthly basis, over the remaining three years. Such awards have a contractual term of ten years from the grant date.

The Company has granted stock options to management for which vesting accelerates upon the achievement of performance-based criteria. Milestone events are specific to the Company's corporate goals, including but not limited to certain clinical development milestones and the Company's ability to execute on its corporate development and financing strategies. Stock-based compensation expense associated with these performance-based stock options is recognized based on the accelerated attribution model. Management evaluates when the achievement of a performance-based milestone is probable based on the expected satisfaction of the performance conditions as of the reporting date. Notwithstanding any vesting in accordance with the achievement of performance-based milestones, such awards vest in full on the sixth anniversary of the vesting commencement date. During each of the years ended December 31, 2020 and 2019, the Company recorded additional stock-based compensation expense of $0.4 million related to the acceleration of vesting of certain stock options associated with the initiation of the Phase 3 clinical trial of tamibarotene at the end of 2020 and the entry into the GBT Collaboration Agreement in December 2019, respectively. As of December 31, 2020, there was no unrecognized

expense related to the performance-based stock options granted to management. The Company did not grant any performance-based stock option to management during the year ended December 31, 2021.

The Company has granted options to purchase 75,000 shares of common stock to an advisor that vest solely upon the achievement of performance-based criteria. As of December 31, 2021, none of these performance-based criteria had been achieved. As of December 31, 2021, there was $0.3 million of unrecognized compensation cost related to this option, with a remaining contractual period of 4.7 years.

A summary of the status of stock options as of December 31, 2021 and December 31, 2020 and changes during the year ended December 31, 2021 is presented below:

	Shares	Weighted Average Exercise Price	Remaining Contractual Life (in years)	Aggregate Intrinsic Value (in thousands)
Outstanding at December 31, 2020	5,468,605	$ 8.90	7.2	$ 13,124
Granted	2,417,600	7.69		
Exercised	(20,134)	7.77		
Cancelled	(1,208,803)	10.00		
Outstanding at December 31, 2021	6,657,268	$ 8.27	7.2	$ 494
Exercisable at December 31, 2021	3,736,652	$ 8.86	5.8	$ 494

The intrinsic value of stock options exercised during the years ended December 31, 2021, 2020 and 2019 was $0.1 million, $0.8 million and $0.2 million, respectively.

As of December 31, 2021, there was $12.8 million of total unrecognized compensation cost related tonon-vested stock options granted to employees, which is expected to be recognized over a weighted-average period of 2.97 years.

Cash received from option exercises during the years ended December 31, 2021, 2020, and 2019 was $0.2 million, $1.1 million, and $0.2 million, respectively.

Restricted Stock Units

From time to time, upon approval by the Company's board of directors, certain employees have been granted restricted stock units with time-based vesting criteria. The majority of these restricted stock units vest annually over a four-year term with 25% vesting on each anniversary of the grant date. Restricted stock units granted to the Company's executive officers vest in full three-years from the date of grant. The fair value of restricted stock units is calculated based on the closing sale price of the Company's common stock on the date of grant.

A summary of the status of restricted stock units as of December 31, 2020 and December 31, 2021 and changes during the year ended December 31, 2021 is presented below:

	Shares	Weighted Average Grant Date Fair Value
Outstanding at December 31, 2020	1,734,383	$ 7.40
Granted	1,747,554	6.31
Vested	(286,837)	7.70
Forfeited	(507,613)	8.15
Outstanding at December 31, 2021	2,687,487	$ 6.52

As of December 31, 2021, there was $12.0 million of unrecognized stock-based compensation expense related to outstanding restricted stock units, with an expected recognition period of 2.07 years.

Stock-based Compensation Expense

The fair value of each stock option granted was estimated on the date of grant using the Black-Scholes option-pricing model based on the following weighted-average assumptions:

	Year Ended December 31,		
	2021	2020	2019
Weighted-average risk-free interest rate	0.99%	1.28%	2.42%
Expected dividend yield	— %	— %	— %
Expected option term (in years)	6.03	5.99	6.00
Volatility	81.56%	78.27%	91.35%

The weighted-average grant date fair value per share of options granted in the years ended December 31, 2021, 2020 and 2019 was $5.33, $5.30 and $5.05, respectively.

The following table summarizes the stock-based compensation expense for stock options, restricted stock units and restricted common stock granted to employees and non-employees and from the 2016 ESPP recorded in the Company's statements of operations:

	Year Ended December 31,		
	2021	2020	2019
Research and development	$ 5,706	$ 4,732	$ 3,472
General and administrative	4,648	6,207	6,367
Total stock-based compensation expense	$ 10,354	$ 10,939	$ 9,839

Due to an operating loss, the Company does not record tax benefits associated withstock-based compensation or option exercises. Tax benefits will be recorded when realized.

13. Income Taxes

The Company accounts for income taxes under FASB Accounting Standards Codification 740 ("ASC 740"). Deferred income tax assets and liabilities are determined based upon differences between financial reporting and tax bases of assets and liabilities and are measured using the enacted tax rates and laws that will be in effect

when the differences are expected to reverse. The components of the income tax provision for the years ended December 31, 2021, 2020 and 2019 are as follows:

	Year Ended December 31,		
	2021	2020	2019
Current	$ 1	$ 4	$ 28
Deferred	—	—	—
Total	$ 1	$ 4	$ 28

A reconciliation of the U.S. statutory income tax rate to the Company's effective tax rate is as follows for the years ended December 31, 2021, 2020 and 2019:

	Year ended December 31,		
	2021	2020	2019
Federal income tax computed at federal statutory tax rate	21.00%	21.00%	21.00%
State income tax, net of federal benefit	7.26	6.12	6.56
Permanent items	3.60	(0.68)	(0.89)
Federal and state research and development credits	5.79	3.89	4.79
Rate change	—	—	—
Other	(1.41)	(0.88)	(0.77)
Change in valuation allowance	(36.24)	(29.45)	(30.73)
Effective income tax rate	— %	— %	(0.04)%

The principal components of the Company's deferred tax assets and liabilities consist of the following at December 31, 2021 and 2020 (in thousands):

	Year ended December 31,	
	2021	2020
Deferred tax assets:		
Federal and state net operating loss carryforwards	$ 109,166	$ 80,658
Tax credit carryforwards	22,446	17,442
Intangible assets	3,000	3,219
Stock-based compensation	5,700	5,117
Deferred revenue	2,810	6,034
Capital lease	6,812	7,284
Other	2,395	1,725
Total deferred tax assets	152,329	121,479
Less valuation allowance	(146,285)	(114,946)
Net deferred tax assets	6,044	6,533
Deferred tax liabilities:		
Right-of-use asset	3,946	4,215
Fixed assets	2,098	2,318
Total deferred tax liabilities	6,044	6,533
Net deferred taxes	$ —	$ —

ASC 740 requires a valuation allowance to reduce the deferred tax assets reported if, based on the weight of the evidence, it is more likely than not that some portion or all of the deferred tax assets will not be realized. After consideration of all the evidence, both positive and negative, the Company has recorded a valuation allowance against its deferred tax assets at December 31, 2021 and 2020, respectively because the Company's management has determined that it is more likely than not that these assets will not be fully realized. The increase in the valuation allowance of $31.3 million in 2021 and $24.7 million in 2020 primarily relates to the net loss incurred by the Company.

As of December 31, 2021, the Company had federal net operating loss ("NOL") carryforwards of approximately $398.9 million and state net operating loss carryforwards of $401.9 million which are available to reduce future taxable income. The Company also had federal tax credits of approximately $19.7 million and state tax credits of $3.5 million which may be used to offset future tax liabilities. Net operating losses generated before 2018 of approximately $135.7 million will expire at various dates through 2037, and net operating loss carryforward of approximately $263.2 million, which were generated after 2017 have an indefinite carryforward period. Federal tax credits will expire at various dates through 2041. State net operating losses will expire at various dates through 2041. State tax credits will expire at various dates through 2036. The NOL and tax credit carryforwards are subject to review and possible adjustment by the Internal Revenue Service and state tax authorities. Net operating loss and tax credit carryforwards may become subject to an annual limitation in the event of certain cumulative changes in the ownership interest of significant shareholders over a three-year period in excess of 50%, as defined under Sections 382 and 383 of the Internal Revenue Code, respectively, as well as similar state provisions. This could limit the amount of tax attributes that can be utilized annually to offset future taxable income or tax liabilities. The amount of the annual limitation is determined based on the value of the Company immediately prior to the ownership change. Subsequent ownership changes may further affect the limitation in future years. The Company has not determined whether an ownership change has occurred and as such, the Company's NOLs may be limited.

The Company's reserves related to taxes are based on a determination of whether and how much of a tax benefit taken by the Company in its tax filings or positions is more likely than not to be realized following resolution of any potential contingencies present related to the tax benefit. As of December 31, 2021 and 2020 the Company had no unrecognized tax benefits or accrued interest or penalties related to unrecognized tax benefits. The Company's policy is to recognize both interest and penalties related to unrecognized tax benefits in income tax expense.

The Company completed a study to document its qualifying research credits for all years ending before December 31, 2018. For the years ending after December 31, 2017, the Company generated research credits but has not conducted a study to document the qualified activities. This study may result in an adjustment to the Company's research and development credit carryforwards; however, until a study is completed and any adjustment is known, no amounts are being presented as an unrecognized tax benefit for the year ended December 31, 2021. A full valuation allowance has been provided against the Company's research and development credits and, if an adjustment is required, this adjustment would be offset by an adjustment to the deferred tax asset established for the research and development credit carryforwards and the valuation allowance.

The federal and state income tax returns are generally subject to examinations for the tax years ended December 31, 2018 through December 31, 2021. To the extent the Company has tax attribute carryforwards, the tax years in which the attribute was generated may still be adjusted upon examination by the Internal Revenue Service or state tax authorities to the extent utilized in a future period. The Company files income tax returns in the U.S. federal and Massachusetts jurisdictions. There are currently no federal or state audits in process.

14. Defined Contribution Plan

The Company established a defined contribution savings plan under Section 401(k) of the Internal Revenue Code. This plan covers substantially all employees who meet minimum age and service requirements and allows participants to defer a portion of their annual compensation on a pretax or post-tax basis. Company contributions to the plan may be made at the discretion of the board of directors. The Company instituted effective September 1, 2017 an employer match of 100% of the amount the employees contribute to the 401(k) plan for each payroll period up to the first 1% of plan compensation plus 50% of the amount the employees contribute between 1% and 6% of plan compensation. During the year ending December 31, 2021, the Company revised its employer match to 100% of the amount the employees contribute to the 401(k) plan for each payroll period up to the first 2% of plan compensation plus 50% of the amount the employees contribute between 2% and 6% of plan compensation. For the years ended December 31, 2021, 2020, and 2019 the Company contributed $0.8 million, $0.5 million and $0.5 million respectively, to the 401(k) plan.

15. Subsequent Events

On January 25, 2022, the Board of Directors adopted a 2022 Inducement Stock Incentive Plan (the "2022 Plan"), pursuant to which the Company may grant non-statutory stock options, stock appreciation rights, restricted stock, restricted stock units and other stock-based awards with respect to an aggregate of 1,000,000 shares of common stock. Awards under the 2022 Plan may only be granted to persons who (i) were not previously an employee or director of the Company or (ii) are commencing employment with the Company following a bona fide period of non-employment, in either case as an inducement material to the individual's entering into employment with the Company and in accordance with the requirements of Nasdaq Stock Market Rule 5635(c)(4).

On March 7, 2022, the Company entered into a Master Collaboration Agreement and a project schedule (collectively, the "Agreement"), with Qiagen Manchester Limited ("Qiagen"). Pursuant to the Agreement, Qiagen has agreed to develop and commercialize an assay as a companion diagnostic test to determine the expression level of the Company's proprietary RARA biomarker for use with tamibarotene, a selective retinoic acid receptor alpha, or RARα, agonist, in newly diagnosed higher-risk MDS patients. Subject to the terms of the Agreement and upon achievement of specified technical and development milestones, the Company is obligated to pay Qiagen an amount up to a high single-digit million-dollar payment over the term of the initial project schedule. In addition, the Company will reimburse Qiagen for certain pass-through costs. Qiagen will retain all proceeds from the commercialization of the companion diagnostic test. Syros has no financial obligations to Qiagen under the Agreement on the commercialization of tamibarotene. The initial term of the Agreement expires on the later to occur of (i) the fifth anniversary of the Agreement and (ii) the expiration or termination of all project schedules executed under the Agreement.

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

Board of Directors and Stockholders
Tyme Technologies, Inc.

Opinion on the financial statements

We have audited the accompanying consolidated balance sheets of Tyme Technologies, Inc. (a Delaware corporation) and subsidiaries (the "Company") as of March 31, 2022 and 2021, the related consolidated statements of operations, changes in stockholders' equity, and cash flows for each of the two years in the period ended March 31, 2022, and the related notes (collectively referred to as the "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company as of March 31, 2022 and 2021, and the results of its operations and its cash flows for each of the two years in the period ended March 31, 2022, in conformity with accounting principles generally accepted in the United States of America.

Basis for opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) ("PCAOB") and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

Critical audit matter

The critical audit matter communicated below is a matter arising from the current period audit of the financial statements that was communicated or required to be communicated to the audit committee and that: (1) relates to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective, or complex judgments. The communication of critical audit matters does not alter in any way our opinion on the financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing a separate opinion on the critical audit matter or on the accounts or disclosures to which it relates.

Stock-based compensation

As described further in Notes 7 and 12 to the consolidated financial statements, the Company has stock-based compensation that is based on fair value measurements. We identified the computation of stock-based compensation as a critical audit matter.

The principal consideration for our determination that stock-based compensation estimates is a critical audit matter is that the model used to determine the grant date fair value includes a significant unobservable input of volatility, which is subject to estimation uncertainty and requires significant auditor subjectivity in evaluating that input and estimate. Volatility is based on a blend of the Company's expected volatility and those of similar companies.

Our audit procedures related to stock-based compensation estimates include the following, among others:

a) We agreed the inputs of the grant date fair value calculation to the key terms of the underlying agreements and read such agreements to assess the completeness of the inputs utilized;

b) We assessed the appropriateness of the similar companies used in the volatility calculation, recomputed expected volatility of the Company and volatility of the similar companies using the changes in the respective stock prices over the term; and with the assistance of our valuation professionals with specialized skills and knowledge, we assessed the methodology used in determining the volatility;

c) We recomputed the fair value of each grant using management's inputs and compared to the fair value calculated by management.

/s/ GRANT THORNTON LLP
We have served as the Company's auditor since 2015.

New York, New York
May 25, 2022

Tyme Technologies, Inc. and Subsidiaries
Consolidated Balance Sheets

	March 31, 2022	March 31, 2021
Assets		
Current assets		
Cash and cash equivalents	$ 13,738,931	$ 107,516,420
Marketable securities	60,611,961	—
Prepaid clinical costs	480,623	987,470
Prepaid expenses and other current assets	4,064,770	1,152,970
Total current assets	78,896,285	109,656,860
Prepaid clinical costs, net of current portion	—	530,989
Operating lease right-of-use asset	38,229	75,471
Marketable securities	9,080,671	—
Total assets	$ 88,015,185	$ 110,263,320
Liabilities and Stockholders' Equity		
Current liabilities		
Accounts payable and other current liabilities (including $153,000 and $87,000 of related party accounts payable, respectively)	$ 3,803,427	$ 3,842,390
Severance payable	2,611,857	726,027
Accrued bonuses	933,082	1,040,710
Operating lease liability	37,332	34,658
Total current liabilities	7,385,698	5,643,785
Long-term liabilities		
Severance payable, net of current portion	421,575	850,709
Operating lease liability, net of current portion	—	41,256
Warrant liability	124,480	1,931,921
Total liabilities	7,931,753	8,467,671
Commitments and contingencies (See Note 9)		
Stockholders' equity		
Preferred stock, $0.0001 par value, 10,000,000 shares authorized, 0 shares issued and outstanding	—	—
Common stock, $0.0001 par value, 300,000,000 shares authorized, 172,206,894 issued and outstanding at March 31, 2022, and 300,000,000 authorized, 172,200,644 issued and outstanding at March 31, 2021	17,223	17,222
Additional paid in capital	241,030,535	238,572,442
Accumulated other comprehensive loss	(544,264)	—
Accumulated deficit	(160,420,062)	(136,794,015)
Total stockholders' equity	80,083,432	101,795,649
Total liabilities and stockholders' equity	$ 88,015,185	$ 110,263,320

The Notes to the Consolidated Financial Statements are an integral part of these statements.

Tyme Technologies, Inc. and Subsidiaries
Consolidated Statements of Operations and Comprehensive Loss

	Years Ended March 31,	
	2022	**2021**
Operating expenses:		
Research and development	$ 13,444,101	$ 16,709,649
General and administrative (including $507,000 and $517,000 of related party legal expenses, respectively)	9,632,103	10,185,537
Severance expense	2,437,379	321,825
Total operating expenses	25,513,583	27,217,011
Loss from operations	(25,513,583)	(27,217,011)
Other income (expense):		
Change in fair value of warrant liability	1,807,441	(3,915,393)
Gain on warrant exchange	—	2,228,697
Other income	150,339	22,077
Interest expense	(70,244)	(97,133)
Total other income (expense)	1,887,536	(1,761,752)
Loss before income taxes	(23,626,047)	(28,978,763)
Net loss	$ (23,626,047)	$ (28,978,763)
Basic and diluted loss per common share	$ (0.14)	$ (0.22)
Basic and diluted weighted average shares outstanding	172,206,534	134,250,722
Statements of Comprehensive Loss		
Net loss	$ (23,626,047)	$ (28,978,763)
Other comprehensive loss		
Unrealized loss on marketable securities, net of tax	(544,264)	—
Comprehensive loss	$ (24,170,311)	$ (28,978,763)

The Notes to the Consolidated Financial Statements are an integral part of these statements.

Tyme Technologies, Inc. and Subsidiaries
Consolidated Statements of Stockholders' Equity
For the Years Ended March 31, 2022 and 2021

	Common Stock		Additional Paid-in capital	Accumulated Deficit	Accumulated Other Comprehensive Loss	Total Stockholders' Equity
	Shares	Amount				
Balance, March 31, 2020	123,312,252	$ 12,333	$ 126,828,055	$ (107,815,252)	$ —	$ 19,025,136
Issuance of common stock from securities purchase agreement, net of associated expenses of $6,228,135	40,000,000	4,000	93,767,865	—	—	93,771,865
Issuance of common stock from at-the-market financing facility, net of associated expenses of $318,425	4,453,939	445	5,774,973	—	—	5,775,418
Proceeds from the exercise of stock options	2,028,203	203	5,351,120	—	—	5,351,323
Warrant to share exchange	2,406,250	241	3,393,534	—	—	3,393,775
Stock based compensation	—	—	3,456,895	—	—	3,456,895
Net loss	—	—	—	(28,978,763)	—	(28,978,763)
Balance, March 31, 2021	172,200,644	$ 17,222	$ 238,572,442	$ (136,794,015)	$ —	$ 101,795,649
Proceeds from the exercise of stock options	6,250	1	6,187	—	—	6,188
Stock based compensation	—	—	2,451,906	—	—	2,451,906
Unrealized gain (loss) on available-for-sale securities	—	—	—	—	(544,264)	(544,264)
Net loss	—	—	—	(23,626,047)	—	(23,626,047)
Balance, March 31, 2022	172,206,894	$ 17,223	$ 241,030,535	$ (160,420,062)	$ (544,264)	$ 80,083,432

The Notes to the Consolidated Financial Statements are an integral part of these statements

Tyme Technologies, Inc. and Subsidiaries
Consolidated Statement of Cash Flows

	Years Ended, March 31	
	2022	**2021**
Cash flows from operating activities:		
Net loss	$ (23,626,047)	$ (28,978,763)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation	—	5,181
Amortization of employees, directors and consultants stock options	2,451,906	3,456,895
Change in fair value of warrant liability	(1,807,441)	3,915,393
Gain on warrant exchange	—	(2,228,697)
Net amortization of premiums and discounts on marketable securities	1,615,332	—
Loss on call redemption of marketable securities	1,416	—
Change in operating assets and liabilities:		
Prepaid clinical costs	1,037,836	144,528
Prepaid expenses and other assets	(2,224,512)	(171,021)
Operating lease right-of-use asset	37,242	150,269
Accounts payable and other current liabilities	(38,963)	1,015,088
Severance payable	1,456,696	(58,896)
Accrued bonuses	(107,628)	(760,269)
Operating lease liability	(38,582)	(54,186)
Net cash used in operating activities	(21,242,745)	(23,564,478)
Cash flows from investing activities:		
Purchases of marketable securities	(95,244,730)	—
Proceeds from maturities of marketable securities	22,703,798	—
Net cash used in investing activities	(72,540,932)	—
Cash flows from financing activities:		
Insurance note payments	—	(518,124)
Proceeds from registered offerings, net of issuance costs	—	99,547,283
Proceeds from exercise of stock options	6,188	5,351,323
Net cash provided by financing activities	6,188	104,380,482
Net (decrease) increase in cash	(93,777,489)	80,816,004
Cash and cash equivalents — beginning of year	107,516,420	26,700,416
Cash and cash equivalents — end of year	$ 13,738,931	$ 107,516,420
Supplemental Cash Flow Information:		
Cash paid for interest and income taxes are as follows:		
Interest	$ 70,244	$ 97,133
Income taxes	$ —	$ —
Noncash investing and financing activities:		
Cashless exchange of April 2019 Warrants to purchase 5,833,333 shares of common stock for 2,406,250 shares in May 2020.	$ —	$ —
Cashless exchange of April 2019 Warrants to purchase 2,166,667 shares of common stock for May 2020 Warrant to purchase the same number of shares common stock.	$ —	$ —
Operating lease right-of-use asset obtained in exchange for lease liabilities	$ —	$ 75,439

The Notes to the Consolidated Financial Statements are an integral part of these statements.

Note 1. Nature of Business

Tyme Technologies, Inc. is a Delaware corporation headquartered in Bedminster, New Jersey, with a wholly owned subsidiary, Tyme Inc. (together, "TYME" or the "Company"). The majority of the Company's research, development and other business activities are conducted by Tyme Inc., which was incorporated in Delaware in 2013.

TYME is an emerging biotechnology company developing CMBTs that are intended to be effective across a broad range of solid tumors and hematologic cancers, while also maintaining patients' quality of life through relatively low toxicity profiles. Unlike targeted therapies that attempt to regulate specific mutations within cancer, the Company's therapeutic approach is designed to take advantage of a cancer cell's innate metabolic requirements to cause cancer cell death.

The Company is currently focused on developing its novel compound,SM-88, its preclinical pipeline of novel CMBT™ programs, and TYME-19 as a potential therapeutic for SARS CoV-2 diseases. The Company believes that early clinical results demonstrated bySM-88 in multiple advanced cancers including breast, sarcomas, pancreatic, and prostate, reinforce the potential of its emerging CMBT™ pipeline.

Ongoing Studies

OASIS Trial in metastatic HR+/HER2- breast cancer

The Company is collaborating with Georgetown University to support a Phase II trial, OASIS, forSM-88 in patients with metastatic breast cancer who have HR+ and HER2- disease ("HR+/HER2-"). This represents approximately 68% of the annual breast cancer diagnoses in the US each year. The OASIS trial is an investigator-initiated prospective open-label Phase II trial evaluating the efficacy and safety of SM-88 with MPS for the treatment of metastatic HR+/HER2- breast cancer after treatment with a CDK4/6 inhibitor. This trial is designed as a two-stage trial, enrolling up to 50 patients who have failed or progressed after receiving two hormonal agents and a CDK4/6 inhibitor to receive SM-88 with MPS without additional cancer therapies. The primary endpoint of this trial is ORR, with secondary endpoints including DOR, CBR at >24 weeks, PFS, and safety. The trial is being conducted at Georgetown University at a total of five sites within the Georgetown/MEDSTAR system located in Washington DC, Maryland, and New Jersey. Patient enrollment began in 2021 with the first patient dosed in September.

HoPES Trial in sarcoma

In early 2020, the open-label Phase 2 investigator-sponsored trial of SM-88 therapy in sarcoma, HoPES, opened. This trial has two cohorts, each expecting to enroll 12 patients. The first is SM-88 with MPS as salvage treatment in patients with mixed rare sarcomas, and the other isSM-88 with MPS as maintenance treatment for patients with metastatic Ewing's sarcoma who had not progressed on prior therapy. The primary objectives are to measure ORR and PFS. Secondary objectives include DOR, OS, CBR using RECIST, and incidence of treatment-emergent AEs. The Joseph Ahmed Foundation is sponsoring this trial, which is being conducted by Principal Investigator Dr. Chawla at the Sarcoma Oncology Center in Santa Monica, CA.

Preclinical Pipeline Programs

The Company has begun a comprehensive translational preclinical program focused onSM-88 MOA and Biomarker Identification/Validation. We have engaged Evotec, a leading global research and development company, to aid in the execution of these activities and we are also incorporating several complementary academic collaborations into this multi-faceted program. The overall goal of these activities is to potentially identify actionable biomarkers of sensitivity and activity to SM-88 in various cancers, complementary combination drugs strategies forSM-88, and other cancer metabolism targets that could benefit from treatment.

TYME-18 is a CMBT™ compound under development that is delivered intratumorally. TYME-18 leverages a member of the bile acid family to create a potential treatment for inoperable tumors. Preliminary observations of the local administration of TYME-18, a combination of a proprietary surfactant system and natural sulfonic acid, suggested its potential as an important regulator of energy metabolism that may impede the ability of tumors to increase in size, which, in addition to its lytic functionality, could prove useful in difficult-to-treat cancers. The Company is assessing development priorities to determine if additional advancement of this program is warranted at this time.

TYME-19 is an oral synthetic member of the bile acid family. The Company also uses bile acids in its anti-cancer drug candidate,TYME-18. Because of its expertise in bile acids and their effects, the Company was able to identify TYME-19 as a well-characterized bile acid with potential antiviral properties. Bile acids have primarily been used for liver disease; however, like all steroids, they are messenger molecules that modulate a number of diverse critical cellular processes. Bile acids can modulate lipid and glucose metabolism and can remediate dysregulated protein folding, with potentially therapeutic effects on cardiovascular, neurologic, immune, and other metabolic systems. Some agents in this class have also previously shown antiviral properties.

The Company has retained virology experts at Evotec to assess the MOAs ofTYME-19 to assist the Company in assessing the path forward for the TYME-19 program. Evotec is a global drug development company with the capability to access the multiple existing and emerging variants of the COVID-19 virus. TYME and Evotec are testing the ability ofTYME-19 to interrupt the cellular pathways commonly used by viruses to produce viral proteins as well as cellular responses to viral infection that cause local inflammation. Prolonged inflammation from SARS-CoV-2 can lead to some of the severe outcomes experienced by infected patients.

Tumor Targeting Technology

TYME has developed a technology (“Tumor Targeting Technology”) by which the tyrosine isomer L metyrosine(L-α-methylparatyrosine) can be fused with a second therapeutic agent in a manner that creates a fusion compound that may allow targeted accumulation of the treatment by the cancer cells in a novel manner. The Company is assessing potential development paths forward for this technology.

Discontinuing Programs

Precision Promise Trial- SM-88 with MPS as 2nd line therapy in metastatic pancreatic cancer

In October 2018 the Company partnered with PanCAN to study SM-88 in an adaptive randomized Phase II/III trial with registration intent known as Precision Promise℠. The objective of Precision Promise is to expedite the study and approval of promising therapies for pancreatic cancer by bringing multiple stakeholders together, including academic, industry and regulatory entities. The trial began in early 2020, with SM-88 (with the conditioning agents MPS) being studied as monotherapy in a treatment arm for patients who have failed one prior line of chemotherapy.

On January 26, 2022, the Company announced the discontinuation ofSM-88 with MPS in the Precision Promise trial in mPDAC upon learning from PanCAN, the trial sponsor, that it terminated the arm due to futility compared to the control of standard of care chemotherapy in second-line mPDAC. Based on the information provided by PanCAN, the OS for SM-88 with MPS in monotherapy was lower compared to standard of care chemotherapies with either Gemcitabine and Abraxane or modified FOLFIRINOX. As of March 31, 2022, remaining estimated costs to close out the trial have been expensed.

TYME-88-PANC (Part 2) (third-line Metastatic Pancreatic Cancer)

In fiscal year 2020, we launched our pivotal study forSM-88 in the third-line treatment of pancreatic cancer through an amendment to our ongoing TYME-88-Panc trial (Part 2), with the first patient dosed in the third

quarter of the fiscal year. As described previously, the COVID-19 pandemic significantly impacted enrollment of this trial such that it appears it is likely to complete enrollment in a similar timeline to the second-line Precision Promise pancreatic cancer trial. There was also a higher than expected dropout of patients randomized to the chemotherapy control arm, which could have potentially impacted the interpretative and regulatory utility of the data.

Following the strategic review, considering, in part, the timeline and regulatory utility for this trial compared to the parallel Precision Promise trial and concentration of investment in this specific cancer, management concluded that it would be best to focus on the second-line Precision Promise trial which offers treatment options to patients earlier in their disease and includes tumor biopsy and biomarker analyses that align with the Company's overall strategic focus on identifying targeted therapies.

Therefore, the Company decided to stop enrollment and begin the process of closing down the trial. Patients currently on therapy are allowed to continue treatment until progression or unacceptable toxicity. The closing of this trial is expected to require several months to complete. During the year ended March 31, 2022, the Company expensed $723,000 of estimated close out costs. The trial's remaining ongoing expense to the Company is approximately $400,000 and is expected to be incurred over the five months following March 31, 2022.

Liquidity

The consolidated financial statements have been prepared on a going-concern basis, which contemplates the realization of assets and the satisfaction of liabilities in the normal course of business. The Company has historically funded its operations primarily through equity offerings.

In February 2021, the Company raised $100 million in gross proceeds through a registered direct offering of 40,000,000 shares of its common stock, at a purchase price of $2.50 per share. The Company incurred $6.2 million of related costs which offset such proceeds.

On January 7, 2020, the Company entered into a Securities Purchase Agreement with Eagle Pharmaceuticals, ("Eagle"), pursuant to which the Company raised $20,000,000 through the issuance and sale to Eagle of 10,000,000 shares of common stock, at a price of $2.00 per share.

On October 18, 2019, TYME entered into an Open Market Sale Agreement℠ (as amended, the "Sale Agreement") with Jefferies LLC ("Jefferies") as sales agent, pursuant to which the Company may, from time to time, sell shares of Common Stock through Jefferies having an aggregate offering price of up to $30.0 million (the "Jefferies ATM"). Under the Sale Agreement the minimum share sales price ("Floor Price") shall not be less than $1.00 without Jefferies prior written consent. During the year ended March 31, 2022, the Company did not sell any shares through the Jefferies ATM. In the year ended March 31, 2021, the Company raised approximately $6.1 million in aggregate gross proceeds before commissions and expenses through the Sale Agreement and paid commissions and expenses of $0.3 million. At March 31, 2022, there remained approximately $22.2 million of availability to sell shares through the Jefferies ATM subject to the terms of the Sale Agreement.

The proceeds of the aforementioned offerings are being used by the Company for continued clinical studies, drug commercialization and development activities and other general corporate and operating expenses.

For the year ended March 31, 2022, the Company had negative cash flow from operations of $21.2 million and net loss of $23.6 million, which included $2.5 million non-cash equity compensation and $1.6 million net amortization expense of premiums and discounts on marketable securities, offset by $1.8 million income change in fair value of warrant liability. As of March 31, 2022, the Company had working capital of approximately $71.5 million.

Management has concluded that substantial doubt does not exist regarding the Company's ability to satisfy its obligations as they come due during the twelve-month period following the issuance of these financial statements. This conclusion is based on the Company's assessment of qualitative and quantitative conditions and

events, considered in aggregate as of the date of issuance of these financial statements that are known and reasonably knowable. Among other relevant conditions and events, the Company has considered its operational plans, liquidity sources, obligations due or expected, funds necessary to maintain the Company's operations, and potential adverse conditions or events as of the issuance date of these financial statements.

Note 2. Basis of Presentation and Summary of Significant Accounting Policies

Basis of Presentation

The accompanying financial statements have been prepared in conformity with GAAP. Any reference in these notes to applicable guidance is meant to refer to GAAP as found in the ASC and ASU of the FASB.

Significant Accounting Policies

Principles of Consolidation

The Company's consolidated financial statements include the accounts of Tyme Technologies, Inc. and its subsidiary, Tyme, Inc. All intercompany transactions and balances have been eliminated in consolidation.

Reclassifications

Certain prior year amounts, primarily severance expense which was broken out to a separate line item on the Consolidated Statements of Operations and Comprehensive Loss, have been reclassified to conform to the current year presentation. These reclassifications have no effect on the previously reported net loss or cash flows.

Risks and Uncertainties

The Company is subject to those risks associated with any biotechnology company that has substantial expenditures for research and development. There can be no assurance that the Company's research and development projects will be successful, that products developed will obtain necessary regulatory approval or that any approved product will be commercially viable. In addition, the Company operates in an environment of rapid technological change and is largely dependent on the services of its employees and consultants, as well as third party contractors.

Current Economic Conditions

The novel COVID-19 pandemic and actions taken by governments and others to reduce its spread, has negatively impacted the global economy, financial markets, and the Company's industry and has disrupted day-to-day life and business operations. Although we have operated within theCOVID-19 environment for approximately two years, outbreaks of infections (including the spread of the new variants) continue to be experienced as conditions evolve and fluctuate around the world. The extent to which the continuing COVID-19 pandemic impacts our product candidates and business, including patients' willingness to participate and remain in clinical trials, the timing of meeting enrollment expectations, the ability of our third-party partners to remain operational and our access to capital markets and financing sources, depends on numerous evolving factors that are highly uncertain, cannot be accurately predicted, and may be significant.

Use of Estimates

The preparation of the consolidated financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the consolidated financial statements and reported amounts of expenses during the reporting period. Significant items subject to such estimation include the calculation of the stock-based compensation and warrant valuation. Actual results could differ from such estimates.

Cash and Cash Equivalents

The Company considers all highly-liquid investments that have maturities of three months or less when acquired to be cash equivalents. Cash equivalents are stated at fair value. The Company's cash and cash equivalents consisted of $13.7 million at March 31, 2022 and $107.5 million at March 31, 2021.

Concentration of Credit Risk

Financial instruments that potentially expose the Company to concentration of credit risk consist primarily of cash and marketable securities. Cash is deposited with major banks and, at times, such balances with any one financial institution may be in excess of FDIC insurance limits. The Company exceeded the FDIC limit of $250,000 by $10.1 million at March 31, 2022 and $107.3 million at March 31, 2021. Although the Company has exceeded the federally insured limit, it has not incurred losses related to these deposits. Management monitors the Company's accounts with these institutions to minimize credit risk.

Marketable Securities

In the first quarter of fiscal year 2022, the Company established an investment policy and invested in a portfolio of highly liquid investments and marketable securities. The primary objectives of the Company's policy are to preserve capital and diversify risk, while maintaining sufficient liquidity to meet cash flow requirements.

All of the Company's marketable securities are debt securities and are classified as available-for-sale in accordance with the ASC Topic 320, "Investments – Debt and Equity Securities." Available for sale securities are carried at fair value and reported in cash equivalents and marketable securities. Marketable securities are further classified as short-term or long-term based on maturity dates and the Company's intent in line with its investment policy to hold the securities to scheduled maturity. Unrealized gains and losses on available-for-sale securities are excluded from net loss and reported in accumulated other comprehensive loss as a separate component of stockholders' equity. Other income includes interest, dividends, amortization of purchase premiums and discounts, gain and losses on sale (or redemptions) of securities and other-than-temporary declines in the fair value of securities, if any.

For individual debt securities classified as available-for-sale securities where there has been a decline in fair value below amortized cost, the Company determines whether the decline resulted from a credit loss or other factors. In making this assessment, the Company considers the extent to which fair value is less than amortized cost, any changes to the rating of the security by a rating agency, and adverse conditions specifically related to the security, among other factors. If this assessment indicates that a credit loss exists, the present value of cash flows expected to be collected from the security is compared to the amortized cost basis of the security. If the present value of cash flows expected to be collected is less than the amortized cost basis, a credit loss exists and an allowance for a credit loss is recorded on our consolidated balance sheet, limited by the amount that the fair value is less than the amortized cost basis. Impairment that has not been recorded through an allowance for credit losses is recorded through other comprehensive loss, net of applicable taxes.

Fair Value of Financial Instruments

The Company records certain financial assets and liabilities at fair value in accordance with the provisions of ASC Topic 820, Fair Value Measurements and Disclosures. Fair value is defined as the price that would be received to sell an asset or paid to transfer a liability in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date.

Fair value should be based on the assumptions that market participants would use when pricing an asset or liability and is based on a fair value hierarchy that prioritizes the information used to develop those assumptions. The fair value hierarchy gives the highest priority to quoted prices in active markets (observable inputs) and the

lowest priority to the Company's assumptions (unobservable inputs). Fair value measurements should be disclosed separately by level within the fair value hierarchy. For assets and liabilities recorded at fair value, it is the Company's policy to maximize the use of observable inputs and minimize the use of unobservable inputs when developing fair value measurements, in accordance with established fair value hierarchy.

Fair value measurements for assets and liabilities where there exists limited or no observable market data are based primarily upon estimates, and often are calculated based on the economic and competitive environment, the characteristics of the asset or liability and other factors. Therefore, the results cannot be determined with precision and may not be realized in an actual sale or immediate settlement of the asset or liability. Additionally, there may be inherent weaknesses in any calculation technique, and changes in the underlying assumptions used, including discount rates and estimates of future cash flows, could significantly affect the results of current or future values.

Additionally, from time to time, the Company may be required to record at fair value other assets on a nonrecurring basis, such as assets held for sale and certain other assets. These nonrecurring fair value adjustments typically involve application of lower-of-cost-or-market accounting or write-downs of individual assets.

Fair value guidance establishes a three-tier fair value hierarchy, which prioritizes the inputs used in measuring fair value. These tiers include:

- Level 1 — Quoted prices in active markets for identical assets or liabilities.
- Level 2 — Inputs other than Level 1 that are observable, either directly or indirectly, such as quoted prices for similar assets or liabilities; quoted prices in markets that are not active; or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the assets or liabilities.
- Level 3 — Unobservable inputs that are supported by little or no market activity and that are significant to the fair value of the assets or liabilities.

Level 3 valuations are for instruments that are not traded in active markets or are subject to transfer restrictions and may be adjusted to reflect illiquidity and/or non-transferability, with such adjustment generally based on available market evidence. In the absence of such evidence, management's best estimate is used.

An adjustment to the pricing method used within either Level 1 or Level 2 inputs could generate a fair value measurement that effectively falls in a lower level in the hierarchy.

The carrying amounts of the Company's financial instruments, including cash, accounts payable and other current liabilities approximates fair value given their short-term nature. The fair value of the severance payable approximates the carrying value, which represents the present value of future severance payments. Cash equivalents, marketable securities and the derivative warrant liability are recorded at fair value. See Note 7.

Prepaid Expenses and Other Current Assets

Prepaid expenses represent expenditures made in advance of when the economic benefit of the cost will be realized, and which will be expensed in future periods with the passage of time. As of March 31, 2022, prepaid expenses and other current assets includes $1.1 million of prepaid insurance, $0.6 million accrued interest receivable on marketable securities and a $2.1 million deposit with our payroll vendor to satisfy the Chief Science Officer severance payment. As of March 31, 2021, prepaid expenses and other current assets includes $1.0 million of prepaid insurance.

Property and Equipment, Net

Property and equipment are recorded at cost and are depreciated on a straight-line basis over their estimated useful lives. The Company estimates a life of three years for equipment and furniture and fixtures. Upon sale or

retirement, the cost and related accumulated depreciation are removed from the accounts and the resulting gain or loss is reflected in results of operations. Repairs and maintenance costs are expensed as incurred.

Impairment of Long-Lived Assets

The Company assesses the recoverability of its long-lived assets, which include fixed assets and operating lease right of use assets, whenever significant events or changes in circumstances indicate impairment may have occurred. If indicators of impairment exist, projected future undiscounted cash flows associated with the asset are compared to its carrying amount to determine whether the asset's value is recoverable. Any resulting impairment is recorded as a reduction in the carrying value of the related asset in excess of fair value and a charge to operating results. For the years ended March 31, 2022 and 2021, the Company determined that there were no triggering events requiring an impairment analysis.

Research and Development

Research and development costs are expensed as incurred and are primarily comprised of, but not limited to, external research and development expenses incurred under arrangements with third parties, such as CROs, CMOs and consultants that conduct clinical and preclinical studies, costs associated with preclinical and development activities, costs associated with regulatory operations, depreciation expense for assets used in research and development activities and employee related expenses, including salaries and benefits for research and development personnel. Costs for certain development activities, such as clinical studies, are accrued, over the service period specified in the contract and recognized based on an evaluation of the progress to completion of specific tasks using data such as patient enrollment, clinical site activations or information provided to us by our vendors on their actual costs incurred. Payments for these activities are based on the terms of the individual arrangements, which may differ from the patterns of costs incurred, and are reflected in the consolidated financial statements as prepaid or accrued expense.

Income Taxes

Income tax expense, deferred tax assets and liabilities, and liabilities for unrecognized tax benefits reflect management's best estimate of current and future taxes to be paid. The Company is subject to income taxes in the United States, for federal and various state jurisdictions. Significant judgments and estimates are required in the determination of the income tax expense.

Deferred income taxes arise from temporary differences between the tax basis of assets and liabilities and their reported amounts in the financial statements, which will result in taxable or deductible amounts in the future. Deferred tax assets and liabilities are measured using enacted tax rates expected to apply to taxable income in the years in which those temporary differences are expected to be recovered or settled. The effect on deferred tax assets and liabilities of a change in tax rates is recognized in income in the period that includes the enactment date.

A valuation allowance is provided when, after consideration of available positive and negative evidence that it is not more likely than not that the benefit from deferred tax assets will be realizable. In recognition of this risk, we have provided a full valuation allowance against the net deferred tax assets. The assumptions about future taxable income require the use of significant judgment and are consistent with the plans and estimates we are using to manage the underlying businesses. In evaluating the objective evidence that historical results provide, we consider three years of cumulative operating income (loss).

The calculation of tax liabilities involves dealing with uncertainties in the application of complex tax laws and regulations in various jurisdictions. ASC 740 "Income Taxes" states that a tax benefit from an uncertain tax position may be recognized when it is more likely than not that the position will be sustained upon examination, including resolutions of any related appeals or litigation processes, on the basis of the technical merits. When and if the Company were to recognize interest and penalties related to unrecognized tax benefits, they would be reported in tax expense.

Segment Information

Operating segments are defined as components of an enterprise about which separate discrete information is available for evaluation by the chief operating decision maker, or decision-making group, in deciding how to allocate resources and in assessing performance. The Company views its operations and manages its business in one segment.

Derivative Warrant Liability

Certain freestanding common stock warrants that are related to the issuance of common stock are classified as liabilities and recorded at fair value due to characteristics that require liability accounting, primarily the obligation to issue registered shares of common stock upon notification of exercise and certain price protection provisions. Warrants of this type are subject to re-measurement at each balance sheet date and any change in fair value is recognized as a component of other income (expense) in the consolidated statement of operations. The Company will continue to adjust the liability for changes in fair value until the earlier of the exercise or expiration of the warrant. The Company utilizes Level 3 fair value criteria to measure the fair value of the warrants.

As noted in Note 8, Stockholders' Equity, the Company classifies a warrant to purchase shares of its common stock as a liability on its consolidated balance sheet if the warrant is a free-standing financial instrument that contains certain price protection features or requires issuance of registered common shares upon exercise which cause the warrants to be treated as derivatives. Each warrant of this type is initially recorded at fair value on date of grant using the Monte Carlo simulation model or the Black-Sholes model and is subsequently re-measured to fair value at each subsequent balance sheet date. Changes in fair value of the warrant are recognized as a component of other income (expense) in the consolidated statement of operations.

Basic and Diluted Loss Per Share

The Company calculates net loss per share in accordance with*Earning per Share (Topic 260).* Basic net loss per share is computed by dividing net loss attributable to the Company by the weighted average number of shares of Company common stock outstanding for the period, and diluted earnings per share is computed by including common stock equivalents outstanding for the period. During the periods presented, the calculation excludes any potential dilutive common shares and any equivalents as they would have been anti-dilutive as the Company incurred losses for the periods then ended.

Stock-based Compensation

The Company follows the authoritative guidance for accounting for stock-based compensation in ASC 718, Compensation-Stock Compensation. The guidance requires that stock-based payment transactions be recognized in the financial statements based on their fair value at the grant date and recognized as compensation expense over the vesting period as services are being provided. (See Note 12, Equity Incentive Plan.)

The fair value of each stock option grant is estimated on the date of grant using the Black-Scholes option-pricing model. The use of the Black-Scholes option pricing model requires management to make assumptions with respect to the expected term of the option, the expected volatility of the common stock consistent with the expected term of the option, risk-free interest rates, the value of the common stock and expected dividend yield of the common stock. For awards subject to time-based vesting conditions, the Company recognizes stock-based compensation expense equal to the grant date fair value of stock options on a straight-line basis over the requisite service period, which is generally the vesting term. The Company accounts for forfeitures as they occur. The Company adopted ASU 2018-07 and, as such, the fair value options granted tonon-employees is estimated at the date of grant only.

Recently Adopted Accounting Pronouncements

In December 2019, the FASB issued ASU2019-12, *Income Taxes (Topic 740): Simplifying the Accounting for Income Taxes*("ASU 2019-12"), as part of its overall simplification initiative to reduce costs and complexity of applying accounting standards while maintaining or improving the usefulness of the information provided to users of financial statements. Amendments include removal of certain exceptions to the general principles of ASC 740, *Income Taxes* and simplification in several other areas such as accounting for a franchise tax (or similar tax) that is partially based on income. ASU2019-12 is effective for public business entities for annual reporting periods beginning after December 15, 2020, and interim periods within those reporting periods. The Company adopted the pronouncement as of April 1, 2021 and the adoption of this standard did not have a material impact on its consolidated financial statements and disclosures.

In June 2016, the FASB issued ASU2016-13, *Financial Instruments-Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments* ("ASU 2016-13") and has since modified the standard with several ASUs (collectively, "Topic 326"). Topic 326 requires companies to present a financial asset (or a group of financial assets) measured at amortized cost and available for sale debt securities net of the amounts expected to be collected. Prior U.S. GAAP delayed recognition of the full amount of credit losses until the loss was probable of occurring. Under this ASU, the income statement will reflect an entity's current estimate of all expected credit losses. The measurement of expected credit losses will be based upon historical experience, current conditions, and reasonable and supportable forecasts that affect the collectability of the reported amount. Credit losses relating to available-for-sale debt securities will be recorded through an allowance for credit losses rather than as a direct write-down of the security. Early adoption is permitted. The guidance is effective for fiscal years beginning after December 15, 2022, including interim periods within those fiscal years. The Company adopted the pronouncement as of April 1, 2021 and the adoption of this standard did not have a material impact on its consolidated financial statements and disclosures.

In August 2020, the FASB issued ASUNo. 2020-06, *Debt – Debt with Conversion and Other Options (Subtopic470-20) and Derivatives and Hedging – Contracts in Entity's Own Equity (Subtopic 815-40)*. ASU No. 2020-06 eliminates the beneficial conversion and cash conversion accounting models for convertible instruments. It also amends the accounting for certain contracts in an entity's own equity that are currently accounted for as derivatives because of specific settlement provisions. In addition, the new guidance modifies how particular convertible instruments and certain contracts that may be settled in cash or shares impact the diluted EPS computation. The amendments in ASU No. 2020-06 are effective for public business entities that meet the definition of an SEC filer, excluding entities eligible to be smaller reporting companies as defined by the SEC, for fiscal years beginning after December 15, 2021, including interim periods within those fiscal years. For all other entities, the amendments are effective for fiscal years beginning after December 15, 2023, including interim periods within those fiscal years. Early adoption is permitted, but no earlier than fiscal years beginning after December 15, 2020, including interim periods within those fiscal years. FASB also specified that an entity should adopt the guidance as of the beginning of its annual fiscal year and is not permitted to adopt the guidance in an interim period. The Company adopted the pronouncement as of April 1, 2021 and the adoption of this standard did not have a material impact on its consolidated financial statements and disclosures.

Note 3. Net Loss Per Common Share.

The following table sets forth the computation of basic and diluted net loss per common share for the periods indicated:

	Year Ended March 31,	
	2022	2021
Basic and diluted net loss per common share calculation		
Net loss	$ (23,626,047)	$ (28,978,763)
Weighted average common shares outstanding — basic and diluted	172,206,534	134,250,722
Net loss per share of common stock — basic and diluted	$ (0.14)	$ (0.22)

The Company calculates net loss per share in accordance with *ASC Topic 260, "Earnings per Share."* Basic net loss per share is computed by dividing net loss attributable to the Company by the weighted average number of shares of Company Common Stock outstanding for the period, and diluted earnings per share is computed by including common stock equivalents outstanding for the period. During the periods presented, the calculation excludes any potential dilutive common shares and any equivalents as they would have been anti-dilutive.

Warrants issued in April 2019, discussed further in Note 8, participated on a one-for-one basis with common stock in the distribution of dividends, if and when declared by the Board of Directors (the "Board") on the Company's Common Stock. For purposes of computing EPS, these warrants were, when outstanding, considered to participate with common stock in the earnings of the Company and, therefore, the Company calculates basic and diluted EPS using the two-class method. Under the two-class method, net income for the period is allocated between common stockholders and participating securities according to dividends declared and participation rights in undistributed earnings. No income was allocated to the warrants for the year ended March 31, 2021 as results of operations was a loss for the period. In May 2020, these warrants were all exchanged for Common Stock or new warrants without such participation rights and are no longer outstanding (see Note 8).

The following outstanding securities at March 31, 2022 and 2021 have been excluded from the computation of diluted weighted average shares outstanding, as they would have been anti-dilutive:

	Year Ended March 31,	
	2022	2021
Stock options	14,504,271	12,588,068
Warrants	3,104,318	3,104,318
Total	17,608,589	15,692,386

Note 4. Available-for-Sale-Securities.

The following table summarizes available-for-sale securities recorded in cash and cash equivalents or marketable securities as of March 31, 2022:

	March 31, 2022			
	Amortized cost	Gross Unrealized Gains	Gross Unrealized Loss	Fair Value
Money market funds	$ 3,409,178	$ —	$ —	$ 3,409,178
Corporate debt securities	32,831,174	—	(343,134)	32,488,040
Municipal debt securities	37,405,722	—	(201,130)	37,204,592
Total	$73,646,074	$	$(544,264)	$73,101,810

The following table summarizes the classification of available-for-sale securities:

	March 31, 2022	March 31, 2021
Cash and cash equivalents	$ 3,409,178	$ —
Marketable securities	69,692,632	—
Total	$73,101,810	$ —

The following table summarizes our portfolio ofavailable-for-sale securities by contractual maturity:

	Less than 12 months		12 months or Longer		Total	
	Fair Value	Net Unrealized Losses	Fair Value	Net Unrealized Losses	Fair Value	Net Unrealized Losses
Money market funds	$ 3,409,178	$ —	$ —	$ —	$ 3,409,178	$ —
Corporate debt securities	26,195,025	(227,300)	6,293,015	(115,834)	32,488,040	(343,134)
Municipal debt securities	34,416,936	(153,855)	2,787,656	(47,275)	37,204,592	(201,130)
Total	$ 64,021,139	$ (381,155)	$ 9,080,671	$ (163,109)	$ 73,101,810	$ (544,264)

Note 5. Accounts Payable and Other Current Liabilities.

Accounts payable (including accounts payable to a related party – see Note 11) and other current liabilities consisted of the following:

	March 31, 2022	March 31, 2021
Legal	$ 263,111	$ 454,139
Consultant and professional services	300,051	176,957
Accounting and auditing	14,410	55,349
Research and development	2,776,594	2,657,202
Board of Directors and Scientific Advisory Board Compensation	418,389	435,594
Other	30,872	63,149
	$ 3,803,427	$ 3,842,390

Note 6. Severance Payable.

The Company entered into a Release Agreement, dated March 24, 2022, pursuant to which the Chief Science Officer resigned and will receive severance that would be payable under his employment agreement in a lump

sum payment of $2.1 million. The Company also entered into Separation and General Release Agreement with three other employees. The agreements provide separation benefits which the Company recorded as severance expense.

In April 2021, the Company entered into a Separation and General Release Agreement related to the separation of employment of its Chief Medical Officer as of March 31, 2021. The agreement provides for separation benefits which the Company recorded as severance expense for the year ended March 31, 2021.

On March 15, 2019 the Company entered into a Release Agreement related to the separation of employment of their Chief Operating Officer, which provides for salary continuance for five years, reimbursement of health benefits for three years and a modification to his outstanding stock options to extend the post-termination exercise period for his vested options from three months to five years. The Company recorded severance expense at its present value of $2.5 million, (using a discount rate of 6%) for the year ended March 31, 2019, including $0.4 million relating to the stock option modification.

The aggregate severance liability payable was $3.0 million and $1.6 million as of March 31, 2022 and March 31, 2021.

Note 7. Fair Value Measurements.

The Company has segregated all financial assets and liabilities that are measured at fair value on a recurring basis into the most appropriate level within the fair value hierarchy based on the inputs used to determine the fair value at the measurement date in the table below. Transfers are calculated on values as of the transfer date. There were no transfers between Levels 1, 2 and 3 during the years ended March 31, 2022 and March 31, 2021.

The Company's financial instruments measured at fair value on a recurring basis are as follows:

March 31, 2022	Total	Quoted prices in active markets (Level 1)	Significant other observable inputs (Level 2)	Significant unobservable inputs (Level 3)
Financial assets				
Cash equivalents				
Money market funds	$ 3,409,178	$ 3,409,178	$ —	$ —
Marketable Securities				
Short-term				
Corporate debt securities	26,195,025	—	26,195,025	—
Municipal debt securities	34,416,936	—	34,416,936	—
Long-term				
Corporate debt securities	6,293,015	—	6,293,015	—
Municipal debt securities	2,787,656	—	2,787,656	—
	$ 73,101,810	$ 3,409,178	$ 69,692,632	$ —
Financial liability				
Warrant liability	$ 124,480	$ —	$ —	$ 124,480
March 31, 2021				
Warrant liability	$ 1,931,921	—	—	$ 1,931,921

Fair values of available-for-sale securities are generally based on prices obtained from commercial pricing services. The fair value of cash equivalents held in money market funds is determined based on "Level 1" inputs. Marketable securities classified as Level 2 within the valuation hierarchy consist of corporate debt securities and

municipal debt securities. We estimate the fair values of these marketable securities by taking into consideration valuations obtained from third-party pricing sources. These pricing sources utilize industry standard valuation models, including both income and market-based approaches, for which all significant inputs are observable, either directly or indirectly, to estimate fair value. These inputs include market pricing based on real-time trade data for the same or similar securities, issuer credit spreads, benchmark yields, and other observable inputs.

The fair value measurement for the warrant issued in conjunction with the Exchange Agreements (see Note 8 for transaction details) (the "May 2020 Warrant") is based on significant inputs not observable in the market and is classified as Level 3 liability as of March 31, 2022 and March 31, 2021.The fair value of the May 2020 Warrant was determined using a Black Scholes model and included significant unobservable inputs such as volatility. The model also incorporated several observable assumptions at each valuation date including: the price of the Company's common stock on the date of valuation, the remaining contractual term of the warrant and the risk free interest rate over the term.

The following table details key inputs and assumptions used to estimate the fair value of the May 2020 Warrant as of March 31, 2022 and March 31, 2021 using a Black Scholes model:

	May 2020 Warrant March 31, 2022	May 2020 Warrant March 31, 2021
Stock price	$ 0.35	$ 1.78
Volatility	98%	78%
Remaining term (years)	2.01	3.01
Expected dividend yield	—	—
Risk-free rate	2.28%	0.35%

The following table summarizes activity for liabilities measured at fair value using Level 3 significant unobservable inputs:

	Warrant liability
Beginning balance, March 31, 2021	**$ 1,931,921**
Change in fair value of May 2020 Warrant liability	(1,807,441)
Ending balance, March 31, 2022	**$ 124,480**

Note 8. Stockholders' Equity.

Preferred Stock

The Company is authorized to issue up to 10,000,000 shares of preferred stock, each with a par value of $0.0001. Shares of Company preferred stock may be issued from time to time in one or more series and/or classes, each of which will have such distinctive designation or title as shall be determined by the Company's Board prior to the issuance of any shares of such series or class. The Company preferred stock will have such voting powers, full or limited or no voting powers and such preferences and relative, participating, optional or other special rights and such qualifications, limitations or restrictions thereof, as shall be stated in such resolution or resolutions providing for the issue of such series or class of Company preferred stock as may be adopted from time to time by the Company's Board prior to the issuance of any shares thereof.

No shares of Company preferred stock are currently issued or outstanding. In connection with the Securities Purchase Agreement, dated January 7, 2020, between the Company and Eagle (the "Eagle SPA"), the Company designated and reserved 10,000 shares as Series A Preferred Stock. The Series A Preferred Stock shares rank senior to the Company's common stock and have no voting rights. The shares, if issued, would be convertible into common stock and will have a conversion ratio equal to the quotient of $1,000 divided by an amount equal to 1.15 times the average of the volume weighted average price of the Company's Common Stock for the seven trading days immediately following announcement of the Milestone Event (as defined in the SPA).

Common Stock

Voting

Each holder of Company common stock is entitled to one vote for each share thereof held by such holder at all meetings of stockholders (and written action in lieu of meetings). The number of authorized shares of Company common stock may be increased or decreased (but not below the number of shares thereof then outstanding) by the affirmative vote of the holders of majority of the combined number of issued and outstanding shares of the Company.

In connection with the Release Agreement, dated March 24, 2022, the Company and Mr. Hoffman also entered into a Voting Agreement, pursuant to which Mr. Hoffman agreed to vote all shares of TYME common stock beneficially owned by him in accordance with the Board's recommendation with respect to any matter presented to the stockholders for a period of one year.

The Company and Michael Demurjian entered into a Voting Agreement, dated April 18, 2022, pursuant to which Mr. Demurjian agreed to vote all shares of TYME common stock beneficially owned by him in accordance with the board of directors of the Company's recommendation with respect to any matter presented to the Company's stockholders for a period of two years from the date of the agreement.

Dividends

Dividends may be declared and paid on the Company common stock from funds lawfully available therefore, as and when determined by the Board.

Liquidation

In the event of the liquidation, dissolution, or winding-up of the Company, holders of Company common stock will be entitled to receive all assets of the Company available for distribution to its stockholders.

Exchange Agreements

On May 20, 2020, the Company entered into exchange agreements with holders (the "Holders") of the warrants issued in April 2019 (the "April 2019 Warrants'). The April 2019 Warrants were offered and issued pursuant to the Company's previous shelf registration statement on Form S-3 (File No. 333-211489).

Pursuant to exchange agreements (the "Share Exchange Agreements") with Holders of the April 2019 Warrants to purchase 5,833,333 shares of Common Stock in the aggregate, the Company issued an aggregate of 2,406,250 shares of common stock (the "Exchange Shares") in exchange for such April 2019 Warrants. Concurrently therewith, each such Holder executed and delivered to the Company a leak-out agreement (a "Share Leak-Out Agreement") that contained trading restrictions with respect to the Exchange Shares, which (i) for the first 90 days, prohibit any sales of Exchange Shares, (ii) for the subsequent 90 days, limit sales of Exchange Shares on any day to 2.5% of that day's trading volume of Common Stock, and (iii) prohibit new short positions or short sales on Common Stock for the combined 180 day period.

The Company also entered into an exchange agreement (the "Warrant Exchange Agreement") with another Holder of April 2019 Warrants to purchase 2,166,667 shares of Common Stock in the aggregate. Pursuant to the Warrant Exchange Agreement, the Company issued such Holder a new warrant (the "May 2020 Warrant") to purchase the same number of shares of Common Stock. The May 2020 Warrant has the same expiration date, April 2, 2024, as the April 2019 Warrants, but has an exercise price of $1.80 and does not include the price protection, anti-dilution provisions or other restrictions on Company action from the April 2019 Warrants. Concurrently therewith, such Holder executed and delivered to the Company a leak-out agreement that contained trading restrictions on sales of Common Stock issued upon exercise of the May 2020 Warrant that are

substantially similar to the restrictions on Exchange Shares in the Share Leak-Out Agreement, provided that the leak-out restrictions will only apply to the first 893,750 shares of Common Stock issued pursuant to the May 2020 Warrant.

The April 2019 Warrants were remeasured as of May 20, 2020, before the exchange, using the Monte Carlo pricing simulation resulting in a fair value of approximately $7.3 million, and the change in fair value from March 31, 2020 to the fair value before the exchange of approximately $3.7 million expense was recorded as a component of other income (expense) within the consolidated statement of operations for the year ended March 31, 2021. The key assumptions in applying the Monte Carlo simulation model were as follows: $1.70 stock price, 73% volatility, 3.87 years remaining term, 0.28% risk free rate and the probability of fundamental transactions occurring.

At May 20, 2020, the fair value of the 2,406,250 shares issued under the Share Exchange Agreements was approximately $3.4 million, which resulted in a gain on exchange of approximately $1.9 million.

The exercise price of the May 2020 Warrant is subject to adjustment upon the occurrence of specific events, including stock dividends, stock splits, combinations and reclassifications of the Company's Common Stock.

The Company determined that the May 2020 Warrant should be recorded as a derivative liability on the consolidated balance sheet due to the May 2020 Warrant's contractual provisions requiring issuance of registered common shares upon exercise. At May 20, 2020, the May 2020 Warrant was recorded at the fair value of $1.7 million as determined using the Black Scholes model and the change in fair value before and after the exchange of $0.3 million was recorded as a gain on warrant exchange as a component of other income (expense) within the consolidated statement of operations. The key assumptions in applying the Black Scholes model were as follows: $1.64 stock price, 73% volatility, 3.87 years remaining term, 0.27% risk free rate and 7% discount for lack of marketability. The change in fair value of the May 2020 Warrant for the year ended March 31, 2022 of $1.8 million income and for the period from May 20, 2020 through March 31, 2021 of $0.3 million expense was recorded as a component of other income (expense) within the consolidated statement of operations.

The following summarizes the common stock warrant activity for the years ended March 31, 2022 and March 31, 2021:

	Warrant Shares of Common Stock	Weighted Average Exercise Price
Outstanding at March 31, 2020	**8,937,651**	**$ 2.31**
Granted	2,166,667	1.80
Exchanged	(8,000,000)	2.00
Outstanding at March 31, 2021	**3,104,318**	**$ 2.77**
Granted	—	—
Exchanged	—	—
Outstanding at March 31, 2022	**3,104,318**	**$ 2.77**

In May 2020, April 2019 Warrants to purchase 5,833,333 shares of common stock were exchanged on a cashless basis for 2,406,250 shares and April 2019 Warrants to purchase 2,166,667 of common stock were exchanged for a May 2020 Warrant to purchase the same number of shares.

At March 31, 2022 and March 31, 2021, 3,074,551 of common stock purchase warrants relating to securities purchase agreements were outstanding and exercisable.

Issued	Classification	Warrants Outstanding	Exercise Price	Expiration
December 2015	Equity	446,500	$ 5.00	December 2025
February 2016	Equity	461,384	$ 5.00	February 2026
July 2016	Equity	29,767	$ 5.00	June 2026
May 2020	Liability	2,166,667	$ 1.80	April 2024

At-the-Market Financing Facility

On October 18, 2019, the Company entered into the Sale Agreement with Jefferies, pursuant to which the Company may, from time to time, sell shares of Common Stock, having an aggregate offering price of up to $30 million through Jefferies, as the Company's sales agent. Under the Sale Agreement the minimum share sales price ("Floor Price") shall not be less than $1.00 without Jefferies prior written consent. As indicated in an amendment, the shares will be offered and sold by the Company pursuant to its currently effective Registration Statement on Form S-3, as amended (Reg. No. 333-245033). Any sales of common stock pursuant to the Sales Agreement will be made by methods deemed to be an "at-the-market offering" as defined in Rule 415 promulgated under the Securities Act, as amended. Jefferies will use commercially reasonable efforts to sell the shares from time to time, based on the instructions of the Company. The Company will pay Jefferies a commission rate of three percent (3%) of the gross proceeds from the sales of shares of Common Stock sold pursuant to the Sale Agreement. Under the Sale Agreement, the Company is not required to use the full available amount authorized and it may, by giving notice as specified in the Sale Agreement, terminate the Sale Agreement at any time.

The Company did not sell any shares through the Jefferies ATM during the year ended March 31, 2022. During the year ended March 31, 2021, the Company raised approximately $6.1 million of gross proceeds via sale of 4,453,939 shares of Common Stock under the Jefferies ATM and incurred $0.3 million of related costs which offset the proceeds. At March 31, 2022, there remained approximately $22.2 million of availability to sell shares through the Jefferies ATM subject to the terms of the Sale Agreement.

Securities Purchase Agreement

On January 7, 2020, the Company and Eagle entered into the Eagle SPA, pursuant to which the Company issued and sold to Eagle 10,000,000 shares of common stock, at a price of $2.00 per share. The Eagle SPA provides that Eagle will, subject to certain conditions, make an additional payment of $20 million upon the occurrence of a milestone event, which is defined as the earlier of (i) achievement of the primary endpoint of overall survival in the TYME-88-Panc pivotal trial; (ii) achievement of the primary endpoint of overall survival in the PanCAN Precision PromiseSM-88 registration arm; or (iii) FDA approval of SM-88 in any cancer indication. This payment would be split into a $10 million milestone cash payment and a $10 million investment in TYME at a 15% premium to the then prevailing market price. Eagle's shares will be restricted from sale until the earlier of three months following the milestone event or the three-year anniversary of the agreement.

Registered Direct Offering

On February 8, 2021, the Company closed on its registered direct offering with several healthcare-focused institutional and other institutional investors (the "Purchasers"), pursuant to which the Company sold to the Purchasers, in a registered direct offering, an aggregate of 40,000,000 shares (the "Shares") of common stock, $0.0001 par value per share. The Shares were sold at a purchase price of $2.50 per share for aggregate gross proceeds to the Company of $100 million, prior to deducting placement agent's fees and other offering expenses payable by TYME. The Company incurred $6.2 million of related costs which offset such proceeds. The Shares

were offered by the Company pursuant to an effective shelf registration statement on Form S-3, which was originally filed with the Securities and Exchange Commission on August 12, 2020 and was declared effective on September 2, 2020 (Reg. No. 333-245033). H.C. Wainwright & Co. acted as the exclusive placement agent for the offering.

Note 9. Commitments and Contingencies.

Contract Service Providers

In the course of the Company's normal business operations, it enters into agreements and arrangements with contract service providers to assist in the performance of its research and development and clinical research activities. At March 31, 2022, the Company's obligations to contract service providers were $0.2 million in the aggregate.

On April 1, 2020, the Company amended the Clinical Research Funding and Drug Supply Agreement, dated October 9, 2018, with PanCAN, to enroll individuals diagnosed with pancreatic cancer in a platform style clinical research study. Stage 1 of the study was initiated in the fourth quarter of fiscal year 2020. On January 26, 2022, the Company announced the discontinuation of SM-88 with MPS in the Precision Promise trial in mPDAC upon learning from PanCAN, the trial sponsor, that it terminated the arm due to futility compared to the control of standard of care chemotherapy in second-line mPDAC. As of March 31, 2022, remaining estimated costs to close out the trial have been expensed.

Purchase Commitments

The Company has entered into contracts with manufacturers to supplySM-88 and certain related conditioning agents, in order to achieve favorable pricing on supplied products. These contracts have non-cancellable elements related to the scheduled deliveries of these products in future periods. Payments are made by us to the manufacturer when the products are delivered and of acceptable quality. The outstanding future contract obligations structured to match clinical supply needs for the Company's ongoing trials and registration activity are approximately $0.9 million and $2.5 million, respectively at March 31, 2022.

Legal Proceedings

The Company is not currently a party to any material legal proceedings and is not aware of any pending or threatened legal proceeding against it that it believes could have a material adverse effect on the Company, its business, operating results or financial condition. From time to time, the Company may be involved in litigation, claims or other contingencies arising in the ordinary course of business. The Company would accrue a liability when a loss is considered probable and the amount can be reasonably estimated. When a material loss contingency is reasonably possible but not probable, the Company would not record a liability, but instead would disclose the nature and the amount of the claim, and an estimate of the loss or range of loss, if such estimate can be made. Legal fees are expensed as incurred.

Note 10. Leases.

The Company has a lease for office space in New Jersey, which expires in February 2023.

Total Company rent expense, including short term rentals, was approximately $62,000 and $165,000 for the years ended March 31, 2022 and 2021, respectively.

Operating lease ROU assets and liabilities on the consolidated balance sheet represents the present value of the remaining lease payments over the remaining lease terms. ROU assets also include any initial direct costs incurred and any lease payments made at or before the lease commencement date, less lease incentives received.

Payments for additional monthly fees to cover the Company's share of certain facility expenses are not included in operating lease ROU assets and liabilities. The Company used its estimated incremental borrowing rate of 11.0% to calculate the present value of its lease payments, as the implicit rate in the lease was not readily determinable.

As of March 31, 2022, the future minimum lease payments undernon-cancellable operating lease agreements for which the Company has recognized operating lease ROU assets and lease liabilities were as follows:

	March 31, 2022
Fiscal year 2023	$ 39,240
Total remaining lease payments	39,240
Less: present value adjustment	(1,908)
Total operating lease liabilities	37,332
Less: current portion	37,332
Operating lease liabilities, net of current portion	$ —

Note 11. Related Party Transactions.

Legal

Faegre Drinker Biddle & Reath ("Faegre Drinker"), formerly Drinker Biddle & Reath LLP ("DBR"), has provided legal services to the Company. The Company's Chief Legal Officer and Corporate Secretary held the consulting role "Senior Counsel" with the Faegre Drinker until December 31, 2021. During the years ended March 31, 2022 and 2021, approximately $0.5 million and $0.6 million ($0.1 million was capitalized into equity in prior year), respectively, have been incurred as legal expenses associated with Faegre Drinker, and the Company had approximately $153,000 and $87,000 in accounts payable and accrued expenses payable to Faegre Drinker at March 31, 2022 and March 31, 2021, respectively.

Note 12. Equity Incentive Plan.

On March 5, 2015, the Company's Board adopted and the Company's stockholders approved, the Company's 2015 Equity Incentive Plan (the "2015 Plan"). Awards under the 2015 Plan may include, but need not be limited to, one or more of the following: options, stock appreciation rights, restricted stock, performance grants, stock bonuses, and any other type of award deemed by the administrator to be consistent with the purposes of the 2015 Plan. The exercise price of all options awarded under the 2015 Plan must be no less than 100% of the fair market value of the Company common stock as determined on the date of the grant and have a term of no greater than ten years from the date of grant. In February 2018, the 2015 Plan was amended making available 12.5% of shares of common stock issued and outstanding. As of March 31, 2022, there were 7,223,029 shares available for grant under the 2015 Plan.

On August 24, 2021 the stockholders approved the Amended and Restated 2016 Option Plan forNon-Employee Directors (the "2016 Director Plan"), which increased the total number of shares of Common Stock authorized and reserved for issuance the 2016 Director Plan by 3,000,000 shares to 5,750,000 shares. On August 24, 2021 the Board of Directors approved: (i) "Initial Grants" upon a director's initial appointment to the Board consisting of an immediate stock option grant of 176,000 shares at fair market value and the shares will vest in equal quarterly increments over a three-year period from the date of grant; and (ii) "Annual Grants" for members who continue in service as members of the Board subsequent to each annual meeting of stockholders occurring subsequent to an Initial Grant, an annual stock option grant of 88,000 shares at fair market value and the shares will vest in equal quarterly increments over a one-year period from the date of grant. The Initial Grants and Annual Grants have a ten year term, subject to applicable termination or forfeiture provisions. As of March 31, 2022, there were 3,411,279 shares available for grant under the 2016 Director Plan.

Stock Options

As of March 31, 2022, and 2021, there was approximately $4.5 million and $3.6 million, respectively, of total unrecognized compensation related to non-vested stock options. The cost is expected to be recognized over the remaining weighted average remaining amortization period of 2.8 years. During the years ended March 31, 2022 and 2021, the Company had stock compensation expense of $2.5 million and $3.5 million, respectively. For the year ended March 31, 2022, stock compensation expense is recognized as $1.9 million in general and administrative expense, $0.6 million in research and development expense. For the year ended March 31, 2021, stock compensation expense recognized was $2.1 million in general and administrative expense and $1.4 million in research and development expense.

The Company uses the Black-Scholes option pricing model to determine the fair value of stock options granted. For employees and non-employees, the compensation expense is amortized on a straight-line basis over the requisite service period, which approximates the vesting period. The Company accounts for forfeitures as they occur, rather than estimating forfeitures as of an award's grant date.

The expected volatility of options granted has been determined using the method described under ASC 718 using a blend of the Company's expected volatility and those of similar companies. The expected term of options granted to employees, non-employees and consultants in the current fiscal period has been based on the term by using the simplified "plain-vanilla" method as allowed under SAB No. 110 and ASU 2018-7.

The assumptions utilized to estimate the fair value of stock options granted are presented in the following table:

	Year Ended March 31,	
	2022	2021
Risk free interest rate	0.280% - 2.34%	0.174% - 0.527%
Expected volatility	95.39% - 105.37%	88.02% - 101.67%
Expected term	2.7 - 6.1 years	2.8 - 6.1 years
Dividend yield	0.0%	0.0%

The following is a summary of the activity of the Company's stock options under the 2015 Plan and 2016 Director Plan as of March 31, 2022:

	Number of Options	Weighted Average Exercise Price
Outstanding at March 31, 2021	12,588,068	$ 2.92
Granted	3,862,388	1.30
Exercised	(6,250)	0.99
Cancelled/Forfeited	(1,939,935)	3.83
Outstanding at March 31, 2022	14,504,271	2.36
Options exercisable at March 31, 2022	9,329,798	$ 2.99

Weighted-average grant date fair value of options granted during the years ended March 31, 2022 and 2021 was $1.00 and $0.89, respectively.

During the year ended March 31, 2022, holders of options issued under the equity incentive plans exercised their right to acquire an aggregate of 6,250 shares of common stock at a weighted average exercise price of $0.99 resulting in $6,000 total proceeds to the Company. During the year ended March 31, 2021, holders of options issued under the equity incentive plans exercised their rights to acquire an aggregate of 2,028,203 shares of

common stock at a weighted average exercise price of $2.64 resulting in $5.4 million total proceeds to the Company.

	Stock Options Outstanding				Stock Options Vested			
Range of Exercise Price	Number Outstanding at March 31, 2022	Weighted Average Exercise Price	Weighted Average Remaining Life (Years)	Aggregate Intrinsic Value	Number Vested at March 31, 2022	Weighted Average Exercise Price	Weighted Average Remaining Life (Years)	Aggregate Intrinsic Value
$0.29 - $8.75	14,504,271	$ 2.36	7	$ 4,610	9,329,798	$ 2.99	6	$ —

The intrinsic value calculated as the excess of the market value as of March 31, 2022 over the exercise price of the options is $4,610. The market value as of March 31, 2022 was $0.35 as reported by the NASDAQ Capital Market. The total intrinsic value of options exercised during the year ended March 31, 2022 was $3,500.

	Options	Weighted Average Grant Date Fair Value Per Share
Non-vested options at March 31, 2021	4,355,171	$ 0.91
Granted	3,862,388	1.00
Vested	(446,522)	0.95
Cancelled/Forfeited	(2,596,564)	0.99
Non-vested options at March 31, 2022	5,174,473	$ 0.93

The fair value of options vested during the years ended March 31, 2022 and 2021 was $2.6 million and $3.7 million, respectively.

Note 13. Income Taxes.

The Company provides for income taxes under ASC 740. Under ASC 740, the liability method is used in accounting for income taxes. Under this method, deferred tax assets and liabilities are determined based on differences between financial reporting and tax bases of assets and liabilities and are measured using the enacted tax rates and laws that will be in effect when the differences are expected to reverse.

The Company has not recorded a current or deferred income tax expense or benefit since its inception.

The Company's loss before income taxes was $23.6 million and $29.0 million for the years ended March 31, 2022 and 2021, respectively, and was generated entirely in the United States. Deferred taxes are recognized for temporary differences between the basis of assets and liabilities for financial statement and income tax purposes. The significant components of the Company's deferred tax assets are comprised of the following:

	March 31,	
	2022	2021
Net operating loss carryforward	$ 27,564,077	$ 20,123,621
Research and development credit carryforward	884,130	1,164,895
Orphan Drug Credit	4,157,360	2,002,559
Stock options – NQSOs	4,765,662	5,267,351
Accruals and other temporary differences	662,754	595,418
Gross deferred tax assets	38,033,983	29,153,844
Deferred tax valuation allowance	(38,033,983)	(29,153,844)
Net deferred taxes	$ —	$ —

Based on the Company's history of operating losses since inception and consideration of available positive and negative evidence, the Company has concluded that it is not more likely than not that the benefit of its deferred tax assets will be realized. Accordingly, the Company continues to maintain a full valuation allowance against its net deferred tax assets as of March 31, 2022. The valuation allowance increased by $8.9 million for the year ended March 31, 2022 primarily due to the increase in the net operating loss carryforward and Orphan Drug credit.

A reconciliation of income tax benefit computed at the statutory federal income tax rate to income taxes as reflected in the financial statements is as follows:

	Year Ended March 31,	
	2022	2021
U.S. statutory income tax rate	21.00%	21.00%
State taxes, net of federal benefit	11.59%	—
Permanent differences	—	(0.02)%
Tax credit carryforwards	7.93%	4.70%
Valuation allowance	(37.08)%	(20.98)%
Stock compensation	(5.05)%	(3.41)%
Warrants	1.61%	(1.29)%
Effective tax rate	— %	— %

As of March 31, 2022, the Company had gross U.S. federal net operating loss carryforwards of approximately $119.1 million, which may be available to offset future income tax liabilities and will begin to expire at various dates starting in 2033. As of March 31, 2022, none of the Company's state net operating losses have value due to the apportionment rule in the states where state income tax returns are currently filed. As permitted under the Protecting Americans Against Tax Hikes Act, which allows the Research and Development tax credit to be applied to Form 941 quarterly payroll tax returns, the Company reduced payroll taxes by $120 thousand and $177 thousand for the years ended March 31, 2022 and March 31, 2021, respectively. As of March 31, 2022, the Company had gross federal research and development tax credit carryforwards of $5.9 million, available to reduce future tax liabilities which will begin to expire at various dates starting in 2030.

Under the provisions of the Internal Revenue Code, the NOL carryforwards are subject to review and possible adjustment by the Internal Revenue Service and state tax authorities. NOL and tax credit carryforwards may become subject to an annual limitation in the event of a 50% cumulative change in the ownership interest of significant stockholders over a three-year period in excess of 50%, as defined under Sections 382 and 383 of the Internal Revenue Code, as well as similar state tax provisions. This could limit the amount of NOLs that the Company can utilize annually to offset future taxable income or tax liabilities. The amount of the annual limitation, if any, will be determined based on the value of the Company immediately prior to the ownership change. Subsequent ownership changes may further affect the limitation in future years. The Company has completed several financing transactions since its inception which may have resulted in a change in control as defined by Sections 382 and 383 of the Internal Revenue Code, or could result in a change in control in the future.

A reconciliation of the beginning and ending amount of unrecognized tax benefits is as follows:

	Year Ended March 31,	
	2022	2021
Gross unrecognized tax benefits at beginning of year	$558,962	$318,394
Increases (decreases) for tax positions in prior period	—	(99,063)
Increase for tax positions in current period	330,712	339,631
Gross unrecognized tax benefits at end of year	$889,674	$558,962

As of March 31, 2022, the Company had $890,000 of unrecognized tax benefits, which were offset with the net operating loss and valuation allowance on the consolidated balance sheets. None of the gross unrecognized tax benefits would affect the effective tax rate at March 31, 2022, if recognized. In addition, the Company did not record any penalties or interest related to uncertain tax positions for the periods presented in these consolidated financial statements. The Company does not have any positions for which it is reasonably possible that there will be significant increase or decrease in the amounts of unrecognized tax benefits within twelve months of the reporting date.

The Company files income tax returns in the United States, and various state jurisdictions. The federal and state income tax returns are generally subject to tax examinations for the period January 1, 2017 through March 31, 2022. To the extent the Company has tax attribute carryforwards, the tax years in which the attribute was generated may still be adjusted upon examination by the Internal Revenue Service or state tax authorities to the extent utilized in a future period.

Annexes

AGREEMENT AND PLAN OF MERGER

by and among

SYROS PHARMACEUTICALS, INC.,

TACK ACQUISITION CORP.,

and

TYME TECHNOLOGIES, INC.

Dated as of July 3, 2022

TABLE OF CONTENTS

TABLE OF DEFINED TERMS

Terms	Cross Reference in Agreement
Accounting Firm	Section 6.15(c)
Acquisition Proposal	Section 6.1(f)(i)
Adjusted Warrant	Section 2.3(c)
Affiliate	Section 2.1(b)
Agreement	Preamble
Alternative Acquisition Agreement	Section 6.1(b)(ii)
Anticipated Closing Date	Section 6.15(a)
Business Day	Section 1.2
Capitalization Date	Sections 3.6(a)
Cash Determination Time	Section 6.15(d)(i)
Certificate of Merger	Section 1.1
Certificates	Section 2.2(a)
Closing	Section 1.2
Closing Date	Section 1.2
COBRA	Section 3.17(p)(i)
Code	Preamble
Confidentiality Agreement	Section 5.3
Consent	Section 3.5(b)
Contemplated Transactions	Section 3.1(b)
Continuing Service Provider	Section 2.3(a)
Contract	Section 3.1(a)
COVID-19 Measures	Section 3.5(a)(v)
DGCL	Preamble
Dispute Notice	Section 6.15(b)
Effect	Section 3.1(b)
Effective Time	Section 1.1
Employee Plan	Section 3.17(p)(ii)
Encumbrance	Section 3.5(a)(v)
Enforceability Exceptions	Section 3.3
Environmental Law	Section 3.18
ERISA	Section 3.17(p)(iii)
ERISA Affiliate	Section 3.17(p)(iv)
Exchange Act	Section 3.7(a)
Exchange Agent	Section 2.2(a)
Exchange Fund	Section 2.2(a)
Exchange Ratio	Section 2.1(c)
FDA	3.14(c)
FDCA	3.14(c)
Financing	Preamble
Financing Agreements	Section 6.19(a)
GAAP	Section 3.5(a)(v)
Governmental Authorization	Section 3.5(a)(iii)
Hazardous Materials	Section 3.18
Indebtedness	Section 6.15(d)(ii)
Indemnified Persons	Section 6.9(a)
Intellectual Property	Section 3.12(j)(i)
Intellectual Property Registrations	Section 3.12(j)(ii)
Intended Tax Treatment	Preamble

Terms	Cross Reference in Agreement
Intervening Event	Section 6.1(f)(ii)
IRS	Section 4.17(b)
Key Employee	Section 3.15(b)
Knowledge	Section 9.8
Law	Section 3.12(j)(iii)
Legal Proceeding	Section 3.15(c)
Lock-Up Agreements	Preamble
Lookback Date	Section 3.7(c)
Merger	Preamble
Merger Share Issuance	Preamble
Merger Sub	Preamble
Multiemployer Plan	Section 3.17(p)(v)
Multiple Employer Plan	Section 3.17(p)(vi)
Multiple Employer Welfare Arrangement	Section 3.17(p)(vii)
Nasdaq	Section 2.2(c)
Nasdaq Listing Application	Section 6.3
Net Cash	Section 6.15(d)(iii)
Organizational Documents	Section 3.2
Order	Section 3.12(j)(viii)
Ordinary Course of Business	Section 3.5(a)(v)
Other Tyme Voting Proposals	Section 3.7(i)
Other Syros Voting Proposals	Section 3.7(i)
Outside Date	Section 8.1(b)
Patent Rights	Section 3.12(j)(ix)
Permitted Encumbrance	Section 3.5(a)(v)
Personal Information	Section 3.22
PIPE Share Issuance	Preamble
Privacy Laws	Section 3.22
Proxy Statement/Prospectus	Section 3.7(i)
Qualified Person	Section 6.1(f)(iii)
Recommendation Change Notice	Section 6.1(b)
Registration Statement	Section 3.7(i)
Regulation M-A Filing	Section 3.7(i)
Representatives	Section 6.1(a)
Required Tyme Voting Proposal	Section 3.7(i)
Required Syros Stockholder Vote	Section 4.4
Required Syros Voting Proposal	Section 3.7(i)
Sarbanes-Oxley Act	Section 3.7(a)
SEC	Section 3.7(a)
Securities Act	Section 3.7(a)
Securities Purchase Agreement	Preamble
Specified Time	Section 6.1(f)(iv)
Subsidiary	Section 2.1(b)
Superior Proposal	Section 6.1(f)(v)
Surviving Corporation	Section 1.3
Syros	Preamble
Syros Associate	Section 4.15(a)
Syros Authorized Stock Increase	Section 3.7(i)
Syros Balance Sheet	Section 4.9
Syros Board	Preamble

Terms	Cross Reference in Agreement
Syros Board Recommendation Change	Section 6.1(b)(i)
Syros Certifications	Sections 4.7(a)
Syros Common Stock	Section 2.1(c)
Syros Contract	Section 4.5(b)
Syros Disclosure Schedule	Article IV
Syros Employee Plan	Section 3.17(p)
Syros Intellectual Property	Section 3.12(j)(x)
Syros Licensed Intellectual Property	Section 3.12(j)(xi)
Syros Material Adverse Effect	Section 4.1(b)
Syros Material Contract	Section 4.13
Syros Meeting	Section 3.7(i)
Syros Option	Section 4.6(c)
Syros Owned Intellectual Property	Section 3.12(j)(xii)
Syros Per Share Price	Section 2.1(c)
Syros Permits	Section 4.14(b)
Syros Product Candidates	Section 4.14(d)
Syros Registrations	Section 3.12(j)(xiii)
Syros Regulatory Permits	Section 4.14(d)
Syros RSU	Section 4.6(c)
Syros SEC Documents	Section 4.7(a)
Syros Stock Plans	Section 4.6(c)
Syros Support Agreement	Preamble
Syros Termination Fee	Section 8.3(c)
Syros Voting Proposals	Section 3.7(i)
Tax Opinion	Section 6.8(b)
Tax Return	Section 3.16(j)
Tax	Section 3.16(j)
Trademarks	Section 3.12(j)(xiv)
Transaction Expenses	Section 6.15(d)(iv)
Treasury Regulations	Section 3.16(g)
Tyme	Preamble
Tyme Associate	Section 3.15(a)
Tyme Balance Sheet	Section 3.9
Tyme Board	Preamble
Tyme Board Recommendation Change	Section 6.1(b)(i)
Tyme Capital Stock	Section 2.1
Tyme Certifications	Sections 3.7(a)
Tyme Common Stock	Section 2.1(b)
Tyme Contract	Section 3.5(b)
Tyme Disclosure Schedule	Article III
Tyme Employee Plan	Section 3.17(p)(viii)
Tyme Intellectual Property	Section 3.12(j)(iv)
Tyme Licensed Intellectual Property	Section 3.12(j)(v)
Tyme Material Adverse Effect	Section 3.1(b)
Tyme Material Contract	Section 3.13
Tyme Meeting	Section 3.4
Tyme Net Cash	Section 6.15(a)
Tyme Net Cash Schedule	Section 6.15(a)
Tyme Options	Section 2.3(a)
Tyme Outstanding Shares	Section 2.1(c)

Terms	Cross Reference in Agreement
Tyme Owned Intellectual Property	Section 3.12(j)(vi)
Tyme Per Share Value	Section 2.1(c)
Tyme Permits	Section 3.14(b)
Tyme Product Candidates	Section 3.14(d)
Tyme Real Estate Leases	Section 3.11
Tyme Registrations	Section 3.12(j)(vii)
Tyme Regulatory Permits	Section 3.14(d)
Tyme SEC Documents	Section 3.7(a)
Tyme Stock Plans	Section 2.3(a)
Tyme Stockholder Approval	Section 3.4
Tyme Support Agreements	Preamble
Tyme Termination Fee	Section 8.3(b)
Tyme Valuation	Section 2.1(c)
Tyme Voting Proposals	Section 3.7(i)
Tyme Warrants	Section 2.3(c)
2020 Tyme Warrants	Section 2.3(c)

AGREEMENT AND PLAN OF MERGER

THIS AGREEMENT AND PLAN OF MERGER (this "Agreement"), dated as of July 3, 2022, is entered into by and among Syros Pharmaceuticals, Inc., a Delaware corporation ("Syros"); Tack Acquisition Corp., a Delaware corporation and a wholly owned subsidiary of Syros (the "Merger Sub"); and Tyme Technologies, Inc., a Delaware corporation ("Tyme").

WHEREAS, the Board of Directors of Syros (the "Syros Board") and the Board of Directors of Tyme (the "Tyme Board") have each (i) determined that the Merger is fair to, and in the best interests of, their respective corporations and stockholders, (ii) approved and declared advisable this Agreement, the Merger and the actions contemplated by this Agreement and (iii) determined to recommend that the stockholders of their respective corporations vote to approve such matters as are contemplated by this Agreement, including, in the case of Tyme, the adoption of this Agreement and, in the case of Syros, the approval of the issuance of shares of Syros Common Stock pursuant to this Agreement (the "Merger Share Issuance") and the Securities Purchase Agreement (as defined below) (the "PIPE Share Issuance" and, together with the Merger Share Issuance, the "Share Issuance") and the Syros Authorized Stock Increase (as defined below);

WHEREAS, the combination of Syros and Tyme shall be effected through a merger (the "Merger") of Merger Sub with and into Tyme in accordance with the terms of this Agreement and the General Corporation Law of the State of Delaware (the "DGCL"), as a result of which Tyme will become a wholly owned subsidiary of Syros;

WHEREAS, concurrently with the execution and delivery of this Agreement and as a condition and inducement to Syros' willingness to enter into this Agreement, each of the stockholders of Tyme named in Section A of the Tyme Disclosure Schedule has entered into (i) a support agreement, dated as of the date of this Agreement, in the form attached hereto as Exhibit A-1 or otherwise in a form satisfactory to Syros (the "Tyme Support Agreements") and (ii) a lock-up agreement in the form attached hereto asExhibit A-2 (the "Lock-Up Agreements");

WHEREAS, concurrently with the execution and delivery of this Agreement and as a condition and inducement to Tyme's willingness to enter into this Agreement, each of the stockholders of Syros named in Section A of the Syros Disclosure Schedule have entered into a support agreement, dated as of the date of this Agreement, in the form attached hereto as Exhibit A-3 (the "Syros Support Agreement") and (ii) Lock-Up Agreements;

WHEREAS, concurrently with the execution and delivery of this Agreement, Syros shall have entered into the Securities Purchase Agreement, dated as of July 3, 2022, by and among Syros and the investors identified on Exhibit A attached thereto (the "Securities Purchase Agreement"), pursuant to which Syros will, at or prior to the Closing, and subject to the satisfaction of the closing conditions set forth in the Securities Purchase Agreement, receive gross proceeds of approximately $130,000,000 (the "Financing"); and

WHEREAS, each of the parties intends that, for U.S. federal income Tax purposes: (i) if Section 368 of the Internal Revenue Code of 1986 (the "Code") applies, (a) this Agreement shall constitute a "plan of reorganization" within the meaning of Section 368 and the Treasury Regulations promulgated thereunder and (b) the Merger shall constitute a "reorganization" within the meaning of Section 368(a) of the Code; and (ii) if Section 351 of the Code applies, the Merger and PIPE Share Issuance, taken together as an integrated transaction, shall constitute a transfer which qualifies under Section 351 of the Code (in either case, the "Intended Tax Treatment").

NOW, THEREFORE, in consideration of the foregoing and the respective representations, warranties, covenants and agreements set forth below, Syros, Merger Sub and Tyme agree as follows:

ARTICLE I

THE MERGER

1.1 Effective Time of the Merger. Upon the terms and subject to the conditions set forth in this Agreement, on the Closing Date the parties hereto will cause the Merger to be consummated by executing and filing a certificate of merger (the "Certificate of Merger") in accordance with the relevant provisions of the DGCL. The Merger shall become effective upon the filing of the Certificate of Merger with the Secretary of State of the State of Delaware or at such subsequent time or date as Syros and Tyme shall agree and specify in the Certificate of Merger (the "Effective Time").

1.2 Closing. Subject to the satisfaction or (to the extent permitted by Law) waiver of the conditions set forth in Article VII, the closing of the Merger (the "Closing") will take place at 11:00 a.m., Eastern time, on a date to be specified by Syros and Tyme (the "Closing Date"), which shall be no later than the second Business Day after satisfaction or (to the extent permitted by Law) waiver of the conditions set forth in Article VII (other than those conditions that by their nature are to be satisfied at the Closing, but subject to the satisfaction or (to the extent permitted by law) waiver of such conditions), at the offices of Wilmer Cutler Pickering Hale and Dorr LLP, 60 State Street, Boston, Massachusetts 02109 (or by remote exchange of electronic documents), unless another date, place or time is agreed to in writing by Syros and Tyme. For the purposes of this Agreement, the term "Business Day" means any day other than a Saturday, Sunday or other day on which commercial banking institutions in New York, New York, Boston, Massachusetts or Wilmington, Delaware are required or permitted by Law to be closed.

1.3 Effects of the Merger. At the Effective Time, (i) the separate existence of Merger Sub shall cease and Merger Sub shall be merged with and into Tyme (Tyme as the surviving corporation following the Merger is sometimes referred to herein as the "Surviving Corporation") and (ii) the certificate of incorporation of Tyme as in effect as of immediately prior to the Effective Time shall be amended and restated in its entirety to read as set forth on Exhibit B-1, and, as so amended and restated, shall be the certificate of incorporation of the Surviving Corporation. In addition, the bylaws of Tyme, as in effect immediately prior to the Effective Time, shall be amended and restated to read as set forth on Exhibit B-2, and, as so amended, shall be the bylaws of the Surviving Corporation. The Merger shall have the effects set forth in the applicable provisions of the DGCL.

1.4 Directors and Officers of the Surviving Corporation.

(a) The individuals named on Section 1.4(a) of the Syros Disclosure Schedule shall be the initial directors of the Surviving Corporation as of the Effective Time, each to hold office in accordance with the certificate of incorporation and bylaws of the Surviving Corporation.

(b) The individuals named on Section 1.4(b) of the Syros Disclosure Schedule shall be the initial officers of the Surviving Corporation as of the Effective Time, each to hold office in accordance with the certificate of incorporation and bylaws of the Surviving Corporation.

1.5 Syros Matters.

(a) Directors. Subject to Section 6.16, until successors are duly elected or appointed and qualified in accordance with applicable Law, the Parties shall use commercially reasonable efforts and take all necessary action so that the current officers and directors of Syros remain in the positions of officers and directors of Syros, to serve in such positions effective as of the Effective Time.

(b) Lock-up Agreements. Syros and Tyme shall use commercially reasonable efforts to have each individual who will serve as a director or officer of Syros following the Closing to execute and deliver a Lock-Up Agreement prior to Closing to the extent not executed and delivered on or prior to the date of this Agreement.

ARTICLE II

CONVERSION OF SECURITIES

2.1 Conversion of Capital Stock. As of the Effective Time, by virtue of the Merger and without any action on the part of the holder of any shares of Tyme Capital Stock or any shares of capital stock of Merger Sub:

(a) Capital Stock of Merger Sub. Each share of the common stock, $0.0001 par value per share, of Merger Sub issued and outstanding immediately prior to the Effective Time shall be converted into and become one fully paid and nonassessable share of common stock, $0.0001 par value per share, of the Surviving Corporation.

(b) Cancellation of Treasury Stock and Syros Owned Stock. All shares of common stock, $0.0001 par value per share, of Tyme ("Tyme Common Stock") that are held in treasury or by any Subsidiary of Tyme and any shares of Tyme Common Stock owned by Syros, Merger Sub or any other Subsidiary of Syros immediately prior to the Effective Time shall be cancelled and shall cease to exist and no stock of Syros or other consideration shall be delivered in exchange therefor. For purposes of this Agreement, (i) "Subsidiary" means, with respect to a person, an Entity in which such person directly or indirectly owns or purports to own, beneficially or of record, (a) an amount of voting securities or other interests in such Entity that is sufficient to enable such person to elect at least a majority of the members of such entity's board of directors or other governing body or (b) at least 50% of the outstanding equity, voting, beneficial or financial interests in such Entity; and (ii) "Affiliate" means, when used with respect to any person, any other person who is an "affiliate" of that party within the meaning of Rule 405 promulgated under the Securities Act.

(c) Conversion of Tyme Common Stock. Subject to Section 2.2, each share of Tyme Common Stock (other than shares to be cancelled in accordance with Section 2.1(b)) shall be automatically converted into the right to receive a number of shares of common stock, $0.001 par value per share, of Syros ("Syros Common Stock") equal to the Exchange Ratio. As of the Effective Time, all such shares of Tyme Common Stock shall cease to be outstanding and shall automatically be cancelled and shall cease to exist, and each holder of a certificate representing any such shares of Tyme Common Stock shall cease to have any rights with respect thereto, except the right to receive the shares of Syros Common Stock pursuant to this Section 2.1(c) and any cash in lieu of fractional shares of Syros Common Stock to be issued or paid in consideration therefor and any amounts payable pursuant to Section 2.2(d) upon the surrender of such certificate in accordance with Section 2.2, without interest. For purposes of this Agreement, "Exchange Ratio" means, subject to Section 2.2(d), the quotient (rounded down to four decimal places) obtained by dividing (x) the Tyme Per Share Value by (y) the Syros Per Share Price, in which:

(i) "Tyme Outstanding Shares" means the total number of shares of Tyme Common Stock actually issued and outstanding immediately prior to the Effective Time.

(ii) "Tyme Per Share Value" means the quotient determined by dividing (A) the Tyme Valuation by (B) the Tyme Outstanding Shares.

(iii) "Tyme Valuation" means $7.5 million plus Tyme Net Cash.

(iv) "Syros Per Share Price" means $0.94.

For the avoidance of doubt and for illustrative purposes only, a sample Exchange Ratio calculation is attached hereto as Annex A.

(d) Certain Adjustments. If, between the date of this Agreement and the Effective Time, the outstanding shares of Tyme Common Stock or Syros Common Stock shall have been changed into, or exchanged for, a different number of shares or a different class, by reason of any stock dividend, subdivision, reclassification, recapitalization, split, combination or exchange of shares or other like change, the Exchange Ratio shall, to the extent necessary, be equitably adjusted to reflect such change to the extent necessary to provide the holders of Tyme Common Stock, Tyme Options and Tyme Warrants with the same economic effect as contemplated by this Agreement prior to such stock dividend, subdivision, reclassification, recapitalization, split, combination or exchange of shares or other like change; provided, however, that nothing herein will be construed to permit the Syros or Tyme to take any action with respect to Syros Common Stock or Tyme Common Stock, respectively, that is prohibited or expressly not permitted by the terms of this Agreement.

2.2 Exchange of Certificates. The procedures for exchanging outstanding shares of Tyme Common Stock for Syros Common Stock pursuant to the Merger are as follows:

(a) Exchange Agent. At or immediately prior to the Effective Time, Syros shall deposit with Computershare Trust Company, N.A. or another bank or trust company designated by Syros and reasonably acceptable to Tyme (the "Exchange Agent"), for the benefit of the holders of shares of Tyme Common Stock, for exchange in accordance with this Section 2.2, through the Exchange Agent, (i) certificates representing the shares of Syros Common Stock (such shares of Syros Common Stock, together with any dividends or distributions with respect thereto with a record date after the Effective Time, being hereinafter referred to as the "Exchange Fund") issuable pursuant to Section 2.1 in exchange for outstanding shares of Tyme Common Stock, (ii) cash in an amount sufficient to make payments for fractional shares required pursuant to Section 2.2(c) and (iii) any dividends or distributions to which holders of certificates or book entry records that, as of immediately prior to the Effective Time, represented outstanding shares of Tyme Common Stock (the "Certificates"), whose shares were converted pursuant to Section 2.1 into the right to receive shares of Syros Common Stock, may be entitled pursuant to Section 2.2(d). Prior to the Effective Time, Syros shall enter into an agreement with the Exchange Agent in form and substance reasonably satisfactory to Tyme.

(b) Exchange Procedures. As soon as reasonably practicable after the Effective Time, the Exchange Agent shall mail to each holder of record of a Certificate (i) a letter of transmittal in customary form specifying that delivery shall be effected, and risk of loss and title to the Certificates shall pass, only upon delivery of the Certificates to the Exchange Agent, and (ii) instructions for use in effecting the surrender of the Certificates in exchange for certificates or book entry records representing shares of Syros Common Stock (plus cash in lieu of fractional shares, if any, of Syros Common Stock and any dividends or distributions as provided below); provided, that, appropriate provision shall be made for electronic delivery and/or acceptance consistent with market practices. Upon surrender of a Certificate for cancellation to the Exchange Agent or to such other agent or agents as may be appointed by Syros, together with such letter of transmittal, duly executed, and such other documents as may reasonably be required by the Exchange Agent and Syros, the holder of such Certificate shall be entitled to receive in exchange therefor a certificate or book entry record representing that number of whole shares of Syros Common Stock which such holder has the right to receive pursuant to the provisions of this Article II plus cash in lieu of fractional shares pursuant to Section 2.2(c) and any dividends or distributions then payable pursuant to Section 2.2(d), and the Certificate so surrendered shall immediately be cancelled. In the event of a transfer of ownership of Tyme Common Stock which is not registered in the transfer records of Tyme, a certificate representing the proper number of whole shares of Syros Common Stock plus cash in lieu of fractional shares pursuant to Section 2.2(c) and any dividends or distributions pursuant to Section 2.2(d) may be issued or paid to a person other than the person in whose name the Certificate so surrendered is registered, only if such Certificate is presented to the Exchange Agent, accompanied by all documents required to evidence and effect such transfer and by evidence that any applicable stock transfer taxes have been paid. Until surrendered as contemplated by this Section 2.2, each Certificate shall be deemed at any time after the Effective Time to

represent only the right to receive shares of Syros Common Stock pursuant to the provisions of this Article II plus cash in lieu of fractional shares pursuant to Section 2.2(c) and any dividends or distributions then payable pursuant to Section 2.2(d) as contemplated by this Section 2.2.

(c) No Fractional Shares. No certificate or scrip representing fractional shares of Syros Common Stock shall be issued upon the surrender for exchange of Certificates, and such fractional share interests shall not entitle the owner thereof to vote or to any other rights of a stockholder of Syros. Notwithstanding any other provision of this Agreement, each holder of shares of Tyme Common Stock converted pursuant to the Merger who would otherwise have been entitled to receive a fraction of a share of Syros Common Stock (after taking into account all Certificates delivered by such holder and the aggregate number of shares of Tyme Common Stock represented thereby) shall receive, in lieu thereof, cash (without interest and subject to applicable Tax withholding) in an amount equal to such fractional part of a share of Syros Common Stock multiplied by the last reported sale price of Syros Common Stock at the 4:00 p.m., Eastern time, end of regular trading hours on The Nasdaq Global Market ("Nasdaq") on the last trading day prior to the Effective Time.

(d) Distributions with Respect to Unexchanged Shares. No dividends or other distributions declared or made after the Effective Time with respect to Syros Common Stock with a record date after the Effective Time shall be paid to the holder of any unsurrendered Certificate until the holder of record of such Certificate shall surrender such Certificate in accordance with this Section 2.2. Subject to the effect of applicable laws, following surrender of any such Certificate, there shall be issued and paid to the record holder of the Certificate, at the time of such surrender the amount of dividends or other distributions with a record date after the Effective Time previously paid with respect to such whole shares of Syros Common Stock, without interest, and at the appropriate payment date, the amount of dividends or other distributions having a record date after the Effective Time but prior to surrender and a payment date subsequent to surrender that are payable with respect to such whole shares of Syros Common Stock.

(e) No Further Ownership Rights in Tyme Common Stock. All shares of Syros Common Stock issued upon the surrender for exchange of Certificates in accordance with the terms hereof (including any cash or dividends or other distributions paid pursuant to Section 2.2(c) or 2.2(d)) shall be deemed to have been issued (and paid) in full satisfaction of all rights pertaining to such shares of Tyme Common Stock, and from and after the Effective Time there shall be no further registration of transfers on the stock transfer books of the Surviving Corporation of the shares of Tyme Common Stock that were outstanding immediately prior to the Effective Time. If, after the Effective Time, Certificates are presented to the Surviving Corporation or the Exchange Agent for any reason, they shall be cancelled and exchanged as provided in this Article II.

(f) Termination of Exchange Fund. Any portion of the Exchange Fund that remains undistributed to the holders of Tyme Common Stock for one year after the Effective Time shall be delivered to Syros, upon demand, and any holder of Tyme Common Stock immediately prior to the Effective Time who has not previously complied with this Section 2.2 shall thereafter look only to Syros, as a general unsecured creditor, for payment of its claim for Syros Common Stock, any cash in lieu of fractional shares of Syros Common Stock and any dividends or distributions with respect to Syros Common Stock.

(g) No Liability. To the extent permitted by applicable law, none of Syros, Merger Sub, Tyme, the Surviving Corporation or the Exchange Agent shall be liable to any holder of shares of Tyme Common Stock or Syros Common Stock, as the case may be, for such shares or any cash amounts required to be delivered to a public official pursuant to any applicable abandoned property, escheat or similar law. If any Certificate shall not have been surrendered immediately prior to such date on which any shares of Syros Common Stock, and any cash payable to the holder of such Certificate or any dividends or distributions payable to the holder of such Certificate pursuant to this Article II would otherwise escheat to or become the property of any Governmental Authority, such Certificate and any such shares of Syros Common Stock or cash, dividends or distributions in respect of such Certificate shall, to the maximum extent permitted by applicable law, become the property of the Surviving Corporation, free and clear of all claims or interest of any person previously entitled thereto.

(h) Withholding Rights. Each of the Exchange Agent, Syros and the Surviving Corporation shall be entitled to deduct and withhold from the amounts otherwise payable pursuant to this Agreement to any holder of shares of Tyme Common Stock and any other recipient of payments hereunder such amounts as it reasonably determines that it is required to deduct and withhold with respect to the making of such payment under the Code, or any other applicable provision of law. To the extent that amounts are so withheld by the Surviving Corporation or Syros, as the case may be, such withheld amounts shall be treated for all purposes of this Agreement as having been paid to the holder of the shares of Tyme Common Stock or other recipient of payments hereunder in respect of which such deduction and withholding was made by the Surviving Corporation or Syros, as the case may be.

(i) Lost Certificates. If any Certificate shall have been lost, stolen or destroyed, upon the making of an affidavit of that fact by the person claiming such Certificate to be lost, stolen or destroyed and, if required by the Surviving Corporation, the posting by such person of a bond in such reasonable amount as the Surviving Corporation may direct as indemnity against any claim that may be made against it with respect to such Certificate, the Exchange Agent shall issue in exchange for such lost, stolen or destroyed Certificate the shares of Syros Common Stock and any cash in lieu of fractional shares, and unpaid dividends and distributions on shares of Syros Common Stock deliverable in respect thereof pursuant to this Agreement.

2.3 Tyme Stock Plans and Tyme Warrants.

(a) At the Effective Time, each outstanding option to purchase Tyme Common Stock (each, a "Tyme Option" and collectively, the "Tyme Options") granted to an individual who continues in the service of the Surviving Corporation at or after the Closing (whether as a director, officer, employee, consultant or other service provider) (each, a "Continuing Service Provider"), whether vested or unvested, and all stock or equity-related plans, agreements or arrangements of Tyme (the "Tyme Stock Plans") themselves, insofar as they relate to outstanding Tyme Options granted to Continuing Service Providers, shall be assumed by Syros and each Tyme Option shall become an option to acquire, on the same terms and conditions as were applicable under such Tyme Option immediately prior to the Effective Time (subject to Section 6.10(b)), such number of shares of Syros Common Stock as is equal to the number of shares of Tyme Common Stock subject to the unexercised portion of such Tyme Option immediately prior to the Effective Time multiplied by the Exchange Ratio (rounded down to the nearest whole share number), at an exercise price per share equal to the exercise price per share of such Tyme Option immediately prior to the Effective Time divided by the Exchange Ratio (rounded up to the nearest whole cent); provided that the assumption of each Tyme Option pursuant to this Section 2.3(a) shall comply with all requirements of Sections 424 and 409A of the Code and the Treasury regulations issued thereunder, as applicable.

(b) At the Effective Time, each outstanding Tyme Option that is not assumed pursuant to Section 2.3(a) will be terminated and shall cease to exist and no consideration shall be delivered in exchange therefor.

(c) Immediately prior to the Effective Time, any outstanding warrants to purchase Tyme Common Stock issued by Tyme on May 20, 2020 (the "2020 Tyme Warrants") shall be purchased by Tyme from the holder thereof on the terms set forth in such warrant agreement. At the Effective Time, by virtue of the Merger, all other warrants (other than 2020 Tyme Warrants) to purchase shares of Tyme Common Stock outstanding immediately prior to the Effective Time (such outstanding warrants, the "Tyme Warrants") shall be automatically assumed by Syros and shall become a warrant to acquire, on the same terms and conditions as were applicable under such Tyme Warrant, such number of shares of Syros Common Stock as is equal to the number of shares of Tyme Common Stock subject to the unexercised portion of such Tyme Warrant immediately prior to the Effective Time multiplied by the Exchange Ratio (rounded down to the nearest whole share number), at an exercise price per share equal to the exercise price per share of such Tyme Warrant immediately prior to the Effective Time divided by the Exchange Ratio (rounded up to the nearest whole cent) (each, as so adjusted, an "Adjusted Warrant").

(d) Tyme shall, prior to the Effective Time, take all actions within its control necessary or desirable in connection with the treatment of Tyme Options contemplated by Sections 2.3(a) and 2.3(b) and Tyme Warrants contemplated by Section 2.3(c), including providing the holder of each Tyme Option that will be terminated at Closing with notice and the opportunity to exercise such Tyme Option prior to Closing (to the extent such notice and opportunity is required under the terms of the applicable agreement, instrument or plan).

(e) Syros shall take all corporate actions necessary to reserve for issuance of shares of Syros Common Stock that will be subject to the assumed Tyme Options and the Adjusted Warrants. Furthermore, Syros shall file with the SEC, as promptly as practicable after the Effective Time, a registration statement on Form S-8 (or any other appropriate form), registering the shares of Syros Common Stock issuable with respect to Tyme Options assumed by Syros in accordance with Sections 2.3(a).

2.4 No Appraisal Rights. In accordance with Section 262(b)(1) of the DGCL, no statutory appraisal rights shall be available for to the holders of Tyme Common Stock in connection with the Contemplated Transaction.

ARTICLE III

REPRESENTATIONS AND WARRANTIES OF TYME

Tyme represents and warrants to Syros and Merger Sub that the statements contained in this Article III are true and correct, except (a) as disclosed in the Tyme SEC Reports filed or furnished prior to the date of this Agreement (but excluding any disclosures under the heading "Risk Factors" and any disclosure of risks included in any "forward looking statements" disclaimers or in any other section to the extent they are forward-looking statements or cautionary, predictive or forward-looking in nature) or (b) as expressly set forth herein or in the disclosure schedule delivered or made available by Tyme to Syros and Merger Sub on the date of this Agreement (the "Tyme Disclosure Schedule"). For purposes hereof, the phrase "to the knowledge of Tyme" and similar expressions mean the actual knowledge of the persons identified on Section K of the Tyme Disclosure Schedule for this purpose, and such knowledge as such persons would reasonably be expected to have obtained in the course of their performance of their duties to Tyme (after due inquiry).

3.1 Due Organization; Subsidiaries.

(a) Each of Tyme and its Subsidiaries is a corporation or other legal entity duly incorporated or otherwise organized, validly existing and in good standing under the Laws of the jurisdiction of its incorporation or organization and has all necessary power and authority: (i) to conduct its business in the manner in which its business is currently being conducted, (ii) to own or lease and use its property and assets in the manner in which its property and assets are currently owned or leased and used and (iii) to perform its obligations under all Contracts (as defined below) by which it is bound. All of Tyme's Subsidiaries are wholly owned by Tyme. For purposes of this Agreement, "Contract" means, with respect to any person, any written agreement, contract, subcontract, lease (whether for real or personal property), mortgage, license, or other legally binding commitment or undertaking of any nature to which such person is a party or by which such person or any of its assets are bound or affected under applicable Law.

(b) Each of Tyme and its Subsidiaries is licensed and qualified to do business, and is in good standing (to the extent applicable in such jurisdiction), under the Laws of all jurisdictions where the nature of its business requires such licensing or qualification other than in jurisdictions where the failure to be so qualified individually or in the aggregate would not be reasonably expected to have a Tyme Material Adverse Effect. For purposes of this Agreement, the term "Tyme Material Adverse Effect" means any effect, change, event, circumstance or development (an "Effect") that, individually or in the aggregate with all other Effects that have occurred through the date of determination, has had, or is reasonably likely to have, a material adverse effect on the assets, liabilities or financial condition of Tyme and its Subsidiaries, taken as a whole; provided, however, that no

Effect, to the extent resulting from or arising out of any of the following, shall be deemed to be a Tyme Material Adverse Effect or be taken into account for purposes of determining whether a Tyme Material Adverse Effect has occurred or is reasonably likely to occur: (A) adverse developments in Tyme's clinical pipeline that have been disclosed in Tyme SEC Reports as of the date of this Agreement, (B) changes after the date of this Agreement in prevailing economic or market conditions in the United States or any other jurisdiction in which such entity has substantial business operations (except to the extent those changes have a disproportionate effect on Tyme and its Subsidiaries relative to the other participants in the industry or industries in which Tyme and its Subsidiaries operate), (C) changes or events after the date of this Agreement affecting the industry or industries in which Tyme and its Subsidiaries operate generally (except to the extent those changes or events have a disproportionate effect on Tyme and its Subsidiaries relative to the other participants in the industry or industries in which Tyme and its Subsidiaries operate), (D) changes after the date of this Agreement in generally accepted accounting principles or requirements (except to the extent those changes have a disproportionate effect on Tyme and its Subsidiaries relative to the other participants in the industry or industries in which Tyme and its Subsidiaries operate), (E) changes after the date of this Agreement in laws, rules or regulations of general applicability or interpretations thereof by any Governmental Authority (except to the extent those changes have a disproportionate effect on Tyme and its Subsidiaries relative to the other participants in the industry or industries in which Tyme and its Subsidiaries operate), (F) any natural disaster, epidemic, pandemic or other disease outbreak (including the COVID-19 pandemic) or any outbreak of major hostilities in which the United States is involved or any act of terrorism within the United States or directed against its facilities or citizens wherever located (except to the extent those changes or events have a disproportionate effect on Tyme and its Subsidiaries relative to the other participants in the industry or industries in which Tyme and its Subsidiaries operate), (G) a change in the public trading price of Tyme Common Stock or the implications hereof, (H) a change in the trading volume of Tyme Common Stock due to the announcement of the Agreement or the pendency of the Merger and the other transactions contemplated by the Agreement (including the Financing) (collectively, the "Contemplated Transactions") or (I) any failure by Tyme to meet any public estimates or expectations of Tyme's revenue, earnings or other financial performance or results of operations for any period, or (J) any failure by Tyme to meet any internal guidance, budgets, plans or forecasts of its revenues, earnings or other financial performance or results of operations (but not, in the case of this clause (K), the underlying cause of such changes or failures, unless such changes or failures would otherwise be excepted from this definition).

(c) Except as set forth on Section 3.1(c) of the Tyme Disclosure Schedule, Tyme has no Subsidiaries and Tyme does not own any capital stock of, or any equity ownership or profit sharing interest of any nature in, or control directly or indirectly, any other Entity. Tyme is not and has not otherwise been, directly or indirectly, a party to, member of or participant in any partnership, joint venture or similar business entity. Tyme has not agreed and is not obligated to make, nor is Tyme bound by any Contract under which it may become obligated to make, any future investment in or capital contribution to any other Entity. Tyme has not, at any time, been a general partner of, and has not otherwise been liable for any of the debts or other obligations of, any general partnership, limited partnership or other Entity.

3.2 Organizational Documents. Tyme has made available to the Company accurate and complete copies of Tyme's Organizational Documents. Tyme is not in breach or violation of its Organizational Documents in any material respect. For purposes of this Agreement, "Organizational Documents" means, with respect to any person (other than an individual), (a) the certificate or articles of association or incorporation or organization or limited partnership or limited liability company, and any joint venture, limited liability company, operating or partnership agreement and other similar documents adopted or filed in connection with the creation, formation or organization of such person and (b) all bylaws, regulations and similar documents or agreements relating to the organization or governance of such person, in each case, as amended or supplemented.

3.3 Authority; Binding Nature of Agreement. Tyme has all necessary corporate power and authority to enter into and to perform its obligations under this Agreement and to consummate the Contemplated Transactions to which it is a party. The Tyme Board (at meetings duly called and held) has: (a) determined that the Contemplated Transactions to which it is a party are fair to, advisable and in the best interests of Tyme and its

stockholders, (b) approved and declared advisable this Agreement and the Contemplated Transactions to which it is a party, and (c) determined to recommend, upon the terms and subject to the conditions set forth in this Agreement, that the stockholders of Tyme vote to approve this Agreement and the Contemplated Transactions to which it is a party. This Agreement has been duly executed and delivered by Tyme and, assuming the due authorization, execution and delivery by Syros, constitutes the legal, valid and binding obligation of Tyme, enforceable against Tyme in accordance with its terms, subject to the (a) Laws of general application relating to bankruptcy, insolvency and the relief of debtors and (b) rules of law governing specific performance, injunctive relief and other equitable remedies (collectively, the "Enforceability Exceptions").

3.4 Vote Required. The affirmative vote of a majority of the outstanding shares of Tyme Common Stock at the meeting of Tyme's stockholders (the "Tyme Meeting") is the only vote of the holders of any class or series of Tyme's capital stock necessary to approve and adopt this Agreement and to approve the Contemplated Transactions (the "Tyme Stockholder Approval").

3.5 Non-Contravention; Consents.

(a) Subject to obtaining the Tyme Stockholder Approval and the filing of the Certificate of Merger required by the DGCL, neither (x) the execution, delivery or performance of this Agreement by Tyme, nor (y) the consummation of the Contemplated Transactions, will directly or indirectly (with or without notice or lapse of time):

(i) contravene, conflict with or result in a violation of any of the provisions of the Organizational Documents of Tyme or its Subsidiaries;

(ii) contravene, conflict with or result in a material violation of, or give any Governmental Authority or other person the right to challenge the Contemplated Transactions or to exercise any remedy or obtain any relief under, any Law or any Order to which Tyme or its Subsidiaries, or any of the assets owned or used by Tyme or its Subsidiaries, is subject;

(iii) contravene, conflict with or result in a material violation of any of the terms or requirements of, or give any Governmental Authority the right to revoke, withdraw, suspend, cancel, terminate or modify, any (a) permit, license, certificate, franchise, permission, variance, exception, order, clearance, registration, qualification or authorization issued, granted, given or otherwise made available by or under the authority of any Governmental Authority or pursuant to any Law or (b) right under any Contract with any Governmental Authority (each, a "Governmental Authorization") that is held by Tyme or its Subsidiaries, or that otherwise relates to the business of Tyme, or any of the assets owned, leased or used by Tyme;

(iv) contravene, conflict with or result in a violation or breach of, or result in a default under, any provision of any Tyme Material Contract, or give any person the right to: (A) declare a default or exercise any remedy under any Tyme Material Contract, (B) any material payment, rebate, chargeback, penalty or change in delivery schedule under any such Tyme Material Contract, (C) accelerate the maturity or performance of any Tyme Material Contract or (D) cancel, terminate or modify any term of any Tyme Material Contract, except in the case of any non-material breach, default, penalty or modification; or

(v) result in the imposition or creation of any Encumbrance upon or with respect to any asset owned or used by Tyme or its Subsidiaries (except for Permitted Encumbrances). For purposes of this Agreement, (a) "Encumbrance" means any lien, pledge, hypothecation, charge, mortgage, security interest, lease, license, option, easement, reservation, servitude, adverse title, claim, infringement, interference, option, right of first refusal, preemptive right, community property interest or restriction or encumbrance of any nature (including any restriction on the voting of any security, any restriction on the transfer of any security or other asset, any restriction on the receipt of any income derived from any asset, any restriction on the use of any asset and any restriction on the possession, exercise or transfer of any other attribute of ownership of any asset);

(b) "Permitted Encumbrance" means (1) any liens for current Taxes not yet due and payable or for Taxes that are being contested in good faith and for which adequate reserves have been made on the Syros Balance Sheet or the Tyme Balance Sheet, as applicable, in accordance with generally accepted accounting principles in the United States ("GAAP") (2) minor liens that have arisen in the Ordinary Course of Business and that do not (in any case or in the aggregate) materially detract from the value of the assets subject thereto or materially impair the operations of Syros and its Subsidiaries or Tyme and its Subsidiaries, as applicable, (3) statutory liens to secure obligations to landlords, lessors or renters under leases or rental agreements, (4) deposits or pledges made in connection with, or to secure payment of, workers' compensation, unemployment insurance or similar programs mandated by Law, (5) statutory liens in favor of carriers, warehousemen, mechanics and materialmen, to secure claims for labor, materials or supplies and (6) other Encumbrances that do not materially and adversely affect the value, use or operation of the asset subject thereto; (c) "Ordinary Course of Business," as applicable to a person, means entered into in the ordinary course of business consistent in all material respects with past practice taking into account any COVID-19 Measures; and (d) "COVID-19 Measures" means any acts or omissions that have been taken to comply with any quarantine, "shelter in place", "stay at home", workforce reduction, social distancing, shutdown, closure, sequester or any other Law, order, guideline or recommendation by any Governmental Authority in connection with or in response to the COVID-19 pandemic.

(b) Except for (i) any approval, consent, ratification, permission, waiver or authorization (including any Governmental Authorization) (each, a "Consent") set forth on Section 3.5(b) of the Tyme Disclosure Schedule under any Contract (a) to which Tyme is a party, (b) by which Tyme or any Tyme Intellectual Property or any other asset of Tyme is or may become bound or under which Tyme has, or may become subject to, any obligation, or (c) under which Tyme has or may acquire any right or interest (each such contract, a "Tyme Contract"); (ii) the Tyme Stockholder Approval; (iii) the filing of the Certificate of Merger with the Secretary of State of the State of Delaware pursuant to the DGCL; and (iv) such consents, waivers, approvals, orders, authorizations, registrations, declarations and filings as may be required under applicable federal and state securities laws, neither Tyme nor any of its Subsidiaries was, is, or will be required to make any filing with or give any notice to, or to obtain any Consent from, any person in connection with (x) the execution, delivery or performance of this Agreement or (y) the consummation of the Contemplated Transactions.

(c) The Tyme Board has taken and will take all actions necessary to ensure that the restrictions applicable to business combinations contained in Section 203 of the DGCL are, and will be, inapplicable to the execution, delivery and performance of this Agreement and to the consummation of the Contemplated Transactions. No other state takeover statute or similar Law applies or purports to apply to the Merger, this Agreement or any of the other Contemplated Transactions.

3.6 Capitalization.

(a) The authorized capital stock of Tyme (the "Tyme Capital Stock") consists of (i) 300,000,000 shares of Tyme Common Stock, par value $0.0001 per share, of which 172,206,894 shares have been issued and are outstanding as of June 30, 2022 (the "Capitalization Date") and (ii) 10,000,000 shares of preferred stock, par value $0.0001 per share, of which no shares have been issued and are outstanding as of the Capitalization Date. Tyme does not hold any shares of its capital stock in its treasury.

(b) All of the outstanding shares of Tyme Common Stock have been duly authorized and validly issued, and are fully paid and nonassessable and are free of any Encumbrances. None of the outstanding shares of Tyme Common Stock is entitled or subject to any preemptive right, right of participation, right of maintenance or any similar right. None of the outstanding shares of Tyme Common Stock is subject to any right of first refusal in favor of Tyme. Except for the Tyme Support Agreement, as contemplated herein or as set forth in Section 3.6(b) of the Tyme Disclosure Schedule, there is no Tyme Contract relating to the voting or registration of, or restricting any person from purchasing, selling, pledging or otherwise disposing of (or granting any option or similar right with respect to), any shares of Tyme Common Stock. Tyme is not under any obligation, nor is Tyme bound by any Contract pursuant to which it may become obligated, to repurchase, redeem or otherwise acquire any

outstanding shares of Tyme Common Stock or other securities. Section 3.6(b) of the Tyme Disclosure Schedule accurately and completely describes all repurchase rights held by Tyme with respect to shares of Tyme Common Stock (including shares issued pursuant to the exercise of stock options) and specifies which of those repurchase rights are currently exercisable.

(c) Except for Tyme's 2015 Equity Incentive Plan and Amended and Restated 2016 Stock Option Plan for Non-Employee Directors, and except as set forth on Section 3.6(c)(i) of the Tyme Disclosure Schedule, Tyme does not have any stock option plan or any other plan, program, agreement or arrangement providing for any equity-based compensation for any person. As of the date of this Agreement, Tyme has reserved 25,138,579 shares of Tyme Common Stock for issuance under the Tyme Stock Plans, of which 112,671 shares have been issued and are currently outstanding, 17,531,806 shares have been reserved for issuance upon exercise or settlement of Tyme Options, as applicable, granted under the Tyme Stock Plans, and 7,606,773 shares remain available for future issuance pursuant to the Tyme Stock Plans. Section 3.6(c)(i) of the Tyme Disclosure Schedule sets forth the following information with respect to each Tyme Option outstanding as of the date of this Agreement, as applicable: (i) the name of the holder, (ii) the number of shares of Tyme Common Stock subject to such Tyme Option at the time of grant, (iii) the number of shares of Tyme Common Stock subject to such Tyme Option as of the date of this Agreement, (iv) the exercise price of such Tyme Option, (v) the date on which such Tyme Option was granted, (vi) the applicable vesting schedule, including any acceleration provisions and the number of vested and unvested shares as of the date of this Agreement, (vii) the date on which such Tyme Option expires and (viii) whether such Tyme Option is intended to be an "incentive stock option" (as defined in the Code) or a non-qualified stock option. Tyme has made available to the Company accurate and complete copies of equity incentive plans pursuant to which Tyme has equity-based awards, the forms of all award agreements evidencing such equity-based awards and evidence of board and stockholder approval of the Tyme Stock Plans and any amendments thereto.

(d) Except for the outstanding Tyme Options or as set forth on Section 3.6(d) of the Tyme Disclosure Schedule, there is no: (i) outstanding subscription, option, call, warrant or right (whether or not currently exercisable) to acquire any shares of the capital stock or other securities of Tyme, (ii) outstanding security, instrument or obligation that is or may become convertible into or exchangeable for any shares of the capital stock or other securities of Tyme, (iii) stockholder rights plan (or similar plan commonly referred to as a "poison pill") or Contract under which Tyme is or may become obligated to sell or otherwise issue any shares of its capital stock or any other securities or (iv) condition or circumstance that may give rise to or provide a basis for the assertion of a claim by any person to the effect that such person is entitled to acquire or receive any shares of capital stock or other securities of Tyme. There are no outstanding or authorized stock appreciation, phantom stock, profit participation or other similar rights with respect to Tyme.

(e) All outstanding shares of Tyme Common Stock, Tyme Options, other equity securities of Tyme have been issued and granted in material compliance with (i) all applicable securities laws and other applicable Law and (ii) all requirements set forth in applicable Contracts.

(f) With respect to Tyme Options granted pursuant to the Tyme Stock Plans, each Tyme Option grant was made in accordance with the terms of the Tyme Stock Plan pursuant to which it was granted and, to the Knowledge of Tyme, all other applicable Law and regulatory rules or requirements.

3.7 SEC Filings; Financial Statements; Information Provided.

(a) Tyme has filed or furnished, as applicable, on a timely basis all forms, statements, certifications, reports and documents required to be filed or furnished by it with the United States Securities and Exchange Commission (the "SEC") under the Securities Exchange Act of 1934 (the "Exchange Act") or the Securities Act of 1933 (the "Securities Act") since December 31, 2021 (the "Tyme SEC Documents"). As of the time it was filed with the SEC (or, if amended or superseded by a filing prior to the date of this Agreement, then on the date of such filing), each of the Tyme SEC Documents complied in all material respects with the applicable

requirements of the Securities Act or the Exchange Act (as the case may be) and, as of the time they were filed, none of the Tyme SEC Documents contained any untrue statement of a material fact or omitted to state a material fact required to be stated therein or necessary in order to make the statements therein, in light of the circumstances under which they were made, not misleading. The certifications and statements required by (i) Rule 13a-14 under the Exchange Act and (ii) 18 U.S.C. §1350 (Section 906 of the Sarbanes-Oxley Act of 2002 (the "Sarbanes-Oxley Act")) relating to the Tyme SEC Documents (collectively, the "Tyme Certifications") are accurate and complete and comply as to form and content with all applicable Laws.

(b) The financial statements (including any related notes) contained or incorporated by reference in the Tyme SEC Documents: (i) complied as to form in all material respects with the published rules and regulations of the SEC applicable thereto, (ii) were prepared in accordance with GAAP (except as may be indicated in the notes to such financial statements or, in the case of unaudited financial statements, as permitted by Form 10-Q of the SEC, and except that the unaudited financial statements may not contain footnotes and are subject to normal and recurringyear-end adjustments that are not reasonably expected to be material in amount) applied on a consistent basis unless otherwise noted therein throughout the periods indicated and (iii) fairly present, in all material respects, the financial position of Tyme as of the respective dates thereof and the results of operations and cash flows of Tyme for the periods covered thereby. Other than as expressly disclosed in the Tyme SEC Documents filed prior to the date hereof, there has been no material change in Tyme's accounting methods or principles that would be required to be disclosed in Tyme's financial statements in accordance with GAAP. The books of account and other financial records of Tyme and each of its Subsidiaries are true and complete in all material respects.

(c) Tyme's auditor has since January 1, 2020 (the "Lookback Date") been: (i) a registered public accounting firm (as defined in Section 2(a)(12) of the Sarbanes-Oxley Act), (ii) to the Knowledge of Tyme, "independent" with respect to Tyme within the meaning of Regulation S-X under the Exchange Act and (iii) to the Knowledge of Tyme, in compliance with subsections (g) through (1) of Section 10A of the Exchange Act and the rules and regulations promulgated by the SEC and the Syros Accounting Oversight Board thereunder.

(d) Tyme has not received any comment letter from the SEC or the staff thereof or any correspondence from Nasdaq or the staff thereof relating to the delisting or maintenance of listing of the Tyme Common Stock on Nasdaq. Tyme has not disclosed any unresolved comments in the Tyme SEC Documents.

(e) There have been no formal internal investigations regarding financial reporting or accounting policies and practices discussed with, reviewed by or initiated at the direction of the chief executive officer, chief financial officer, or general counsel of Tyme, the Tyme Board or any committee thereof, other than ordinary course audits or reviews of accounting policies and practices or internal controls required by the Sarbanes-Oxley Act.

(f) Tyme is in compliance in all material respects with the applicable provisions of the Sarbanes-Oxley Act, the Exchange Act and the applicable listing and governance rules and regulations of Nasdaq.

(g) Tyme maintains a system of internal control over financial reporting (as defined in Rules13a-15(f) and 15d-15(f) of the Exchange Act) that is sufficient to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with GAAP, including policies and procedures sufficient to provide reasonable assurance (i) that Tyme maintains records that in reasonable detail accurately and fairly reflect Tyme's transactions and dispositions of assets, (ii) that transactions are recorded as necessary to permit preparation of financial statements in accordance with GAAP, (iii) that receipts and expenditures are made only in accordance with authorizations of management and the Tyme Board and (iv) regarding prevention or timely detection of the unauthorized acquisition, use or disposition of Tyme's assets that could have a material effect on Tyme's financial statements. Tyme has evaluated the effectiveness of Tyme's internal control over financial reporting and, to the extent required by applicable Law, presented in any applicable Tyme SEC Document that is a report on Form 10-K or Form 10-Q

(or any amendment thereto) its conclusions about the effectiveness of the internal control over financial reporting as of the end of the period covered by such report or amendment based on such evaluation. Tyme has disclosed to Tyme's auditors and the Audit Committee of the Tyme Board (and made available to the Company a summary of the significant aspects of such disclosure) (A) all significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting that are reasonably likely to adversely affect Tyme's ability to record, process, summarize and report financial information and (B) any fraud, whether or not material, that involves management or other employees who have a significant role in Tyme's or its Subsidiaries' internal control over financial reporting. Except as disclosed in the Tyme SEC Documents filed prior to the date hereof, Tyme has not identified any material weaknesses in the design or operation of Tyme's internal control over financial reporting.

(h) Tyme's "disclosure controls and procedures" (as defined in Rules 13a-15(e) and 15d-15(e) of the Exchange Act) are reasonably designed to ensure that all information (both financial and non-financial) required to be disclosed by Tyme in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the rules and forms of the SEC, and that all such information is accumulated and communicated to Tyme's management as appropriate to allow timely decisions regarding required disclosure and to make the Tyme Certifications.

(i) The information to be supplied by or on behalf of Tyme for inclusion or incorporation by reference in the registration statement on Form S-4 to be filed by Syros pursuant to which shares of Syros Common Stock issued in connection with the Merger shall be registered under the Securities Act (the "Registration Statement"), or to be included or supplied by or on behalf of Tyme for inclusion in any filing pursuant to Rule 165 and Rule 425 under the Securities Act or Rule 14a-12 under the Exchange Act (each a "Regulation M-A Filing"), shall not at the time the Registration Statement or any such Regulation M-A Filing is filed with the SEC, at any time it is amended or supplemented or at the time the Registration Statement is declared effective by the SEC, as applicable, contain any untrue statement of a material fact or omit to state any material fact required to be stated therein or necessary in order to make the statements therein not misleading. The information to be supplied by or on behalf of Tyme for inclusion in the joint proxy statement/prospectus/information statement (the "Proxy Statement/Prospectus") to be sent to the stockholders of Syros in connection with the meeting of Syros' stockholders (the "Syros Meeting") and the stockholders of Tyme in connection with the Tyme Meeting to solicit the approval of (a) Syros' stockholders of (i) the Merger Share Issuance under Nasdaq Rules (the "Required Syros Voting Proposal"), (ii) the PIPE Share Issuance under Nasdaq Rules, (iii) an increase in the number of authorized shares of Syros Common Stock to be effectuated prior to the Effective Time (the "Syros Authorized Stock Increase"), and (iv) such other matters as may require approval of the Syros' stockholders pursuant to the DGCL with respect to the Financing ((ii), (iii) and (iv), together, the "Other Syros Voting Proposals" and collectively with the Required Syros Voting Proposal, the "Syros Voting Proposals"); and (b) Tyme's stockholders of (i) the Tyme Stockholder Approval (the "Required Tyme Voting Proposal") and (ii) certain other proposals (the "Other Tyme Voting Proposals" and collectively with the Required Tyme Voting Proposal, the "Tyme Voting Proposals"). Such information shall be deemed to include all information about or relating to Tyme and its Subsidiaries and/or the Required Tyme Voting Proposal and shall not, on the date the Proxy Statement/Prospectus is first mailed to stockholders of Syros, or at the time of the Syros Meeting, at the time of the Tyme Meeting or as of the Effective Time, contain any statement that, at such time and in light of the circumstances under which it shall be made, is false or misleading with respect to any material fact, or omit to state any material fact necessary in order to make the statements made in the Proxy Statement/Prospectus not false or misleading; or omit to state any material fact necessary to correct any statement in any earlier communication with respect to the solicitation of proxies for the Syros Meeting or the Tyme Meeting that has become false or misleading.

3.8 Absence of Changes. Between March 31, 2022 and the date of this Agreement, Tyme has conducted its business only in the Ordinary Course of Business (except for the execution and performance of this Agreement and the discussions, negotiations and transactions related thereto) and there has not been any (a) Tyme Material Adverse Effect or (b) action, event or occurrence that would have required consent of Syros

pursuant to Section 5.1 of this Agreement had such action, event or occurrence taken place after the execution and delivery of this Agreement.

3.9 Absence of Undisclosed Liabilities. Neither Tyme nor any of its Subsidiaries has any Liability of a type required to be reflected or reserved for on a balance sheet prepared in accordance with GAAP, except for: (a) Liabilities disclosed, reflected or reserved against in the audited balance sheet of Tyme as of March 31, 2022, included in Tyme's Annual Report on Form 10-K for the fiscal quarter then ended, as filed with the SEC (the "Tyme Balance Sheet"), (b) normal and recurring current Liabilities that have been incurred by Tyme or its Subsidiaries since the date of the Tyme Balance Sheet in the Ordinary Course of Business (none of which relates to any breach of contract, breach of warranty, tort, infringement, or violation of Law), (c) Liabilities for performance of obligations of Tyme or any of its Subsidiaries under Tyme Contracts, (d) Liabilities incurred in connection with the Contemplated Transactions and (e) Liabilities described in Section 3.9 of the Tyme Disclosure Schedule.

3.10 Title to Assets. Each of Tyme and its Subsidiaries owns, and has good and valid title to, or, in the case of leased properties and assets, valid leasehold interests in, all tangible properties or assets and equipment used or held for use in its business or operations or purported to be owned by it, including: (a) all assets reflected on the Tyme Balance Sheet and (b) all other assets reflected in the books and records of Tyme or any of its Subsidiaries as being owned by Tyme. All of such assets are owned or, in the case of leased assets, leased by Tyme or any of its Subsidiaries free and clear of any Encumbrances, other than Permitted Encumbrances.

3.11 Real Property; Leasehold. Neither Tyme nor any of its Subsidiaries owns or has ever owned any real property. Tyme has made available to the Company (a) an accurate and complete list of all real properties with respect to which Tyme directly or indirectly holds a valid leasehold interest as well as any other real estate that is in the possession of or leased by Tyme or any of its Subsidiaries and (b) copies of all leases under which any such real property is possessed (the "Tyme Real Estate Leases"), each of which is in full force and effect, with no existing material default thereunder.

3.12 Intellectual Property.

(a) Tyme, directly or through any of its Subsidiaries, owns, or has the right to use, and has the right to bring actions for the infringement of, all Tyme Intellectual Property.

(b) Section 3.12(b) of the Tyme Disclosure Schedule is an accurate, true and complete listing of all Tyme Registrations.

(c) Section 3.12(c) of the Tyme Disclosure Schedule accurately identifies (i) all Tyme Contracts pursuant to which Tyme Intellectual Property is licensed to Tyme or any of its Subsidiaries (other than (A) any non-customized software that (1) is so licensed solely in executable or object code form pursuant to a non-exclusive, internal use software license and other Intellectual Property associated with such software and (2) is not incorporated into, or material to the development, manufacturing, or distribution of, any of Tyme's or any of its Subsidiaries' products or services, (B) any Intellectual Property licensed on a non-exclusive basis ancillary to the purchase or use of equipment, reagents or other materials and (C) any confidential information provided under confidentiality agreements) and (ii) whether the license or licenses granted to Tyme or any of its Subsidiaries are exclusive or non-exclusive.

(d) Section 3.12(d) of the Tyme Disclosure Schedule accurately identifies each Tyme Contract pursuant to which any person has been granted any license under, or otherwise has received or acquired any right (whether or not currently exercisable) or interest in, any Tyme Intellectual Property (other than (i) any confidential information provided under confidentiality agreements and (ii) any Tyme Intellectual Property non-exclusively licensed to suppliers or service providers for the sole purpose of enabling such supplier or service providers to provide services for Tyme's benefit).

(e) Tyme has delivered, or made available to the Company, a complete and accurate copy of all instruments or agreements governing, related or pertaining to any Tyme Intellectual Property.

(f) Neither the manufacture, marketing, license, offering for sale, sale, importation, use or intended use or other disposal of any product or technology currently licensed or sold or under development by Tyme, to the Knowledge of Tyme, infringes or misappropriates any valid Intellectual Property right of any other party, which infringement or misappropriation would reasonably be expected to have a Tyme Material Adverse Effect. To the Knowledge of Tyme, no third party is infringing upon any Tyme Intellectual Property, or violating any license or agreement with Tyme relating to any Tyme Intellectual Property.

(g) To the Knowledge of Tyme, there is no current or pending Legal Proceeding (including, but not limited to, opposition, interference or other proceeding in any patent or other government office) contesting the validity, ownership or right to use, sell, offer for sale, license or dispose of any Tyme Registrations. Tyme has not received any written notice or, to the Knowledge of Tyme, any oral notice asserting that any Tyme Registrations or the proposed use, sale, offer for sale, license or disposition of any products, methods, or processes claimed or covered thereunder conflicts with or infringes or misappropriates or will conflict with or infringe or misappropriate the rights of any other person or that Tyme or any of its Subsidiaries have otherwise infringed, misappropriated or otherwise violated any Intellectual Property of any person.

(h) To the Knowledge of Tyme, no Trademark or trade name owned, used, or applied for by Tyme conflicts or interferes with any Trademark or trade name owned, used, or applied for by any other person except as would not have a Tyme Material Adverse Effect. None of the goodwill associated with or inherent in any Trademark in which Tyme has or purports to have an ownership interest has been impaired as determined by Tyme in accordance with GAAP.

(i) Except as may be set forth in the Contracts listed on Section 3.12(c) or 4.12(d) of the Tyme Disclosure Schedule (i) Tyme is not bound by any Contract to indemnify, defend, hold harmless, or reimburse any other person with respect to any Intellectual Property infringement, misappropriation, or similar claim which is material to Tyme taken as a whole and (ii) Tyme has never assumed, or agreed to discharge or otherwise take responsibility for, any existing or potential liability of another person for infringement, misappropriation, or violation of any Intellectual Property right, which assumption, agreement or responsibility remains in force as of the date of this Agreement.

(j) For purposes of this Agreement, the following terms shall have the following meanings:

(i) "Intellectual Property" means the following subsisting throughout the world: (i) Patent Rights; (ii) Trademarks and all goodwill in the Trademarks; (iii) copyrights, designs, data and database rights and registrations and applications for registration thereof, including moral rights of authors; (iv) mask works and registrations and applications for registration thereof and any other rights in semiconductor topologies under the Laws of any jurisdiction; (v) inventions, invention disclosures, statutory invention registrations, trade secrets and confidential business information, know-how, scientific and technical information, data and technology, including medical, clinical, toxicological and other scientific data, manufacturing and product processes, algorithms, techniques and analytical methodology, research and development information, financial, marketing and business data, pricing and cost information, business and marketing plans and customer and supplier lists and information, whether patentable or nonpatentable, whether copyrightable or noncopyrightable and whether or not reduced to practice; and (vi) other proprietary rights relating to any of the foregoing (including remedies against infringement thereof and rights of protection of interest therein under the Laws of all jurisdictions).

(ii) "Intellectual Property Registrations" means Patent Rights, applications and registrations for Trademarks, applications and registrations for copyrights and designs, mask work registrations and applications for each of the foregoing.

(iii) "Law" means each applicable transnational, domestic or foreign federal, state or local law (statutory, common or otherwise) law, order, judgment, rule, code, statute, regulation, requirement, variance, decree, writ, injunction, award, ruling, permit or ordinance of any Governmental Authority, including any applicable stock exchange rule or requirement.

(iv) "Tyme Intellectual Property" means the Tyme Owned Intellectual Property and the Tyme Licensed Intellectual Property.

(v) "Tyme Licensed Intellectual Property" means all Intellectual Property that is licensed to Tyme or any of its Subsidiaries by any individual or entity other than Tyme or any of its Subsidiaries.

(vi) "Tyme Owned Intellectual Property" means all Intellectual Property owned or purported to be owned by Tyme or any of its Subsidiaries, in whole or in part.

(vii) "Tyme Registrations" means Intellectual Property Registrations that are registered or filed in the name of Tyme or where Tyme is the assignee thereof, in each case, alone or jointly with others.

(viii) "Order" means any judgment, order, writ, injunction, ruling, decision or decree of (that is binding on a party), or any plea agreement, corporate integrity agreement, resolution agreement, or deferred prosecution agreement with, or any settlement under the jurisdiction of, any court or Governmental Authority.

(ix) "Patent Rights" means all patents, patent applications, utility models, design registrations and certificates of invention and other governmental grants for the protection of inventions or industrial designs (including all related continuations, continuations-in-part, divisionals, post-grant proceedings, oppositions, reissues and reexaminations).

(x) "Syros Intellectual Property" means the Syros Owned Intellectual Property and the Syros Licensed Intellectual Property.

(xi) "Syros Licensed Intellectual Property" means all Intellectual Property that is licensed to Syros or any of its Subsidiaries by any individual or entity other than Syros or any of its Subsidiaries.

(xii) "Syros Owned Intellectual Property" means all Intellectual Property owned or purported to be owned by Syros or any of its Subsidiaries, in whole or in part.

(xiii) "Syros Registrations" means Intellectual Property Registrations that are registered or filed in the name of Syros or where Syros is the assignee thereof, in each case, alone or jointly with others.

(xiv) "Trademarks" means all registered trademarks and service marks, logos, Internet domain names, social media accounts and identifiers, corporate names and doing business designations and all registrations and applications for registration of the foregoing, common Law trademarks and service marks and trade dress.

3.13 Agreements, Contracts and Commitments. Section 3.13 of the Tyme Disclosure Schedule identifies each Tyme Contract that is in effect as of the date of this Agreement and is (a) a material contract as defined in Item 601(b)(10) of Regulation S-K as promulgated under the Securities Act, (b) a Contract to which Tyme is a party or by which any of its assets and properties is currently bound, which, pursuant to the express terms thereof, require obligations of payment by, or payments to, Tyme on or after the date of this Agreement in excess of $100,000 in any twelve-month period, (c) a Tyme Real Estate Lease, (d) a Contract disclosed in or required to be disclosed in Section 3.12(c) or Section 3.12(d) of the Tyme Disclosure Schedule, (e) relating to any bonus, deferred compensation, severance, incentive compensation, or any other similar employee arrangements, or (f) requiring payments by Tyme or the Surviving Corporation after the date of this Agreement in excess of

$100,000 pursuant to its express terms relating to the employment of, or the performance of employment-related services by, any person, including any employee, consultant or independent contractor, or Entity providing employment related, consulting or independent contractor services, not terminable by the Company or its Subsidiaries on 30 days' or less notice without liability (other than for accrued but unpaid salary and vacation), except to the extent general principles of wrongful termination Law may limit the Company's, its Subsidiaries' or such successor's ability to terminate employees at will. Tyme has delivered or made available to the Company accurate and complete copies of all Contracts to which Tyme or any of its Subsidiaries is a party or by which it is bound of the type described in clauses (a)-(f) of the immediately preceding sentence (any such Contract, a "Tyme Material Contract"), including all amendments thereto. Tyme has not nor, to Tyme's Knowledge as of the date of this Agreement, has any other party to a Tyme Material Contract, breached, violated or defaulted under, or received notice that it breached, violated or defaulted under, any of the terms or conditions of any Tyme Material Contract in such manner as would permit any other party to cancel or terminate any such Tyme Material Contract, or would permit any other party to seek damages which would reasonably be expected to have a Tyme Material Adverse Effect. As to Tyme, as of the date of this Agreement, each Tyme Material Contract is valid, binding, enforceable and in full force and effect, subject to the Enforceability Exceptions. No person is renegotiating, or has a right pursuant to the terms of any Tyme Material Contract to change, any material amount paid or payable to Tyme under any Tyme Material Contract or any other material term or provision of any Tyme Material Contract.

3.14 Compliance; Permits; Restrictions.

(a) Tyme and each of its Subsidiaries is, and has been, in material compliance with all applicable Laws. No investigation, claim, suit, proceeding, audit, Order, or other action by any Governmental Authority is pending or, to the Knowledge of Tyme, threatened against Tyme or any of its Subsidiaries. There is no agreement or Order binding upon Tyme or any of its Subsidiaries which (i) has or would reasonably be expected to have the effect of prohibiting or materially impairing any business practice of Tyme or any of its Subsidiaries, any acquisition of material property by Tyme or any of its Subsidiaries or the conduct of business by Tyme or any of its Subsidiaries as currently conducted, (ii) is reasonably likely to have an adverse effect on Tyme's ability to comply with or perform any covenant or obligation under this Agreement or (iii) is reasonably likely to have the effect of preventing, delaying, making illegal or otherwise interfering with the Contemplated Transactions.

(b) Each of Tyme and its Subsidiaries holds all required Governmental Authorizations that are material to the operation of the business of Tyme as currently conducted (collectively, the "Tyme Permits"). Section 3.14(b) of the Tyme Disclosure Schedule identifies each Tyme Permit. Each of Tyme and its Subsidiaries is in material compliance with the terms of the Tyme Permits. No Legal Proceeding is pending or, to the Knowledge of Tyme, threatened, which seeks to revoke, substantially limit, suspend, or materially modify any Tyme Permit. The rights and benefits of each Tyme Permit will be available to Tyme and Surviving Corporation immediately after the Effective Time on terms substantially identical to those enjoyed by Tyme and its Subsidiaries as of the date of this Agreement and immediately prior to the Effective Time.

(c) There are no Legal Proceedings pending or, to the Knowledge of Tyme, threatened with respect to an alleged material violation by Tyme or any of its Subsidiaries of the Federal Food, Drug, and Cosmetic Act (the "FDCA"), U.S. Food and Drug Administration ("FDA") regulations adopted thereunder, the Controlled Substance Act or any other similar Law promulgated by a Drug Regulatory Agency.

(d) Each of Tyme and its Subsidiaries holds all required Governmental Authorizations issuable by any Drug Regulatory Agency necessary for the conduct of the business of Tyme as currently conducted, and, as applicable, the development, testing, manufacturing, processing, storage, labeling, sale, marketing, advertising, distribution and importation or exportation, as currently conducted, of any of its products or product candidates (the "Tyme Product Candidates") (the "Tyme Regulatory Permits") and no such Tyme Regulatory Permit has been (i) revoked, withdrawn, suspended, cancelled or terminated or (ii) modified in any adverse manner other than immaterial adverse modifications. Tyme has timely maintained and is in compliance in all material respects

with the Tyme Regulatory Permits and neither Tyme nor any of its Subsidiaries has received any written notice or other written communication from any Drug Regulatory Agency regarding (A) any material violation of or failure to comply materially with any term or requirement of any Tyme Regulatory Permit or (B) any revocation, withdrawal, suspension, cancellation, termination or material modification of any Tyme Regulatory Permit. Tyme has made available to the Company all information requested by the Company in Tyme's or its Subsidiaries' possession or control relating to the Tyme Product Candidates and the development, testing, manufacturing, processing, storage, labeling, sale, marketing, advertising, distribution and importation or exportation of the Tyme Product Candidates, including, but not limited to, complete copies of the following (to the extent there are any): (x) adverse event reports; pre-clinical, clinical and other study reports and material study data; inspection reports, notices of adverse findings, untitled letters, warning letters, filings and letters and other written correspondence to and from any Drug Regulatory Agency; and meeting minutes with any Drug Regulatory Agency and (y) similar reports, material study data, notices, letters, filings, correspondence and meeting minutes with any other Governmental Authority. All such information is accurate and complete in all material respects.

(e) All clinical, pre-clinical and other studies and tests conducted by or on behalf of, or sponsored by, Tyme or its Subsidiaries, in which Tyme or its Subsidiaries or their respective products or product candidates, including the Tyme Product Candidates, have participated were and, if still pending, are being conducted in all material respects in accordance with standard medical and scientific research procedures and in compliance in all material respects with the applicable regulations of the Drug Regulatory Agencies and other applicable Law, including, without limitation, 21 C.F.R. Parts 50, 54, 56, 58 and 312. Neither Tyme nor any of its Subsidiaries has received any written notices, correspondence, or other communications from any Drug Regulatory Agency requiring or, to the Knowledge of Tyme, any action to place a clinical hold order on, or otherwise terminate, delay, or suspend any clinical studies conducted by or on behalf of, or sponsored by, Tyme or any of its Subsidiaries or in which Tyme or any of its Subsidiaries or its current products or product candidates, including the Tyme Product Candidates, have participated. Further, no clinical investigator, researcher, or clinical staff participating in any clinical study conducted by or, to the Knowledge of Tyme, on behalf of Tyme or any of its Subsidiaries has been disqualified from participating in studies involving the Tyme Product Candidates, and to the Knowledge of Tyme, no such administrative action to disqualify such clinical investigators, researchers or clinical staff has been threatened or is pending.

(f) Neither Tyme nor any of its Subsidiaries, and to the Knowledge of Tyme, no contract manufacturer with respect to any Tyme Product Candidate is the subject of any pending or, to the Knowledge of Tyme, threatened investigation in respect of its business or products by the FDA pursuant to its "Fraud, Untrue Statements of Material Facts, Bribery, and Illegal Gratuities" Final Policy set forth in 56 Fed. Reg. 46191 (September 10, 1991) and any amendments thereto. To the Knowledge of Tyme, neither Tyme nor any of its Subsidiaries and no contract manufacturer with respect to any Tyme Product Candidate has not committed any acts, made any statement, or failed to make any statement, in each case in respect of its business or products that would violate FDA's "Fraud, Untrue Statements of Material Facts, Bribery, and Illegal Gratuities" Final Policy, and any amendments thereto. None of Tyme, any of its Subsidiaries, and to the Knowledge of Tyme, any contract manufacturer with respect to any Tyme Product Candidate, or any of their respective officers, employees or agents has been convicted of any crime or engaged in any conduct that could result in a material debarment or exclusion (i) under 21 U.S.C. Section 335a or (ii) any similar applicable Law. To the Knowledge of Tyme, no material debarment or exclusionary claims, actions, proceedings or investigations in respect of their business or products are pending or threatened against Tyme, any of its Subsidiaries, and to the Knowledge of Tyme, any contract manufacturer with respect to any Tyme Product Candidate, or any of its officers, employees or agents.

(g) All manufacturing operations conducted by, or, to the Knowledge of Tyme, for the benefit of Tyme or its Subsidiaries in connection with any Tyme Product Candidate, since the Lookback Date, have been and are being conducted in compliance in all material respects with applicable Laws, including the FDA's standards for current good manufacturing practices, including applicable requirements contains in 21 C.F.R.

Parts 210 and 211, and the respective counterparts thereof promulgated by Governmental Authorities in countries outside the United States.

(h) No manufacturing site owned by Tyme or its Subsidiaries, and to the Knowledge of Tyme, no manufacturing site of a contract manufacturer, with respect to any Tyme Product Candidate, (i) is subject to a Drug Regulatory Agency shutdown or import or export prohibition or (ii) has received any Form FDA 483, notice of violation, warning letter, untitled letter, or similar correspondence or notice from the FDA or other Governmental Authority alleging or asserting noncompliance with any applicable Law, in each case, that have not be complied with or closed to the satisfaction of the relevant Governmental Authority, and, to the Knowledge of Tyme, neither the FDA nor any other Governmental Authority is considering such action.

3.15 Legal Proceedings; Orders.

(a) There is no pending Legal Proceeding and, to the Knowledge of Tyme, no person has threatened in writing to commence any Legal Proceeding: (i) that involves Tyme or any of its Subsidiaries or any current or former employee, independent contractor, officer or director of Tyme or any of its Subsidiaries (in his or her capacity as such) (a "Tyme Associate") or any of the material assets owned or used by Tyme or its Subsidiaries or (ii) that challenges, or that may have the effect of preventing, delaying, making illegal or otherwise interfering with, the Contemplated Transactions.

(b) There is no Order to which Tyme or any of its Subsidiaries, or any of the assets owned or used by Tyme or any of its Subsidiaries is subject. To the Knowledge of Tyme, no officer or other Key Employee of Tyme or any of its Subsidiaries is subject to any Order that prohibits such officer or employee from engaging in or continuing any conduct, activity or practice relating to the business of Tyme or any of its Subsidiaries or to any material assets owned or used by Tyme or any of its Subsidiaries. For purposes of this Agreement, "Key Employee" means, with respect to a person, an executive officer of such person or any employee of such person that reports directly to the board of directors of such person or to the principal executive, financial or accounting officer of such person.

(c) For the purposes of this Agreement, the term "Legal Proceeding" means any action, suit, litigation, arbitration, proceeding (including any civil, criminal, administrative, investigative or appellate proceeding), hearing, inquiry, audit, examination or investigation commenced, brought, conducted or heard by or before, or otherwise involving, any court or other Governmental Authority or any arbitrator or arbitration panel.

3.16 Tax Matters.

(a) Each of Tyme and its Subsidiaries has timely filed all income Tax Returns and other material Tax Returns that they were required to file under applicable Law. All such Tax Returns were correct and complete in all material respects and have been prepared in material compliance with all applicable Law. No claim has ever been made by a Governmental Authority in writing in a jurisdiction where Tyme or any of its Subsidiaries does not file Tax Returns that Tyme or such Subsidiary is subject to taxation by that jurisdiction.

(b) All material Taxes due and owing by Tyme and each of its Subsidiaries (whether or not shown on any Tax Return) have been paid. Since the date of the Tyme Balance Sheet, neither Tyme nor any of its Subsidiaries has incurred any material Liability for Taxes outside the Ordinary Course of Business or otherwise inconsistent with past custom and practice.

(c) Each of Tyme and its Subsidiaries has withheld and paid all material Taxes required to have been withheld and paid in connection with any amounts paid or owing to any employee, independent contractor, creditor, stockholder, or other third party.

(d) There are no Encumbrances for material Taxes (other than Taxes not yet due and payable or for Taxes that are being contested in good faith, in each case, for which adequate reserves have been established in accordance with GAAP) upon any of the assets of Tyme or any of its Subsidiaries.

(e) No outstanding deficiencies for Taxes with respect to Tyme or any of its Subsidiaries have been claimed, proposed or assessed by any Governmental Authority in writing. There are no pending (or, based on written notice, threatened) audits, assessments or other actions for or relating to any liability in respect of Taxes of Tyme or any of its Subsidiaries. Neither Tyme nor any of its Subsidiaries has waived any statute of limitations in respect of Taxes or agreed to any extension of time with respect to a Tax assessment or deficiency, which waiver or extension is currently in effect.

(f) Neither Tyme nor any of its Subsidiaries is a party to any Tax allocation, Tax sharing or similar agreement (including indemnity arrangements), other than customary provisions in commercial contracts entered into in the Ordinary Course of Business with vendors, customers, lenders and landlords.

(g) Neither Tyme nor any of its Subsidiaries has been a member of an affiliated group filing a consolidated U.S. federal income Tax Return (other than a group the common parent of which is Tyme). Neither Tyme nor any of its Subsidiaries has any material Liability for the Taxes of any person (other than Tyme and any of its Subsidiaries) under Section 1.1502-6 of the United States Treasury regulations promulgated under the Code (the "Treasury Regulations") (or any similar provision of state, local, or foreign law) or as a transferee or successor.

(h) Neither Tyme nor any of its Subsidiaries has distributed stock of another person, or had its stock distributed by another person, in a transaction that was purported or intended to be governed in whole or in part by Section 355 of the Code or Section 361 of the Code.

(i) Neither Tyme nor any of its Subsidiaries has entered into any transaction identified as a "listed transaction" for purposes of Treasury Regulations Sections 1.6011-4(b)(2) or 301.6111-2(b)(2).

(j) To the Knowledge of Tyme and its Subsidiaries, neither Tyme nor any of its Subsidiaries has taken or agreed to take any action that would reasonably be expected to prevent the Transactions from qualifying for the Intended Tax Treatment.

(k) For purposes of this Agreement, (i) "Tax" means any federal, state, local, foreign or other tax, including any income tax, franchise tax, capital gains tax, gross receipts tax, value-added tax, surtax, estimated tax, unemployment tax, national health insurance tax, excise tax, ad valorem tax, transfer tax, stamp tax, sales tax, use tax, property tax, business tax, withholding tax, payroll tax, customs duty, alternative or add-on minimum or other tax of any kind whatsoever, and including any fine, penalty, addition to tax or interest imposed by a Governmental Authority with respect thereto, and (ii) "Tax Return" means any return (including any information return), report, statement, declaration, estimate, schedule, notice, notification, form, election, certificate or other document or information, and any amendment or supplement to any of the foregoing, filed or required to be filed with any Governmental Authority in connection with the determination, assessment, collection or payment of any Tax or in connection with the administration, implementation or enforcement of or compliance with any Law relating to any Tax.

3.17 Employee and Labor Matters; Benefit Plans.

(a) The employment of Tyme's and any of its Subsidiaries' employees is terminable by Tyme or the applicable Subsidiary at will. Tyme has made available to Syros accurate and complete copies of all employee manuals and handbooks, disclosure materials, policy statements and other materials relating to the employment of Tyme Associates to the extent currently effective and material.

(b) Neither Tyme nor any of its Subsidiaries is a party to, bound by, or has a duty to bargain under, any collective bargaining agreement or other Contract with a labor organization representing any of its employees, and there are no labor organizations representing or, to the Knowledge of Tyme, purporting to represent or seeking to represent any employees of Tyme or its Subsidiaries.

(c) Section 3.17(c) of the Tyme Disclosure Schedule lists all Tyme Employee Plans.

(d) Neither Tyme nor any of its Subsidiaries maintains or has maintained any plan intended to be qualified under Section 401(a) of the Code.

(e) Each Tyme Employee Plan has been established, maintained and operated in compliance, in all material respects, with its terms and all applicable Law, including the Code ERISA and the Affordable Care Act. No Legal Proceeding (other than those relating to routine claims for benefits) is pending or, to the Knowledge of Tyme, threatened with respect to any Tyme Employee Plan. All payments and/or contributions required to have been made with respect to all Tyme Employee Plans either have been made or have been accrued, where required by GAAP, in accordance with the terms of the applicable Tyme Employee Plan and applicable Law.

(f) Neither Tyme nor any of its ERISA Affiliates has, within the past 6 years, maintained, contributed to, or been required to contribute to (i) any employee benefit plan that is or was subject to Title IV or Section 302 of ERISA or Section 412 of the Code, (ii) a Multiemployer Plan, (iii) any funded welfare benefit plan within the meaning of Section 419 of the Code, (iv) any Multiple Employer Plan, or (v) any Multiple Employer Welfare Arrangement. Neither Tyme nor any of its ERISA Affiliates has ever incurred any liability under Title IV of ERISA that has not been paid in full.

(g) No Tyme Employee Plan provides for medical or other welfare benefits beyond termination of service or retirement, other than (i) pursuant to COBRA or an analogous state law requirement, (ii) continuation coverage through the end of the month in which such termination or retirement occurs, or (iii) any otherwise disclosed express severance arrangement. Tyme does not sponsor or maintain any self-funded medical or long-term disability benefit plan

(h) No Tyme Employee Plan is subject to any law of a foreign jurisdiction outside of the United States.

(i) No Tyme Options or other equity-based awards issued or granted by Tyme are subject to the requirements of Code Section 409A. Each Tyme Employee Plan that constitutes in any part a "nonqualified deferred compensation plan" (as such term is defined under Section 409A(d)(1) of the Code and the guidance thereunder) (each, a "Tyme 409A Plan") complies in all material respects, in both form and operation, with the requirements of Code Section 409A and the guidance thereunder. No payment to be made under any Tyme 409A Plan is or, when made in accordance with the terms of the Tyme 409A Plan, will be subject to the penalties of Code Section 409A(a)(1).

(j) Tyme and each of its Subsidiaries is, and since the Lookback Date has been, in material compliance with all applicable federal, state and local laws, rules and regulations respecting employment, employment practices, terms and conditions of employment, worker classification, tax withholding, prohibited discrimination, equal employment, fair employment practices, meal and rest periods, immigration status, employee safety and health, wages (including overtime wages), compensation, and hours of work, and in each case, with respect to the employees of Tyme and its Subsidiaries: (i) since the Lookback Date, has withheld and reported all material amounts required by law or by agreement to be withheld and reported with respect to wages, salaries and other payments to employees, (ii) is not liable for any arrears of wages, severance pay or any Taxes or any penalty for failure to comply with any of the foregoing and (iii) is not liable for any material payment to any trust or other fund governed by or maintained by or on behalf of any Governmental Authority, with respect to unemployment compensation benefits, social security or other benefits or obligations for employees (other than routine payments to be made in the Ordinary Course of Business). There are no actions, suits, claims or administrative matters pending or, to the Knowledge of Tyme or any of its Subsidiaries, threatened or reasonably anticipated against Tyme relating to any employee, employment agreement or Tyme Employee Plan (other than routine claims for benefits). To the Knowledge of Tyme or any of its Subsidiaries, there are no pending or threatened or reasonably anticipated claims or actions against Tyme or any of its Subsidiaries, any Tyme trustee

or any trustee of any Subsidiary under any workers' compensation policy or long-term disability policy. Neither Tyme nor any of its Subsidiaries is a party to a conciliation agreement, consent decree or other agreement or Order with any federal, state, or local agency or Governmental Authority with respect to employment practices.

(k) Neither Tyme nor any of its Subsidiaries has material liability with respect to any misclassification within the past three years of: (i) any person as an independent contractor rather than as an employee, (ii) any employee leased from another employer or (iii) any employee currently or formerly classified as exempt from overtime wages. Neither Tyme nor any of its Subsidiaries has taken any action which would constitute a "plant closing" or "mass layoff" within the meaning of the WARN Act or similar state or local law, issued any notification of a plant closing or mass layoff required by the WARN Act or similar state or local law, or incurred any liability or obligation under WARN or any similar state or local law that remains unsatisfied.

(l) There has never been, nor has there been any threat of, any strike, slowdown, work stoppage, lockout, job action, union organizing activity, question concerning representation or any similar activity or dispute, affecting Tyme or any of its Subsidiaries. No event has occurred within the past six months, and no condition or circumstance exists, that might directly or indirectly be likely to give rise to or provide a basis for the commencement of any such strike, slowdown, work stoppage, lockout, job action, union organizing activity, question concerning representation or any similar activity or dispute.

(m) Neither Tyme nor any of its Subsidiaries is, nor has Tyme or any of its Subsidiaries been, engaged in any unfair labor practice within the meaning of the National Labor Relations Act. There is no Legal Proceeding, claim, labor dispute or grievance pending or, to the Knowledge of Tyme, threatened or reasonably anticipated relating to any employment contract, privacy right, labor dispute, wages and hours, leave of absence, plant closing notification, workers' compensation policy, long-term disability policy, harassment, retaliation, immigration, employment statute or regulation, safety or discrimination matter involving any Tyme Associate, including charges of unfair labor practices or discrimination complaints.

(n) There is no Contract, plan or arrangement to which Tyme or any person that is (or at any relevant time was) under common control with Tyme within the meaning of Sections 414(b), (c), (m) and (o) of the Code, and the regulations issued thereunder is a party or by which it is bound to compensate any of its employees for excise taxes paid pursuant to Section 4999 or Section 409A of the Code.

(o) Neither Tyme nor any of its Subsidiaries is a party to any Contract that could, due to the Merger (either alone or in conjunction with any other event) (i) result in the payment of any "parachute payment" within the meaning of Section 280G of the Code or (ii) result in, or cause the accelerated vesting, payment, funding or delivery of, or increase the amount or value of, any payment or benefit to any employee, officer, director or other service provider of Tyme or any of its Subsidiaries.

(p) For purposes of this Agreement, the following terms shall have the following meanings:

(i) "COBRA" means the Consolidated Omnibus Budget Reconciliation Act of 1985, as set forth in Section 4980B of the Code and Part 6 of Title I of ERISA.

(ii) "Employee Plan" means (A) an employee benefit plan within the meaning of Section 3(3) of ERISA whether or not subject to ERISA; (B) stock option plans, stock purchase plans, bonus (including annual bonus and retention bonus) or incentive plans, severance pay plans, programs or arrangements, deferred compensation arrangements or agreements, employment agreements, compensation plans, programs, agreements or arrangements, change in control plans, programs or arrangements, supplemental income arrangements, vacation plans, and all other employee benefit plans, agreements, and arrangements, not described in (A) above (including, with respect to the Tyme Employee Plans, any Tyme Stock Plan and with respect to the Syros Employees, any Syros Stock Plan); and (C) plans or arrangements providing compensation to employee and non-employee directors.

(iii) "ERISA" means the Employee Retirement Income Security Act of 1974, as amended.

(iv) "ERISA Affiliate" means, with respect to any Entity, any other person that is, or within the past 6 years, would be considered a single employer with such Entity or part of the same "controlled group" as such Entity under Sections 414(b), (c), (m) or (o) of the Code.

(v) "Multiemployer Plan" means (a) a "multiemployer plan," as defined in Section 3(37) or 4001(a)(3) of ERISA or (b) a plan which if maintained or administered in or otherwise subject to the laws of the United States would be described in paragraph (a).

(vi) "Multiple Employer Plan" means (a) a "multiple employer plan" within the meaning of Section 413(c) of the Code or Section 3(40) of ERISA or (b) a plan which if maintained or administered in or otherwise subject to the laws of the United States would be described in paragraph (a).

(vii) "Multiple Employer Welfare Arrangement" means (a) a "multiple employer welfare arrangement" within the meaning of Section 3(40) of ERISA or (b) a plan which if maintained or administered in or otherwise subject to the laws of the United States would be described in paragraph (a) of this definition.

(viii) "Tyme Employee Plan" means any Employee Plan that Tyme or any of its Subsidiaries sponsors, contributes to, or provides benefits under or through such plan, or has any obligation to contribute to or provide benefits under or through such plan, or if such plan provides benefits to or otherwise covers any current or former employee, officer or director of Tyme or any of its Subsidiaries (or their spouses, dependents, or beneficiaries), including any plan provided by or through a professional employer organization.

(ix) "Syros Employee Plan" means any Employee Plan that Syros or any of its Subsidiaries sponsors, contributes to, or provides benefits under or through such plan, or has any obligation to contribute to or provide benefits under or through such plan, or if such plan provides benefits to or otherwise covers any current or former employee, officer or director of Syros or any of its Subsidiaries (or their spouses, dependents, or beneficiaries), including any plan provided by or through a professional employer organization.

3.18 Environmental Matters. Since the Lookback Date, Tyme and each of its Subsidiaries has complied with all applicable federal, state, local or foreign Laws relating to pollution or protection of human health or the environment (including ambient air, surface water, ground water, land surface or subsurface strata), including any law or regulation relating to emissions, discharges, releases or threatened releases of Hazardous Materials (as defined below), or otherwise relating to the manufacture, processing, distribution, use, treatment, storage, disposal, transport or handling of Hazardous Materials (each, an "Environmental Law"), which compliance includes the possession by Tyme of all permits and other Governmental Authorizations required under applicable Environmental Laws and compliance with the terms and conditions thereof, except for any failure to be in compliance that, individually or in the aggregate, would not result in a Tyme Material Adverse Effect. Neither Tyme nor any of its Subsidiaries has received, since the Lookback Date, any written notice or other communication (in writing or otherwise), whether from a Governmental Authority, citizens group, employee or otherwise, that alleges that Tyme or any of its Subsidiaries is not in compliance with any Environmental Law, and, to the Knowledge of Tyme, there are no circumstances that may prevent or interfere with Tyme's or any of its Subsidiaries' compliance with any Environmental Law in the future, except where such failure to comply would not reasonably be expected to have a Tyme Material Adverse Effect. To the Knowledge of Tyme: (i) no current or prior owner of any property leased or controlled by Tyme or any of its Subsidiaries has received, since the Lookback Date, any written notice or other communication relating to property owned or leased at any time by Tyme or any of its Subsidiaries, whether from a Governmental Authority, citizens group, employee or otherwise, that alleges that such current or prior owner or Tyme or any of its Subsidiaries is not in compliance with or violated any Environmental Law relating to such property and (ii) neither Tyme nor any of its Subsidiaries has no material liability under any Environmental Law. For purposes of this Agreement, "Hazardous Materials" means any pollutant, chemical, substance and any toxic, infectious, carcinogenic, reactive, corrosive,

ignitable or flammable chemical, or chemical compound, or hazardous substance, material or waste, whether solid, liquid or gas, that is subject to regulation, control or remediation under any Environmental Law, including without limitation, crude oil or any fraction thereof, and petroleum products or by-products.

3.19 Insurance. Tyme has made available to the Company accurate and complete copies of all material insurance policies and all material self-insurance programs and arrangements relating to the business, assets, liabilities and operations of Tyme. Each of such insurance policies is in full force and effect and Tyme is in compliance in all material respects with the terms thereof. Other than customary end of policy notifications from insurance carriers, since the Lookback Date, Tyme has not received any notice or other communication regarding any actual or possible: (i) cancellation or invalidation of any insurance policy or (ii) refusal or denial of any coverage, reservation of rights or rejection of any material claim under any insurance policy. Tyme has provided timely written notice to the appropriate insurance carrier(s) of each Legal Proceeding pending against Tyme for which Tyme has insurance coverage, and no such carrier has issued a denial of coverage or a reservation of rights with respect to any such Legal Proceeding, or informed Tyme of its intent to do so.

3.20 Transactions with Affiliates. Except as set forth in the Tyme SEC Documents filed prior to the date of this Agreement, since the date of Tyme's last annual proxy statement filed with the SEC, no event has occurred that would be required to be reported by Tyme pursuant to Item 404 of Regulation S-K promulgated by the SEC.

3.21 Financial Advisors. Except as set forth on Section 3.21 of the Tyme Disclosure Schedule, no broker, finder or investment banker is entitled to any brokerage fee, finder's fee, opinion fee, success fee, transaction fee or other fee or commission in connection with the Contemplated Transactions based upon arrangements made by or on behalf of Tyme.

3.22 Privacy and Data Security. Tyme has complied with all applicable Privacy Laws relating to Personal Information of any individuals (including clinical trial participants, patients, patient family members, caregivers or advocates, physicians and other health care professionals, clinical trial investigators, researchers, pharmacists) that interact with Tyme in connection with the operation of Tyme's business, except for such non-compliance as has not had, and would not reasonably be expected to have, individually or in the aggregate, a Tyme Material Adverse Effect. To the Knowledge of Tyme, Tyme has complied with its Privacy Policies, except for such non-compliance as has not had, and would not reasonably be expected to have, individually or in the aggregate, a Tyme Material Adverse Effect. To the Knowledge of Tyme, as of the date hereof, no claims have been asserted or threatened against Tyme by any person alleging a violation of Privacy Laws and/or Privacy Policies. For purposes of this Agreement, (a) "Privacy Laws" means Laws relating to privacy, security and/or collection and use of Personal Information, and (b) "Personal Information" means data and information concerning an identifiable natural person.

3.23 No Other Representations or Warranties. Tyme hereby acknowledges and agrees that, except for the representations and warranties contained in this Agreement, neither the Company nor any of its Subsidiaries nor any other person on behalf of the Company or its Subsidiaries makes any express or implied representation or warranty with respect to the Company or its Subsidiaries or with respect to any other information provided to Tyme, its stockholders or any of their respective Affiliates in connection with the Contemplated Transactions, and (subject to the express representations and warranties of the Company set forth in Article IV (in each case as qualified and limited by the Company Disclosure Schedule)) none of Tyme or any of its Representatives or stockholders has relied on any such information (including the accuracy or completeness thereof).

ARTICLE IV

REPRESENTATIONS AND WARRANTIES OF SYROS AND THE MERGER SUB

Syros and Merger Sub represent and warrant to Tyme that the statements contained in this Article IV are true and correct, except (a) as disclosed in the Syros SEC Reports filed or furnished prior to the date of this

Agreement (but excluding any disclosures under the heading "Risk Factors" and any disclosure of risks included in any "forward looking statements" disclaimers or in any other section to the extent they are forward-looking statements or cautionary, predictive or forward-looking in nature) or (b) as expressly set forth herein or in the disclosure schedule delivered by Syros and Merger Sub to Tyme on the date of this Agreement (the "Syros Disclosure Schedule"). For purposes hereof, the phrase "to the knowledge of Syros" and similar expressions mean the actual knowledge of the persons identified on Section K of the Syros Disclosure Schedule for this purpose, and such knowledge as such persons would reasonably be expected to have obtained in the course of their performance of their duties to the Syros (after due inquiry).

4.1 Due Organization; Subsidiaries.

(a) Each of Syros and its Subsidiaries (including Merger Sub) is a corporation or other legal entity duly incorporated or otherwise organized, validly existing and in good standing under the Laws of the jurisdiction of its incorporation or organization and has all necessary power and authority: (i) to conduct its business in the manner in which its business is currently being conducted, (ii) to own or lease and use its property and assets in the manner in which its property and assets are currently owned or leased and used and (iii) to perform its obligations under all Contracts by which it is bound. Since the date of its incorporation, Merger Sub has not engaged in any activities other than in connection with or as contemplated by this Agreement. All of Syros' Subsidiaries are wholly owned by Syros.

(b) Each of Syros and its Subsidiaries is licensed and qualified to do business, and is in good standing (to the extent applicable in such jurisdiction), under the Laws of all jurisdictions where the nature of its business requires such licensing or qualification other than in jurisdictions where the failure to be so qualified individually or in the aggregate would not be reasonably expected to have a Syros Material Adverse Effect. For purposes of this Agreement, the term "Syros Material Adverse Effect" means any Effect that, individually or in the aggregate with all other Effects that have occurred through the date of determination, has had, or is reasonably likely to have, a material adverse effect on the business, assets, liabilities, capitalization, financial condition or results of operations of Syros and its Subsidiaries, taken as a whole; provided, however, that no Effect, to the extent resulting from or arising out of any of the following, shall be deemed to be a Syros Material Adverse Effect or be taken into account for purposes of determining whether a Syros Material Adverse Effect has occurred or is reasonably likely to occur: (A) adverse developments in Syros' clinical pipeline that have been disclosed in Syros SEC Reports as of the date of this Agreement, (B) changes after the date of this Agreement in prevailing economic or market conditions in the United States or any other jurisdiction in which such entity has substantial business operations (except to the extent those changes have a disproportionate effect on Syros and its Subsidiaries relative to the other participants in the industry or industries in which Syros and its Subsidiaries operate), (C) changes or events after the date of this Agreement affecting the industry or industries in which Syros and its Subsidiaries operate generally (except to the extent those changes or events have a disproportionate effect on Syros and its Subsidiaries relative to the other participants in the industry or industries in which Syros and its Subsidiaries operate), (D) changes after the date of this Agreement in generally accepted accounting principles or requirements (except to the extent those changes have a disproportionate effect on Syros and its Subsidiaries relative to the other participants in the industry or industries in which Syros and its Subsidiaries operate), (E) changes after the date of this Agreement in laws, rules or regulations of general applicability or interpretations thereof by any Governmental Authority (except to the extent those changes have a disproportionate effect on Syros and its Subsidiaries relative to the other participants in the industry or industries in which Syros and its Subsidiaries operate), (F) any natural disaster, epidemic, pandemic or other disease outbreak (including the COVID-19 pandemic) or any outbreak of major hostilities in which the United States is involved or any act of terrorism within the United States or directed against its facilities or citizens wherever located (except to the extent those changes or events have a disproportionate effect on Syros and its Subsidiaries relative to the other participants in the industry or industries in which Syros and its Subsidiaries operate), (G) a change in the public trading price of Syros Common Stock or the implications hereof, (H) a change in the trading volume of Syros Common Stock due to the announcement of the Agreement or the pendency of the Contemplated Transactions or (I) any failure by Syros to meet any public estimates or expectations of Syros'

revenue, earnings or other financial performance or results of operations for any period, or (J) any failure by Syros to meet any internal guidance, budgets, plans or forecasts of its revenues, earnings or other financial performance or results of operations (but not, in the case of this clause (J), the underlying cause of such changes or failures, unless such changes or failures would otherwise be excepted from this definition).

(c) Except as set forth on Section 4.1(c) of the Syros Disclosure Schedule, Syros has no Subsidiaries other than Merger Sub and Syros does not own any capital stock of, or any equity ownership or profit sharing interest of any nature in, or control directly or indirectly, any other Entity other than Merger Sub. Syros is not and has not otherwise been, directly or indirectly, a party to, member of or participant in any partnership, joint venture or similar business entity. Syros has not agreed and is not obligated to make, nor is Syros bound by any Contract under which it may become obligated to make, any future investment in or capital contribution to any other Entity. Syros has not, at any time, been a general partner of, and has not otherwise been liable for any of the debts or other obligations of, any general partnership, limited partnership or other Entity.

4.2 Organizational Documents. Syros has made available to Tyme accurate and complete copies of Syros' Organizational Documents. Syros is not in breach or violation of its Organizational Documents in any material respect.

4.3 Authority; Binding Nature of Agreement. Each of Syros and Merger Sub has all necessary corporate power and authority to enter into and to perform its obligations under this Agreement and the Securities Purchase Agreement and to consummate the Contemplated Transactions. The Syros Board (at meetings duly called and held) has: (a) determined that the Contemplated Transactions are fair to, advisable and in the best interests of Syros and its stockholders, (b) approved and declared advisable this Agreement, the Securities Purchase Agreement and the Contemplated Transactions, including the Share Issuance, and (c) determined to recommend, upon the terms and subject to the conditions set forth in this Agreement, that the stockholders of Syros vote to approve this Agreement, the Securities Purchase Agreement and the Contemplated Transactions, including the Share Issuance. The Board of Directors of Merger Sub (by unanimous written consent) has: (x) determined that the Contemplated Transactions are fair to, advisable, and in the best interests of Merger Sub and its sole stockholder, (y) deemed advisable and approved this Agreement and the Contemplated Transactions and (z) determined to recommend, upon the terms and subject to the conditions set forth in this Agreement, that the stockholder of Merger Sub vote to adopt this Agreement and thereby approve the Contemplated Transactions to which it is a party. This Agreement has been duly executed and delivered by Syros and Merger Sub and, assuming the due authorization, execution and delivery by the Company, constitutes the legal, valid and binding obligation of Syros and Merger Sub, enforceable against each of Syros and Merger Sub in accordance with its terms, subject to the Enforceability Exceptions.

4.4 Vote Required. The affirmative vote of a majority of (a) the votes cast at the Syros Stockholder Meeting is the only vote of the holders of any class or series of Syros' capital stock necessary to approve the Required Syros Voting Proposal and to approve the PIPE Share Issuance under Nasdaq Rules and (b) the shares of outstanding Syros Common Stock entitled to vote thereon is the only vote of the holders of any class or series of Syros' capital stock necessary to approve the Other Syros Voting Proposals (collectively, the "Required Syros Stockholder Vote").

4.5 Non-Contravention; Consents.

(a) Subject to obtaining the Required Syros Stockholder Vote and the filing of the Certificate of Merger required by the DGCL, neither (x) the execution, delivery or performance of this Agreement by Syros or Merger Sub, nor (y) the consummation of the Contemplated Transactions, will directly or indirectly (with or without notice or lapse of time):

(i) contravene, conflict with or result in a violation of any of the provisions of the Organizational Documents of Syros or its Subsidiaries;

(ii) contravene, conflict with or result in a material violation of, or give any Governmental Authority or other person the right to challenge the Contemplated Transactions or to exercise any remedy or obtain any relief under, any Law or any Order to which Syros or its Subsidiaries, or any of the assets owned or used by Syros or its Subsidiaries, is subject;

(iii) contravene, conflict with or result in a material violation of any of the terms or requirements of, or give any Governmental Authority the right to revoke, withdraw, suspend, cancel, terminate or modify, any Governmental Authorization that is held by Syros or its Subsidiaries, or that otherwise relates to the business of Syros, or any of the assets owned, leased or used by Syros;

(iv) contravene, conflict with or result in a violation or breach of, or result in a default under, any provision of any Syros Material Contract, or give any person the right to: (A) declare a default or exercise any remedy under any Syros Material Contract, (B) any material payment, rebate, chargeback, penalty or change in delivery schedule under any such Syros Material Contract, (C) accelerate the maturity or performance of any Syros Material Contract or (D) cancel, terminate or modify any term of any Syros Material Contract, except in the case of any non-material breach, default, penalty or modification; or

(v) result in the imposition or creation of any Encumbrance upon or with respect to any asset owned or used by Syros or its Subsidiaries (except for Permitted Encumbrances).

(b) Except for (i) any Consent set forth on Section 4.5 of the Syros Disclosure Schedule under any Contract (a) to which the Company or any of its Subsidiaries is a Party, (b) by which the Company or any of its Subsidiaries or any Company Intellectual Property or any other asset of the Company or its Subsidiaries is or may become bound or under which the Company or any of its Subsidiaries has, or may become subject to, any obligation, or (c) under which the Company or any of its Subsidiaries has or may acquire any right or interest (each such contract, a "Syros Contract"); (ii) the Required Syros Stockholder Vote; (iii) the filing of the Certificate of Merger with the Secretary of State of the State of Delaware pursuant to the DGCL; and (iv) such consents, waivers, approvals, orders, authorizations, registrations, declarations and filings as may be required under applicable federal and state securities laws, neither Syros nor any of its Subsidiaries was, is, or will be required to make any filing with or give any notice to, or to obtain any Consent from, any person in connection with (x) the execution, delivery or performance of this Agreement or (y) the consummation of the Contemplated Transactions.

(c) The Syros Board and the Board of Directors of Merger Sub have taken and will take all actions necessary to ensure that the restrictions applicable to business combinations contained in Section 203 of the DGCL are, and will be, inapplicable to the execution, delivery and performance of this Agreement, the Syros Support Agreement and to the consummation of the Contemplated Transactions. No other state takeover statute or similar Law applies or purports to apply to the Merger, this Agreement or any of the other Contemplated Transactions.

4.6 Capitalization.

(a) The authorized capital stock of Syros consists of (i) 200,000,000 shares of Syros Common Stock, par value $0.001 per share, of which 62,989,020 shares have been issued and are outstanding as of the Capitalization Date and (ii) 10,000,000 shares of preferred stock, par value $0.001 per share, of which no shares have been issued and are outstanding as of the Capitalization Date. Syros does not hold any shares of its capital stock in its treasury.

(b) All of the outstanding shares of Syros Common Stock have been duly authorized and validly issued, and are fully paid and nonassessable and are free of any Encumbrances. None of the outstanding shares of Syros Common Stock is entitled or subject to any preemptive right, right of participation, right of maintenance or any similar right. None of the outstanding shares of Syros Common Stock is subject to any right of first refusal in

favor of Syros. Except for the Syros Support Agreement, as contemplated herein or as set forth in Section 4.6(b) of the Syros Disclosure Schedule, there is no Syros Contract relating to the voting or registration of, or restricting any person from purchasing, selling, pledging or otherwise disposing of (or granting any option or similar right with respect to), any shares of Syros Common Stock. Syros is not under any obligation, nor is Syros bound by any Contract pursuant to which it may become obligated, to repurchase, redeem or otherwise acquire any outstanding shares of Syros Common Stock or other securities. Section 4.6(b) of the Syros Disclosure Schedule accurately and completely describes all repurchase rights held by Syros with respect to shares of Syros Common Stock (including shares issued pursuant to the exercise of stock options) and specifies which of those repurchase rights are currently exercisable.

(c) Section 4.6(c) of the Syros Disclosure Schedule sets forth a complete and accurate list of all stock or equity-related plans, agreements or arrangements of Syros (each, a "Syros Stock Plan"), and except as set forth on Section 4.6(c)(i) of the Syros Disclosure Schedule, Syros does not have any stock option plan or any other plan, program, agreement or arrangement providing for any equity-based compensation for any person. As of the Capitalization Date, Syros has reserved 20,821,015 shares of Syros Common Stock for issuance under the Syros Stock Plans, of which 4,647,255 shares have been issued and are currently outstanding, 7,649,178 shares have been reserved for issuance upon exercise or settlement of options or other rights to purchase shares of Syros Common Stock issued by Syros (collectively, "Syros Options"), 4,588,169 shares have been reserved for issuance upon settlement of restricted stock units with respect to shares of Syros Common Stock issued by Syros (collectively, "Syros RSUs") and 3,936,413 shares remain available for future issuance pursuant to the Syros Stock Plans. Syros has made available to the Company accurate and complete copies of equity incentive plans pursuant to which Syros has equity-based awards and the forms of all award agreements evidencing such equity-based awards.

(d) Except for the outstanding Syros Options or as set forth on Section 4.6(d) of the Syros Disclosure Schedule, there is no: (i) outstanding subscription, option, call, warrant or right (whether or not currently exercisable) to acquire any shares of the capital stock or other securities of Syros, (ii) outstanding security, instrument or obligation that is or may become convertible into or exchangeable for any shares of the capital stock or other securities of Syros, (iii) stockholder rights plan (or similar plan commonly referred to as a "poison pill") or Contract under which Syros is or may become obligated to sell or otherwise issue any shares of its capital stock or any other securities or (iv) condition or circumstance that may give rise to or provide a basis for the assertion of a claim by any person to the effect that such person is entitled to acquire or receive any shares of capital stock or other securities of Syros. There are no outstanding or authorized stock appreciation, phantom stock, profit participation or other similar rights with respect to Syros.

(e) All outstanding shares of Syros Common Stock, Syros Options, other equity securities of Syros have been issued and granted in material compliance with (i) all applicable securities laws and other applicable Law and (ii) all requirements set forth in applicable Contracts.

(f) With respect to Syros Options granted pursuant to the Syros Stock Plans, each Syros Option grant was made in accordance with the terms of the Syros Stock Plan pursuant to which it was granted and, to the Knowledge of Syros, all other applicable Law and regulatory rules or requirements.

4.7 SEC Filings; Financial Statements.

(a) Syros has filed or furnished, as applicable, on a timely basis all forms, statements, certifications, reports and documents required to be filed or furnished by it with the SEC under the Exchange Act or the Securities Act since December 31, 2021 (the "Syros SEC Documents"). As of the time it was filed with the SEC (or, if amended or superseded by a filing prior to the date of this Agreement, then on the date of such filing), each of the Syros SEC Documents complied in all material respects with the applicable requirements of the Securities Act or the Exchange Act (as the case may be) and, as of the time they were filed, none of the Syros SEC Documents contained any untrue statement of a material fact or omitted to state a material fact required to be

stated therein or necessary in order to make the statements therein, in light of the circumstances under which they were made, not misleading. The certifications and statements required by (i) Rule 13a-14 under the Exchange Act and (ii) 18 U.S.C. §1350 (Section 906 of the Sarbanes-Oxley Act) relating to the Syros SEC Documents (collectively, the "Syros Certifications") are accurate and complete and comply as to form and content with all applicable Laws.

(b) The financial statements (including any related notes) contained or incorporated by reference in the Syros SEC Documents: (i) complied as to form in all material respects with the published rules and regulations of the SEC applicable thereto, (ii) were prepared in accordance with GAAP (except as may be indicated in the notes to such financial statements or, in the case of unaudited financial statements, as permitted by Form 10-Q of the SEC, and except that the unaudited financial statements may not contain footnotes and are subject to normal and recurringyear-end adjustments that are not reasonably expected to be material in amount) applied on a consistent basis unless otherwise noted therein throughout the periods indicated and (iii) fairly present, in all material respects, the financial position of Syros as of the respective dates thereof and the results of operations and cash flows of Syros for the periods covered thereby. Other than as expressly disclosed in the Syros SEC Documents filed prior to the date hereof, there has been no material change in Syros' accounting methods or principles that would be required to be disclosed in Syros' financial statements in accordance with GAAP. The books of account and other financial records of Syros and each of its Subsidiaries are true and complete in all material respects.

(c) Syros' auditor has since the Lookback Date been: (i) a registered public accounting firm (as defined in Section 2(a)(12) of the Sarbanes-Oxley Act), (ii) to the Knowledge of Syros, "independent" with respect to Syros within the meaning of Regulation S-X under the Exchange Act and (iii) to the Knowledge of Syros, in compliance with subsections (g) through (1) of Section 10A of the Exchange Act and the rules and regulations promulgated by the SEC and the Syros Accounting Oversight Board thereunder.

(d) Syros has not received any comment letter from the SEC or the staff thereof or any correspondence from Nasdaq or the staff thereof relating to the delisting or maintenance of listing of the Syros Common Stock on Nasdaq. Syros has not disclosed any unresolved comments in the Syros SEC Documents.

(e) There have been no formal internal investigations regarding financial reporting or accounting policies and practices discussed with, reviewed by or initiated at the direction of the chief executive officer, chief financial officer, or general counsel of Syros, the Syros Board or any committee thereof, other than ordinary course audits or reviews of accounting policies and practices or internal controls required by the Sarbanes-Oxley Act.

(f) Syros is in compliance in all material respects with the applicable provisions of the Sarbanes-Oxley Act, the Exchange Act and the applicable listing and governance rules and regulations of Nasdaq.

(g) Syros maintains a system of internal control over financial reporting (as defined inRules 13a-15(f) and 15d-15(f) of the Exchange Act) that is sufficient to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with GAAP, including policies and procedures sufficient to provide reasonable assurance (i) that Syros maintains records that in reasonable detail accurately and fairly reflect Syros' transactions and dispositions of assets, (ii) that transactions are recorded as necessary to permit preparation of financial statements in accordance with GAAP, (iii) that receipts and expenditures are made only in accordance with authorizations of management and the Syros Board and (iv) regarding prevention or timely detection of the unauthorized acquisition, use or disposition of Syros' assets that could have a material effect on Syros' financial statements. Syros has evaluated the effectiveness of Syros' internal control over financial reporting and, to the extent required by applicable Law, presented in any applicable Syros SEC Document that is a report on Form 10-K or Form 10-Q (or any amendment thereto) its conclusions about the effectiveness of the internal control over financial reporting as of the end of the period covered by such report or amendment based on such evaluation.

Syros has disclosed to Syros' auditors and the Audit Committee of the Syros Board (and made available to the Company a summary of the significant aspects of such disclosure) (A) all significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting that are reasonably likely to adversely affect Syros' ability to record, process, summarize and report financial information and (B) any fraud, whether or not material, that involves management or other employees who have a significant role in Syros' or its Subsidiaries' internal control over financial reporting. Except as disclosed in the Syros SEC Documents filed prior to the date hereof, Syros has not identified any material weaknesses in the design or operation of Syros' internal control over financial reporting.

(h) Syros' "disclosure controls and procedures" (as defined in Rules 13a-15(e) and 15d-15(e) of the Exchange Act) are reasonably designed to ensure that all information (both financial and non-financial) required to be disclosed by Syros in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the rules and forms of the SEC, and that all such information is accumulated and communicated to Syros' management as appropriate to allow timely decisions regarding required disclosure and to make the Syros Certifications.

(i) The information to be supplied by or on behalf of Syros for inclusion or incorporation by reference in the Registration Statement, or to be included or supplied by or on behalf of Tyme for inclusion in any Regulation M-A Filing, shall not at the time the Registration Statement or any such Regulation M-A Filing is filed with the SEC, at any time it is amended or supplemented or at the time the Registration Statement is declared effective by the SEC, as applicable, contain any untrue statement of a material fact or omit to state any material fact required to be stated therein or necessary in order to make the statements therein not misleading. The information to be supplied by or on behalf of Syros for Proxy Statement/Prospectus to be sent to the stockholders of Syros in connection with the Syros Meeting and the stockholders of Tyme in connection with the Tyme Meeting to solicit the approval of (a) Syros' stockholders for the Required Syros Voting Proposal and the Other Syros Voting Proposals; and (b) Tyme's stockholders of the Required Tyme Voting Proposal and the Other Tyme Voting Proposals. Such information shall be deemed to include all information about or relating to Syros and its Subsidiaries and/or the Syros Voting Proposal and Other Syros Voting Proposals and shall not, on the date the Proxy Statement/Prospectus is first mailed to stockholders of Syros, or at the time of the Syros Meeting, at the time of the Tyme Meeting or as of the Effective Time, contain any statement that, at such time and in light of the circumstances under which it shall be made, is false or misleading with respect to any material fact, or omit to state any material fact necessary in order to make the statements made in the Proxy Statement/Prospectus not false or misleading; or omit to state any material fact necessary to correct any statement in any earlier communication with respect to the solicitation of proxies for the Syros Meeting or the Tyme Meeting that has become false or misleading.

4.8 Absence of Changes. Between March 31, 2022 and the date of this Agreement, Syros has conducted its business only in the Ordinary Course of Business (except for the execution and performance of this Agreement and the discussions, negotiations and transactions related thereto) and there has not been any (a) Syros Material Adverse Effect or (b) action, event or occurrence that would have required consent of Tyme pursuant to Section 5.2 of this Agreement had such action, event or occurrence taken place after the execution and delivery of this Agreement.

4.9 Absence of Undisclosed Liabilities. Neither Syros nor any of its Subsidiaries has any Liability of a type required to be reflected or reserved for on a balance sheet prepared in accordance with GAAP, except for: (a) Liabilities disclosed, reflected or reserved against in the unaudited balance sheet of Syros as of March 31, 2022, included in Syros' Quarterly Report on Form 10-Q for the fiscal quarter then ended, as filed with the SEC (the 'Syros Balance Sheet"), (b) normal and recurring current Liabilities that have been incurred by Syros or its Subsidiaries since the date of the Syros Balance Sheet in the Ordinary Course of Business (none of which relates to any breach of contract, breach of warranty, tort, infringement, or violation of Law), (c) Liabilities for performance of obligations of Syros or any of its Subsidiaries under Syros Contracts, (d) Liabilities incurred in connection with the Contemplated Transactions and (e) Liabilities described in Section 4.9 of the Syros Disclosure Schedule.

4.10 Title to Assets. Each of Syros and its Subsidiaries owns, and has good and valid title to, or, in the case of leased properties and assets, valid leasehold interests in, all tangible properties or assets and equipment used or held for use in its business or operations or purported to be owned by it, including: (a) all assets reflected on the Syros Balance Sheet and (b) all other assets reflected in the books and records of Syros or any of its Subsidiaries as being owned by Syros. All of such assets are owned or, in the case of leased assets, leased by Syros or any of its Subsidiaries free and clear of any Encumbrances, other than Permitted Encumbrances.

4.11 Real Property; Leasehold. Neither Syros nor any of its Subsidiaries owns or has ever owned any real property. Syros has made available to the Company (a) an accurate and complete list of all real properties with respect to which Syros directly or indirectly holds a valid leasehold interest as well as any other real estate that is in the possession of or leased by Syros or any of its Subsidiaries and (b) copies of all leases under which any such real property is possessed, each of which is in full force and effect, with no existing material default thereunder.

4.12 Intellectual Property.

(a) Syros, directly or through any of its Subsidiaries, owns, or has the right to use, and has the right to bring actions for the infringement of, all Syros Intellectual Property.

(b) Section 4.12(b) of the Syros Disclosure Schedule is an accurate, true and complete listing of all Syros Registrations.

(c) Section 4.12(c) of the Syros Disclosure Schedule accurately identifies (i) all Syros Contracts pursuant to which Syros Intellectual Property is licensed to Syros or any of its Subsidiaries (other than (A) any non-customized software that (1) is so licensed solely in executable or object code form pursuant to a non-exclusive, internal use software license and other Intellectual Property associated with such software and (2) is not incorporated into, or material to the development, manufacturing, or distribution of, any of Syros' or any of its Subsidiaries' products or services, (B) any Intellectual Property licensed on a non-exclusive basis ancillary to the purchase or use of equipment, reagents or other materials and (C) any confidential information provided under confidentiality agreements) and (ii) whether the license or licenses granted to Syros or any of its Subsidiaries are exclusive or non-exclusive.

(d) Section 4.12(d) of the Syros Disclosure Schedule accurately identifies each Syros Contract pursuant to which any person has been granted any license under, or otherwise has received or acquired any right (whether or not currently exercisable) or interest in, any Syros Intellectual Property (other than (i) any confidential information provided under confidentiality agreements and (ii) any Syros Intellectual Property non-exclusively licensed to suppliers or service providers for the sole purpose of enabling such supplier or service providers to provide services for Syros' benefit).

(e) Syros has delivered, or made available to the Company, a complete and accurate copy of all material instruments or agreements governing, related or pertaining to any Syros Intellectual Property.

(f) Neither the manufacture, marketing, license, offering for sale, sale, importation, use or intended use or other disposal of any product or technology currently licensed or sold or under development by Syros, to the Knowledge of Syros, infringes or misappropriates any valid Intellectual Property right of any other party, which infringement or misappropriation would reasonably be expected to have a Syros Material Adverse Effect. To the Knowledge of Syros, no third party is infringing upon any Syros Intellectual Property, or violating any license or agreement with Syros relating to any Syros Intellectual Property.

(g) To the Knowledge of Syros, there is no current or pending Legal Proceeding (including, but not limited to, opposition, interference or other proceeding in any patent or other government office) contesting the validity, ownership or right to use, sell, offer for sale, license or dispose of any Syros Registrations. Syros has not

received any written notice or, to the Knowledge of Syros, any oral notice asserting that any Syros Registrations or the proposed use, sale, offer for sale, license or disposition of any products, methods, or processes claimed or covered thereunder conflicts with or infringes or misappropriates or will conflict with or infringe or misappropriate the rights of any other person or that Syros or any of its Subsidiaries have otherwise infringed, misappropriated or otherwise violated any Intellectual Property of any person.

(h) To the Knowledge of Syros, no Trademark or trade name owned, used, or applied for by Syros conflicts or interferes with any Trademark or trade name owned, used, or applied for by any other person except as would not have a Syros Material Adverse Effect. None of the goodwill associated with or inherent in any Trademark in which Syros has or purports to have an ownership interest has been impaired as determined by Syros in accordance with GAAP.

(i) Except as may be set forth in the Contracts listed onSection 4.12(c) or 4.12(d) of the Syros Disclosure Schedule (i) Syros is not bound by any Contract to indemnify, defend, hold harmless, or reimburse any other person with respect to any Intellectual Property infringement, misappropriation, or similar claim which is material to Syros taken as a whole and (ii) Syros has never assumed, or agreed to discharge or otherwise take responsibility for, any existing or potential liability of another person for infringement, misappropriation, or violation of any Intellectual Property right, which assumption, agreement or responsibility remains in force as of the date of this Agreement.

4.13 Agreements, Contracts and Commitments. Section 4.13 of the Syros Disclosure Schedule identifies each Syros Contract that is in effect as of the date of this Agreement and is (a) a material contract as defined in Item 601(b)(10) of Regulation S-K as promulgated under the Securities Act, (b) a Syros Real Estate Lease or (c) a Contract disclosed in or required to be disclosed in Section 4.12(c) or Section 4.12(d) of the Syros Disclosure Schedule. Syros has delivered or made available to the Company accurate and complete copies of all Contracts to which Syros or any of its Subsidiaries is a party or by which it is bound of the type described in clauses (a)-(d) of the immediately preceding sentence (any such Contract, a "Syros Material Contract"), including all amendments thereto. Syros has not nor, to Syros' Knowledge as of the date of this Agreement, has any other party to a Syros Material Contract, breached, violated or defaulted under, or received notice that it breached, violated or defaulted under, any of the terms or conditions of any Syros Material Contract in such manner as would permit any other party to cancel or terminate any such Syros Material Contract, or would permit any other party to seek damages which would reasonably be expected to have a Syros Material Adverse Effect. As to Syros, as of the date of this Agreement, each Syros Material Contract is valid, binding, enforceable and in full force and effect, subject to the Enforceability Exceptions. No person is renegotiating, or has a right pursuant to the terms of any Syros Material Contract to change, any material amount paid or payable to Syros under any Syros Material Contract or any other material term or provision of any Syros Material Contract.

4.14 Compliance; Permits; Restrictions.

(a) Syros and each of its Subsidiaries is, and has been, in material compliance with all applicable Laws. No investigation, claim, suit, proceeding, audit, Order, or other action by any Governmental Authority is pending or, to the Knowledge of Syros, threatened against Syros or any of its Subsidiaries. There is no agreement or Order binding upon Syros or any of its Subsidiaries which (i) has or would reasonably be expected to have the effect of prohibiting or materially impairing any business practice of Syros or any of its Subsidiaries, any acquisition of material property by Syros or any of its Subsidiaries or the conduct of business by Syros or any of its Subsidiaries as currently conducted, (ii) is reasonably likely to have an adverse effect on Syros' ability to comply with or perform any covenant or obligation under this Agreement or (iii) is reasonably likely to have the effect of preventing, delaying, making illegal or otherwise interfering with the Contemplated Transactions.

(b) Each of Syros and its Subsidiaries holds all required Governmental Authorizations that are material to the operation of the business of Syros and Merger Sub as currently conducted (collectively, the "Syros Permits"). Section 4.14(b) of the Syros Disclosure Schedule identifies each Syros Permit. Each of Syros

and its Subsidiaries is in material compliance with the terms of the Syros Permits. No Legal Proceeding is pending or, to the Knowledge of Syros, threatened, which seeks to revoke, substantially limit, suspend, or materially modify any Syros Permit. The rights and benefits of each Syros Permit will be available to Syros and Surviving Corporation immediately after the Effective Time on terms substantially identical to those enjoyed by Syros and its Subsidiaries as of the date of this Agreement and immediately prior to the Effective Time.

(c) There are no Legal Proceedings pending or, to the Knowledge of Syros, threatened with respect to an alleged material violation by Syros or any of its Subsidiaries of the FDCA, FDA regulations adopted thereunder, the Controlled Substance Act or any other similar Law promulgated by a Drug Regulatory Agency.

(d) Each of Syros and its Subsidiaries holds all required Governmental Authorizations issuable by any Drug Regulatory Agency necessary for the conduct of the business of Syros and Merger Sub as currently conducted, and, as applicable, the development, testing, manufacturing, processing, storage, labeling, sale, marketing, advertising, distribution and importation or exportation, as currently conducted, of any of its products or product candidates (the "Syros Product Candidates") (the "Syros Regulatory Permits") and no such Syros Regulatory Permit has been (i) revoked, withdrawn, suspended, cancelled or terminated or (ii) modified in any adverse manner other than immaterial adverse modifications. Syros has timely maintained and is in compliance in all material respects with the Syros Regulatory Permits and neither Syros nor any of its Subsidiaries has received any written notice or other written communication from any Drug Regulatory Agency regarding (A) any material violation of or failure to comply materially with any term or requirement of any Syros Regulatory Permit or (B) any revocation, withdrawal, suspension, cancellation, termination or material modification of any Syros Regulatory Permit. Syros has made available to the Company all information requested by the Company in Syros' or its Subsidiaries' possession or control relating to the Syros Product Candidates and the development, testing, manufacturing, processing, storage, labeling, sale, marketing, advertising, distribution and importation or exportation of the Syros Product Candidates, including, but not limited to, complete copies of the following (to the extent there are any): (x) adverse event reports; pre-clinical, clinical and other study reports and material study data; inspection reports, notices of adverse findings, untitled letters, warning letters, filings and letters and other written correspondence to and from any Drug Regulatory Agency; and meeting minutes with any Drug Regulatory Agency and (y) similar reports, material study data, notices, letters, filings, correspondence and meeting minutes with any other Governmental Authority. All such information is accurate and complete in all material respects.

(e) All clinical, pre-clinical and other studies and tests conducted by or on behalf of, or sponsored by, Syros or its Subsidiaries, in which Syros or its Subsidiaries or their respective products or product candidates, including the Syros Product Candidates, have participated were and, if still pending, are being conducted in all material respects in accordance with standard medical and scientific research procedures and in compliance in all material respects with the applicable regulations of the Drug Regulatory Agencies and other applicable Law, including, without limitation, 21 C.F.R. Parts 50, 54, 56, 58 and 312. Neither Syros nor any of its Subsidiaries has received any written notices, correspondence, or other communications from any Drug Regulatory Agency requiring or, to the Knowledge of Syros, any action to place a clinical hold order on, or otherwise terminate, delay, or suspend any clinical studies conducted by or on behalf of, or sponsored by, Syros or any of its Subsidiaries or in which Syros or any of its Subsidiaries or its current products or product candidates, including the Syros Product Candidates, have participated. Further, no clinical investigator, researcher, or clinical staff participating in any clinical study conducted by or, to the Knowledge of Syros, on behalf of Syros or any of its Subsidiaries has been disqualified from participating in studies involving the Syros Product Candidates, and to the Knowledge of Syros, no such administrative action to disqualify such clinical investigators, researchers or clinical staff has been threatened or is pending.

(f) Neither Syros nor any of its Subsidiaries, and to the Knowledge of Syros, no contract manufacturer with respect to any Syros Product Candidate is the subject of any pending or, to the Knowledge of Syros, threatened investigation in respect of its business or products by the FDA pursuant to its "Fraud, Untrue Statements of Material Facts, Bribery, and Illegal Gratuities" Final Policy set forth in 56 Fed. Reg. 46191

(September 10, 1991) and any amendments thereto. To the Knowledge of Syros, neither Syros nor any of its Subsidiaries and no contract manufacturer with respect to any Syros Product Candidate has not committed any acts, made any statement, or failed to make any statement, in each case in respect of its business or products that would violate FDA's "Fraud, Untrue Statements of Material Facts, Bribery, and Illegal Gratuities" Final Policy, and any amendments thereto. None of Syros, any of its Subsidiaries, and to the Knowledge of Syros, any contract manufacturer with respect to any Syros Product Candidate, or any of their respective officers, employees or agents has been convicted of any crime or engaged in any conduct that could result in a material debarment or exclusion (i) under 21 U.S.C. Section 335a or (ii) any similar applicable Law. To the Knowledge of Syros, no material debarment or exclusionary claims, actions, proceedings or investigations in respect of their business or products are pending or threatened against Syros, any of its Subsidiaries, and to the Knowledge of Syros, any contract manufacturer with respect to any Syros Product Candidate, or any of its officers, employees or agents.

(g) All manufacturing operations conducted by, or, to the Knowledge of Syros, for the benefit of Syros or its Subsidiaries in connection with any Syros Product Candidate, since the Lookback Date, have been and are being conducted in compliance in all material respects with applicable Laws, including the FDA's standards for current good manufacturing practices, including applicable requirements contains in 21 C.F.R. Parts 210 and 211, and the respective counterparts thereof promulgated by Governmental Authorities in countries outside the United States.

(h) No manufacturing site owned by Syros or its Subsidiaries, and to the Knowledge of Syros, no manufacturing site of a contract manufacturer, with respect to any Syros Product Candidate, (i) is subject to a Drug Regulatory Agency shutdown or import or export prohibition or (ii) has received any Form FDA 483, notice of violation, warning letter, untitled letter, or similar correspondence or notice from the FDA or other Governmental Authority alleging or asserting noncompliance with any applicable Law, in each case, that have not be complied with or closed to the satisfaction of the relevant Governmental Authority, and, to the Knowledge of Syros, neither the FDA nor any other Governmental Authority is considering such action.

4.15 Legal Proceedings; Orders.

(a) There is no pending Legal Proceeding and, to the Knowledge of Syros, no person has threatened in writing to commence any Legal Proceeding: (i) that involves Syros or any of its Subsidiaries or any current or former employee, independent contractor, officer or director of Syros or any of its Subsidiaries (in his or her capacity as such) (a "Syros Associate") or any of the material assets owned or used by Syros or its Subsidiaries or (ii) that challenges, or that may have the effect of preventing, delaying, making illegal or otherwise interfering with, the Contemplated Transactions.

(b) There is no Order to which Syros or any of its Subsidiaries, or any of the material assets owned or used by Syros or any of its Subsidiaries is subject. To the Knowledge of Syros, no officer or other Key Employee of Syros or any of its Subsidiaries is subject to any Order that prohibits such officer or employee from engaging in or continuing any conduct, activity or practice relating to the business of Syros or any of its Subsidiaries or to any material assets owned or used by Syros or any of its Subsidiaries.

4.16 Tax Matters.

(a) Each of Syros and its Subsidiaries has timely filed all federal income Tax Returns and other material Tax Returns that they were required to file under applicable Law. All such Tax Returns were correct and complete in all material respects and have been prepared in material compliance with all applicable Law. No claim has ever been made by a Governmental Authority in writing in a jurisdiction where Syros or any of its Subsidiaries does not file Tax Returns that Syros or such Subsidiary is subject to taxation by that jurisdiction.

(b) All material Taxes due and owing by Syros and each of its Subsidiaries (whether or not shown on any Tax Return) have been paid. Since the date of the Syros Balance Sheet, neither Syros nor any of its

Subsidiaries has incurred any material Liability for Taxes outside the Ordinary Course of Business or otherwise inconsistent with past custom and practice.

(c) Each of Syros and its Subsidiaries has withheld and paid all material Taxes required to have been withheld and paid in connection with any amounts paid or owing to any employee, independent contractor, creditor, stockholder, or other third party.

(d) There are no Encumbrances for material Taxes (other than Taxes not yet due and payable or for Taxes that are being contested in good faith, in each case, for which adequate reserves have been established in accordance with GAAP) upon any of the assets of Syros or any of its Subsidiaries.

(e) No outstanding deficiencies for Taxes with respect to Syros or any of its Subsidiaries have been claimed, proposed or assessed by any Governmental Authority in writing. There are no pending (or, based on written notice, threatened) audits, assessments or other actions for or relating to any liability in respect of Taxes of Syros or any of its Subsidiaries. Neither Syros nor any of its Subsidiaries has waived any statute of limitations in respect of Taxes or agreed to any extension of time with respect to a Tax assessment or deficiency, which waiver or extension is currently in effect.

(f) Neither Syros nor any of its Subsidiaries is a party to any Tax allocation, Tax sharing or similar agreement (including indemnity arrangements), other than customary provisions in commercial contracts entered into in the Ordinary Course of Business with vendors, customers, lenders and landlords.

(g) Neither Syros nor any of its Subsidiaries has been a member of an affiliated group filing a consolidated U.S. federal income Tax Return (other than a group the common parent of which is Syros). Neither Syros nor any of its Subsidiaries has any material Liability for the Taxes of any person (other than Syros and any of its Subsidiaries) under Treasury Regulations Section 1.1502-6 (or any similar provision of state, local, or foreign law) or as a transferee or successor.

(h) Neither Syros nor any of its Subsidiaries has distributed stock of another person, or had its stock distributed by another person, in a transaction that was purported or intended to be governed in whole or in part by Section 355 of the Code or Section 361 of the Code.

(i) To the Knowledge of Syros, except as provided in Section 6.17, neither Syros nor any of its Subsidiaries has taken or agreed to take any action that would reasonably be expected to prevent the Transactions from qualifying for the Intended Tax Treatment.

(j) Neither Syros nor any of its Subsidiaries has entered into any transaction identified as a "listed transaction" for purposes of Treasury Regulations Sections 1.6011-4(b)(2) or 301.6111-2(b)(2).

4.17 Employee and Labor Matters; Benefit Plans.

(a) The employment of Syros' and any of its Subsidiaries' employees is terminable by Syros or the applicable Subsidiary at will. Syros has made available to Tyme accurate and complete copies of its code of conduct, employee handbook and insider trading policy. Neither Syros nor any of its Subsidiaries is a party to, bound by, or has a duty to bargain under, any collective bargaining agreement or other Contract with a labor organization representing any of its employees, and there are no labor organizations representing or, to the Knowledge of Syros, purporting to represent or seeking to represent any employees of Syros or its Subsidiaries.

(b) Each Syros Employee Plan that is intended to be qualified under Section 401(a) of the Code has received a favorable determination or is the subject of a favorable opinion letter with respect to such qualified status from the United States Internal Revenue Service (the "IRS"). To the Knowledge of Syros, nothing has occurred that would reasonably be expected to adversely affect the qualified status of any such Syros Employee Plan or the exempt status of any related trust.

(c) Each Syros Employee Plan has been established, maintained and operated in compliance, in all material respects, with its terms and all applicable Law, including the Code, ERISA and the Affordable Care Act. No Legal Proceeding (other than those relating to routine claims for benefits) is pending or, to the Knowledge of Syros, threatened with respect to any Syros Employee Plan. All payments and/or contributions required to have been made with respect to all Syros Employee Plans either have been made or have been accrued, where required by GAAP, in accordance with the terms of the applicable Syros Employee Plan and applicable Law.

(d) Neither Syros nor any of its ERISA Affiliates has, within the past 6 years, maintained, contributed to, or been required to contribute to (i) any employee benefit plan that is or was subject to Title IV or Section 302 of ERISA or Section 412 of the Code, (ii) a Multiemployer Plan, (iii) any funded welfare benefit plan within the meaning of Section 419 of the Code, (iv) any Multiple Employer Plan, or (v) any Multiple Employer Welfare Arrangement. Neither Syros nor any of its ERISA Affiliates has ever incurred any liability under Title IV of ERISA that has not been paid in full.

(e) No Syros Employee Plan provides for medical or other welfare benefits beyond termination of service or retirement, other than (i) pursuant to COBRA or an analogous state law requirement, (ii) continuation coverage through the end of the month in which such termination or retirement occurs, or (iii) any otherwise disclosed express severance arrangement. Syros does not sponsor or maintain any self-funded medical or long-term disability benefit plan.

(f) No Syros Employee Plan is subject to any law of a foreign jurisdiction outside of the United States.

(g) No Syros Options or other equity-based awards issued or granted by Syros are subject to the requirements of Code Section 409A. Each Syros Employee Plan that constitutes in any part a "nonqualified deferred compensation plan" (as such term is defined under Section 409A(d)(1) of the Code and the guidance thereunder) (each, a "Syros 409A Plan") complies in all material respects, in both form and operation, with the requirements of Code Section 409A and the guidance thereunder. No payment to be made under any Syros 409A Plan is or, when made in accordance with the terms of the Syros 409A Plan, will be subject to the penalties of Code Section 409A(a)(1).

(h) Syros and each of its Subsidiaries is, and since the Lookback Date has been, in material compliance with all applicable federal, state and local laws, rules and regulations respecting employment, employment practices, terms and conditions of employment, worker classification, tax withholding, prohibited discrimination, equal employment, fair employment practices, meal and rest periods, immigration status, employee safety and health, wages (including overtime wages), compensation, and hours of work, and in each case, with respect to the employees of Syros and its Subsidiaries: (i) since the Lookback Date, has withheld and reported all material amounts required by law or by agreement to be withheld and reported with respect to wages, salaries and other payments to employees, (ii) is not liable for any arrears of wages, severance pay or any Taxes or any penalty for failure to comply with any of the foregoing and (iii) is not liable for any material payment to any trust or other fund governed by or maintained by or on behalf of any Governmental Authority, with respect to unemployment compensation benefits, social security or other benefits or obligations for employees (other than routine payments to be made in the Ordinary Course of Business). There are no actions, suits, claims or administrative matters pending or, to the Knowledge of Syros or any of its Subsidiaries, threatened or reasonably anticipated against Syros relating to any employee, employment agreement or Syros Employee Plan (other than routine claims for benefits). To the Knowledge of Syros or any of its Subsidiaries, there are no pending or threatened or reasonably anticipated claims or actions against Syros or any of its Subsidiaries, any Syros trustee or any trustee of any Subsidiary under any workers' compensation policy or long-term disability policy. Neither Syros nor any of its Subsidiaries is a party to a conciliation agreement, consent decree or other agreement or Order with any federal, state, or local agency or Governmental Authority with respect to employment practices.

(i) Neither Syros nor any of its Subsidiaries has material liability with respect to any misclassification within the past three years of: (i) any person as an independent contractor rather than as an

employee, (ii) any employee leased from another employer or (iii) any employee currently or formerly classified as exempt from overtime wages. Neither Syros nor any of its Subsidiaries has taken any action which would constitute a "plant closing" or "mass layoff" within the meaning of the WARN Act or similar state or local law, issued any notification of a plant closing or mass layoff required by the WARN Act or similar state or local law, or incurred any liability or obligation under WARN or any similar state or local law that remains unsatisfied.

(j) There has never been, nor has there been any threat of, any strike, slowdown, work stoppage, lockout, job action, union organizing activity, question concerning representation or any similar activity or dispute, affecting Syros or any of its Subsidiaries. No event has occurred within the past six months, and no condition or circumstance exists, that might directly or indirectly be likely to give rise to or provide a basis for the commencement of any such strike, slowdown, work stoppage, lockout, job action, union organizing activity, question concerning representation or any similar activity or dispute.

(k) Neither Syros nor any of its Subsidiaries is, nor has Syros or any of its Subsidiaries been, engaged in any unfair labor practice within the meaning of the National Labor Relations Act. There is no Legal Proceeding, claim, labor dispute or grievance pending or, to the Knowledge of Syros, threatened or reasonably anticipated relating to any employment contract, privacy right, labor dispute, wages and hours, leave of absence, plant closing notification, workers' compensation policy, long-term disability policy, harassment, retaliation, immigration, employment statute or regulation, safety or discrimination matter involving any Syros Associate, including charges of unfair labor practices or discrimination complaints.

(l) There is no contract, agreement, plan or arrangement to which Syros or any person that is (or at any relevant time was) under common control with Syros within the meaning of Sections 414(b), (c), (m) and (o) of the Code, and the regulations issued thereunder is a party or by which it is bound to compensate any of its employees for excise taxes paid pursuant to Section 4999 or Section 409A of the Code.

(m) Neither Syros nor any of its Subsidiaries is a party to any Contract that could, due to the Merger (either alone or in conjunction with any other event) (i) result in the payment of any "parachute payment" within the meaning of Section 280G of the Code or (ii) result in, or cause the accelerated vesting, payment, funding or delivery of, or increase the amount or value of, any payment or benefit to any employee, officer, director or other service provider of Syros or any of its Subsidiaries.

4.18 Environmental Matters. Since the Lookback Date, Syros and each of its Subsidiaries has complied with all applicable Environmental Laws, which compliance includes the possession by Syros of all permits and other Governmental Authorizations required under applicable Environmental Laws and compliance with the terms and conditions thereof, except for any failure to be in compliance that, individually or in the aggregate, would not result in a Syros Material Adverse Effect. Neither Syros nor any of its Subsidiaries has received, since the Lookback Date, any written notice or other communication (in writing or otherwise), whether from a Governmental Authority, citizens group, employee or otherwise, that alleges that Syros or any of its Subsidiaries is not in compliance with any Environmental Law, and, to the Knowledge of Syros, there are no circumstances that may prevent or interfere with Syros' or any of its Subsidiaries' compliance with any Environmental Law in the future, except where such failure to comply would not reasonably be expected to have a Syros Material Adverse Effect. To the Knowledge of Syros: (i) no current or prior owner of any property leased or controlled by Syros or any of its Subsidiaries has received, since the Lookback Date, any written notice or other communication relating to property owned or leased at any time by Syros or any of its Subsidiaries, whether from a Governmental Authority, citizens group, employee or otherwise, that alleges that such current or prior owner or Syros or any of its Subsidiaries is not in compliance with or violated any Environmental Law relating to such property and (ii) neither Syros nor any of its Subsidiaries has no material liability under any Environmental Law.

4.19 Insurance. Syros has made available to the Company accurate and complete copies of all material insurance policies and all material self-insurance programs and arrangements relating to the business, assets, liabilities and operations of Syros and Merger Sub. Each of such insurance policies is in full force and effect and

Syros and Merger Sub are in compliance in all material respects with the terms thereof. Other than customary end of policy notifications from insurance carriers, since the Lookback Date, Syros has not received any notice or other communication regarding any actual or possible: (i) cancellation or invalidation of any insurance policy or (ii) refusal or denial of any coverage, reservation of rights or rejection of any material claim under any insurance policy. Each of Syros and Merger Sub has provided timely written notice to the appropriate insurance carrier(s) of each Legal Proceeding pending against Syros for which Syros has insurance coverage, and no such carrier has issued a denial of coverage or a reservation of rights with respect to any such Legal Proceeding, or informed Syros of its intent to do so.

4.20 Transactions with Affiliates. Except as set forth in the Syros SEC Documents filed prior to the date of this Agreement, since the date of Syros' last annual proxy statement filed with the SEC, no event has occurred that would be required to be reported by Syros pursuant to Item 404 of Regulation S-K promulgated by the SEC.

4.21 Financial Advisors. Except as set forth on Section 4.21 of the Syros Disclosure Schedule, no broker, finder or investment banker is entitled to any brokerage fee, finder's fee, opinion fee, success fee, transaction fee or other fee or commission in connection with the Contemplated Transactions based upon arrangements made by or on behalf of Syros.

4.22 Valid Issuance. The Syros Common Stock to be issued in the Merger will, when issued in accordance with the provisions of this Agreement, be validly issued, fully paid and nonassessable.

4.23 Privacy and Data Security. Syros has complied with all applicable Privacy Laws relating to privacy, security, collection or use of Personal Information of any individuals (including clinical trial participants, patients, patient family members, caregivers or advocates, physicians and other health care professionals, clinical trial investigators, researchers, pharmacists) that interact with Syros in connection with the operation of Syros' business, except for such non-compliance as has not had, and would not reasonably be expected to have, individually or in the aggregate, a Syros Material Adverse Effect. To the Knowledge of Syros, Syros has complied with its Privacy Policies, except for such non-compliance as has not had, and would not reasonably be expected to have, individually or in the aggregate, a Syros Material Adverse Effect. To the Knowledge of Syros, as of the date hereof, no claims have been asserted or threatened against Syros by any person alleging a violation of Privacy Laws and/or Privacy Policies.

4.24 Securities Purchase Agreement. Syros has delivered to Tyme a true, correct and complete copy of the fully executed Securities Purchase Agreement for the Financing. To the knowledge of Syros, (i) the Securities Purchase Agreement has not been amended or modified; (ii) no such amendment or modification is contemplated except as otherwise expressly set forth therein; and (iii) the respective commitments contained in the Securities Purchase Agreement have not been withdrawn (or contemplated to be), terminated or rescinded in any respect by Syros and the other parties thereto. There are no other Contracts, agreements, supplements, side letters or arrangements to which Syros or any of its Affiliates is a party that would reasonably be expected to affect the conditionality or availability of the Financing in a manner adverse to Tyme or Syros. The Securities Purchase Agreement (in the form delivered by Syros to Tyme) is (a) in full force and effect, and constitutes the legal, valid and binding obligations of Syros and, to the knowledge of Syros, the other parties thereto, and (b) enforceable against Syros and, to the knowledge of Syros, the other parties thereto, in accordance with its terms, subject to the Enforceability Exceptions. Other than as expressly set forth in the Securities Purchase Agreement, there are no conditions precedent related to the funding of the Financing pursuant to any agreement relating to the Financing to which Syros is a party. To the knowledge of Syros, as of the date hereof, no event has occurred that, with or without notice or lapse of time or both, would, or would reasonably be expected to, (A) constitute a default, breach or failure to satisfy a condition precedent set forth in the Securities Purchase Agreement, or (B) result in any portion of the committed financing contemplated by the Financing being unavailable on the Closing Date, assuming the conditions to such financing are satisfied or waived in accordance with the terms thereof. Assuming the satisfaction of the conditions set forth in Article VII, as of the date of this Agreement, Syros has no reason to believe that it will be unable to satisfy in all material respects on a timely basis any term

or condition of closing to be satisfied by it contained in the Securities Purchase Agreement. As of date of this Agreement, (1) no party to the Securities Purchase Agreement has notified Syros of its intention to terminate any of the commitments set forth in the Securities Purchase Agreement or not to provide the financings contemplated thereto and (2) no termination of any commitment set forth in the Securities Purchase Agreement is contemplated by Syros.

4.25 No Other Representations or Warranties. Syros hereby acknowledges and agrees that, except for the representations and warranties contained in this Agreement, neither the Company nor any of its Subsidiaries nor any other person on behalf of the Company or its Subsidiaries makes any express or implied representation or warranty with respect to the Company or its Subsidiaries or with respect to any other information provided to Syros, Merger Sub or stockholders or any of their respective Affiliates in connection with the Contemplated Transactions, and (subject to the express representations and warranties of the Company set forth in Article III (in each case as qualified and limited by the Company Disclosure Schedule)) none of Syros, Merger Sub or any of their respective Representatives or stockholders, has relied on any such information (including the accuracy or completeness thereof).

ARTICLE V

CONDUCT OF BUSINESSES

5.1 Covenants of Tyme. Except as set forth inSection 5.1 of the Tyme Disclosure Schedule (or as disclosed in any Tyme SEC Report) or as expressly provided herein or as consented to in writing by Syros (which consent shall not be unreasonably withheld, conditioned or delayed), or to the extent necessary to comply with any COVID-19 Measures, from and after the date of this Agreement until the earlier of the termination of this Agreement in accordance with its terms and the Effective Time, Tyme shall, and shall cause each of its Subsidiaries to, use commercially reasonable efforts to act and carry on its business in the Ordinary Course of Business, pay its debts and Taxes and perform its other obligations when due (subject to good faith disputes over such debts, Taxes or obligations), comply with applicable laws, rules and regulations, and maintain and preserve its and each of its Subsidiaries' business organization, assets and properties, keep available the services of its present officers and key employees and preserve its advantageous business relationships with customers, strategic partners, suppliers, distributors and others having business dealings with it. Without limiting the generality of the foregoing, except as set forth in Section 5.1 of the Tyme Disclosure Schedule (or as disclosed in any Tyme SEC Report) or as expressly provided herein, or to the extent necessary to comply with any COVID-19 Measures, from and after the date of this Agreement until the earlier of the termination of this Agreement in accordance with its terms and the Effective Time, Tyme shall not, and shall not permit any of its Subsidiaries to, directly or indirectly, do any of the following without the prior written consent of Syros (which consent shall not, in the case of the actions set forth in clauses (k) and (l) of this Section 5.1, be unreasonably withheld, conditioned or delayed):

(a) (i) declare, set aside or pay any dividends on, or make any other distributions (whether in cash, securities or other property) in respect of, any of its capital stock (other than dividends and distributions by a direct or indirect wholly owned Subsidiary of Tyme to its parent); (ii) split, combine or reclassify any of its capital stock or issue or authorize the issuance of any other securities in respect of, in lieu of or in substitution for shares of its capital stock or any of its other securities; or (iii) purchase, redeem or otherwise acquire any shares of its capital stock or any other of its securities or any rights, warrants or options to acquire any such shares or other securities, other than, in the case of this clause (iii), from former employees, directors and consultants in accordance with Tyme Stock Plans in effect on the date of this Agreement providing for the repurchase of shares at no or nominal consideration in connection with any termination of services to Tyme or any of its Subsidiaries (or as part of a cashless exercise or to settle tax obligations with respect to the exercise of Tyme Options or Tyme Warrants outstanding on the date of this Agreement);

(b) issue, deliver, sell, grant, pledge or otherwise dispose of or encumber any shares of its capital stock, any other voting securities or any securities convertible into or exchangeable for, or any rights, warrants or options to acquire, any such shares, voting securities or convertible or exchangeable securities (other than the issuance of shares of Tyme Common Stock upon the exercise of Tyme Options or Tyme Warrants outstanding on the date of this Agreement and set forth in Section 3.2(c) or Section 3.2(d) of the Tyme Disclosure Schedule in accordance with their present terms (including cashless exercises);

(c) amend its certificate of incorporation, bylaws or other comparable charter or organizational documents or effect or be a party to any merger, consolidation, share exchange, business combination, recapitalization, reclassification of shares, stock split or reverse stock split or form any new Subsidiary or acquire any equity interest or other interest in any other person;

(d) acquire (i) by merging or consolidating with, or by purchasing all or a substantial portion of the assets or any stock of, or by any other manner, any business or any corporation, partnership, joint venture, limited liability company, association or other business organization or division thereof or (ii) any assets that are material, in the aggregate, to Tyme and its Subsidiaries, taken as a whole;

(e) whether or not in the Ordinary Course of Business, sell, lease, license, pledge, or otherwise dispose of or encumber any material properties or assets of Tyme or of any of its Subsidiaries;

(f) whether or not in the Ordinary Course of Business, sell, dispose of or otherwise transfer any assets material to Tyme and its Subsidiaries, taken as a whole (including any accounts, leases, contracts or Intellectual Property or any assets or the stock of any of its Subsidiaries, but excluding the sale or license of products in the Ordinary Course of Business);

(g) (i) incur or suffer to exist any indebtedness for borrowed money other than such indebtedness that existed as of the date of the Tyme Balance Sheet to the extent reflected on the Tyme Balance Sheet or guarantee any such indebtedness of another person, (ii) issue, sell or amend any debt securities or warrants or other rights to acquire any debt securities of Tyme or any of its Subsidiaries, guarantee any debt securities of another person, enter into any "keep well" or other agreement to maintain any financial statement condition of another person or enter into any arrangement having the economic effect of any of the foregoing, (iii) make any loans, advances (other than routine advances to employees of Tyme in the Ordinary Course of Business pursuant to Tyme Employee Plans) or capital contributions to, or investment in, any other person, other than Tyme or any of its direct or indirect wholly owned Subsidiaries or (iv) enter into any hedging agreement or other financial agreement or arrangement designed to protect Tyme or its Subsidiaries against fluctuations in commodities prices or exchange rates;

(h) make any capital expenditures or other expenditures with respect to property, plant or equipment for Tyme and its Subsidiaries, taken as a whole, other than as set forth in Tyme's budget for capital expenditures previously made available to Syros or the specific capital expenditures disclosed and set forth in Section 5.1(h) of the Tyme Disclosure Schedule;

(i) make any changes in accounting methods, principles or practices, except insofar as may have been required by a change in GAAP or, except as so required, change any assumption underlying, or method of calculating, any bad debt, contingency or other reserve;

(j) except (i) in the Ordinary Course of Business or (ii) in connection with terminations of any contract not expected to continue after Closing or as a result of the expiration of any contract that expires in accordance with terms, (A) modify or amend in any material respect, or terminate, any material contract or agreement to which Tyme or any of its Subsidiaries is party, or (B) knowingly waive, release or assign any material rights or claims (including any write-off or other compromise of any accounts receivable of Tyme of any of its Subsidiaries);

(k) except in the Ordinary Course of Business, (i) enter into any material contract or agreement relating to the rendering of services or the distribution, sale or marketing by third parties of the products, of, or products licensed by, Tyme or any of its Subsidiaries or (ii) license any material Intellectual Property rights to or from any third party;

(l) except as required to comply with applicable Law or required by a Tyme Employee Plan, (i) take any action with respect to, adopt, enter into, terminate (other than terminations for cause) or amend any Tyme Employee Plan (or any other employee benefit or compensation plan, program, policy, agreement or arrangement that would have constituted a Tyme Employee Plan had it been in effect on the date of this Agreement) or any collective bargaining agreement, (ii) increase in any material respect the compensation or fringe benefits of, or pay any material bonus to, any director, officer, employee or consultant (except for annual increases of the salaries of non-officer employees in the Ordinary Course of Business), (iii) amend or accelerate the payment, right to payment or vesting of any compensation or benefits, including any outstanding equity or equity-based incentive awards, (iv) pay any material benefit not provided for as of the date of this Agreement under any Tyme Employee Plan, (v) grant any awards under any Tyme Employee Plan (or under any other employee benefit or compensation plan, program, policy, agreement or arrangement that would have constituted a Tyme Employee Plan had it been in effect on the date of this Agreement), or (vi) take any action other than in the Ordinary Course of Business to fund or in any other way secure the payment of compensation or benefits under any Tyme Employee Plan (or under any other employee benefit or compensation plan, program, policy, agreement or arrangement that would have constituted a Tyme Employee Plan had it been in effect on the date of this Agreement);

(m) make or change any material Tax election, change an annual accounting period, enter into any closing agreement, waive or extend any statute of limitations with respect to Taxes, settle or compromise any material Tax liability, claim or assessment, surrender any right to claim a refund of material Taxes, or amend any income or other material Tax Return;

(n) commence any offering of shares of Tyme Common Stock pursuant to any employee stock purchase plan;

(o) initiate, compromise or settle any material litigation or arbitration proceeding;

(p) open any facility or office, or close any facility or office without prior consultation with Syros;

(q) fail to use commercially reasonable efforts to maintain insurance at levels substantially comparable to levels existing as of the date of this Agreement;

(r) fail to pay accounts payable and other obligations in the Ordinary Course of Business;

(s) suspend any clinical trials sponsored by Tyme or involving any products marketed or in development by Tyme; or

(t) authorize any of, or commit or agree, in writing or otherwise, to take any of, the foregoing actions or any action that would make any representation or warranty of Tyme in this Agreement untrue or incorrect in any material respect, or would materially impair, delay or prevent the satisfaction of any conditions in Article VII hereof.

5.2 Covenants of Syros. Except as set forth in Section 5.2 of the Syros Disclosure Schedule (or as disclosed in any Syros SEC Report) or as expressly provided herein or as consented to in writing by Tyme (which consent shall not be unreasonably withheld, conditioned or delayed), or to the extent necessary to comply with any COVID-19 Measures, from and after the date of this Agreement until the earlier of the termination of this Agreement in accordance with its terms and the Effective Time, Syros shall, and shall cause each of its

Subsidiaries to, use commercially reasonable efforts to act and carry on its business in the Ordinary Course of Business, pay its debts and Taxes and perform its other obligations when due (subject to good faith disputes over such debts, Taxes or obligations), comply with applicable laws, rules and regulations, and, maintain and preserve its and each of its Subsidiaries' business organization, assets and properties, keep available the services of its present officers and key employees and preserve its advantageous business relationships with customers, strategic partners, suppliers, distributors and others having business dealings with it. Without limiting the generality of the foregoing, except as set forth in Section 5.2 of the Syros Disclosure Schedule (or as disclosed in any Syros SEC Report) or as expressly provided herein, or to the extent necessary to comply with any COVID-19 Measures, from and after the date of this Agreement until the earlier of the termination of this Agreement in accordance with its terms and the Effective Time, Syros shall not, and shall not permit any of its Subsidiaries to, directly or indirectly, do any of the following without the prior written consent of Tyme (which consent shall not, in the case of the actions set forth in clauses (k) and (l) of this Section 5.2, be unreasonably withheld, conditioned or delayed):

(a) (i) declare, set aside or pay any dividends on, or make any other distributions (whether in cash, securities or other property) in respect of, any of its capital stocks (other than dividends and distributions by a direct or indirect wholly owned subsidiary of Syros to its parent), (ii) except as contemplated by the Syros Authorized Stock Increase, split, combine or reclassify any of its capital stock or issue or authorize the issuance of any other securities in respect of, in lieu of or in substitution for shares of its capital stock or any of its other securities; or (iii) purchase, redeem or otherwise acquire any shares of its capital stock or any other of its securities or any rights, warrants or options to acquire any such shares or other securities, other than, in the case of this clause (iii), from former employees, directors and consultants in accordance with Syros Stock Plans in effect on the date of this Agreement providing for the repurchase of shares at no or nominal consideration in connection with any termination of services to Syros or any of its Subsidiaries;

(b) Except pursuant to the Securities Purchase Agreement, issue, deliver, sell, grant, pledge or otherwise dispose of or encumber any shares of its capital stock, any other voting securities or any securities convertible into or exchangeable for, or any rights, warrants or options to acquire, any such shares, voting securities or convertible or exchangeable securities (in each case other than the issuance of shares of Syros Common Stock upon the exercise of Syros Stock Options or warrants of Syros or the settlement of Syros RSUs outstanding on the date of this Agreement in accordance with their present terms (including cashless exercises));

(c) except as contemplated by the Syros Authorized Stock Increase, amend its certificate of incorporation, bylaws or other comparable charter or organizational documents or effect or be a party to any merger, consolidation, share exchange, business combination, recapitalization, reclassification of shares, stock split or reverse stock split or form any new Subsidiary or acquire any equity interest or other interest in any other person;

(d) acquire (i) by merging or consolidating with, or by purchasing all or a substantial portion of the assets or any stock of, or by any other manner, any business or any corporation, partnership, joint venture, limited liability company, association or other business organization or division thereof or (ii) any assets, except for purchases of inventory and raw materials in the Ordinary Course of Business, that are material, in the aggregate, to Syros and its Subsidiaries, taken as a whole;

(e) except in the Ordinary Course of Business and except as contemplated bySection 5.2, sell, lease, license, pledge, or otherwise dispose of or encumber any properties or assets of Syros or of any of its Subsidiaries;

(f) whether or not in the Ordinary Course of Business, sell, dispose of or otherwise transfer any assets material to Syros and its Subsidiaries, taken as a whole (including any accounts, leases, contracts or Intellectual Property or any assets or the stock of any of its Subsidiaries, but excluding the sale or license of products in the Ordinary Course of Business);

(g) (i) incur or suffer to exist any indebtedness for borrowed money or guarantee any such indebtedness of another person, (ii) issue, sell or amend any debt securities or warrants or other rights to acquire any debt securities of Syros or any of its Subsidiaries, guarantee any debt securities of another person, enter into any "keep well" or other agreement to maintain any financial statement condition of another person or enter into any arrangement having the economic effect of any of the foregoing, (iii) make any loans, advances (other than routine advances to employees of Syros in the Ordinary Course of Business pursuant to Syros Employee Plans) or capital contributions to, or investment in, any other person, other than Syros or any of its direct or indirect wholly owned Subsidiaries or (iv) enter into any hedging agreement or other financial agreement or arrangement designed to protect Syros or its Subsidiaries against fluctuations in commodities prices or exchange rates;

(h) make any capital expenditures or other expenditures with respect to property, plant or equipment in excess of $500,000 in the aggregate for Syros and its Subsidiaries, taken as a whole, other than as set forth in Syros' budget for capital expenditures previously made available to Tyme or the specific capital expenditures disclosed and set forth in Section 5.2 of the Syros Disclosure Schedule;

(i) make any changes in accounting methods, principles or practices, except insofar as may have been required by the SEC or a change in GAAP or, except as so required, change any assumption underlying, or method of calculating, any bad debt, contingency or other reserve;

(j) except (i) in the Ordinary Course of Business or (ii) for terminations as a result of the expiration of any contract that expires in accordance with its terms, (A) modify or amend in any material respect, or terminate, any material contract or agreement to which Syros or any of its Subsidiaries is party, or (B) knowingly waive, release or assign any material rights or claims (including any write-off or other compromise of any accounts receivable of Syros of any of its Subsidiaries);

(k) terminate the Securities Purchase Agreement or make any amendment, modification or waiver with respect to the Securities Purchase Agreement that would have the effect of (i) decreasing the price per share issuable thereunder, (ii) increasing the warrant coverage, lowering the warrant exercise price, extending the warrant term, or otherwise modifying the terms of the warrants issuable thereunder in a manner adverse to Syros or Tyme, (iii) increasing the gross proceeds to be realized from such Financing or reducing the amount of the gross proceeds to be realized from such Financing to an amount less than $100,000,000, (iv) conditioning or delaying consummation of the Financing, (v) preventing the Intended Tax Treatment, or (vi) any other change that would be material and adverse to Tyme or Syros;

(l) except in the Ordinary Course of Business, (i) enter into any material contract or agreement relating to the rendering of services or the distribution, sale or marketing by third parties of the products, of, or products licensed by, Syros or any of its Subsidiaries or (ii) license any material Intellectual Property rights to or from any third party;

(m) other than in the Ordinary Course of Business, as required to comply with applicable Law or as required by a Syros Employee Plan, (i) take any action with respect to, adopt, enter into, terminate (other than terminations for cause) or amend any Syros Employee Plan (or any other employee benefit or compensation plan, program, policy, agreement or arrangement that would have constituted a Syros Employee Plan had it been in effect on the date of this Agreement) or any collective bargaining agreement, (ii) increase in any material respect the compensation or fringe benefits of, or pay any material bonus to, any director, officer, employee or consultant, (iii) amend or accelerate the payment, right to payment or vesting of any compensation or benefits, including any outstanding equity or equity-based incentive awards, (iv) pay any material benefit not provided for as of the date of this Agreement under any Syros Employee Plan, (v) grant any awards under any Syros Employee Plan (or under any other employee benefit or compensation plan, program, policy, agreement or arrangement that would have constituted a Syros Employee Plan had it been in effect on the date of this Agreement), or (vi) take any action to fund or in any other way secure the payment of compensation or benefits under any Syros Employee Plan (or under any other employee benefit or compensation plan, program, policy,

agreement or arrangement that would have constituted a Syros Employee Plan had it been in effect on the date of this Agreement);

(n) make or change any material Tax election, change an annual accounting period, enter into any closing agreement, waive or extend any statute of limitations with respect to Taxes, settle or compromise any material Tax liability, claim or assessment, surrender any right to claim a refund of material Taxes, or amend any income or other material Tax Return;

(o) commence any offering of shares of Syros Common Stock pursuant to any employee stock purchase plan;

(p) initiate, compromise or settle any material litigation or arbitration proceeding;

(q) open or close any facility or office;

(r) fail to use commercially reasonable efforts to maintain insurance at levels substantially comparable to levels existing as of the date of this Agreement;

(s) suspend any clinical trials sponsored by Syros or involving any products marketed or in development by Syros;

(t) fail to pay accounts payable and other obligations in the Ordinary Course of Business; or

(u) authorize any of, or commit or agree, in writing or otherwise, to take any of, the foregoing actions or any action that would make any representation or warranty of Syros in this Agreement untrue or incorrect in any material respect, or would materially impair, delay or prevent the satisfaction of any conditions in Article VII hereof.

5.3 Confidentiality. The parties acknowledge that Syros and Tyme have previously executed a confidentiality agreement, dated as of April 8, 2022 (the "Confidentiality Agreement"), which Confidentiality Agreement shall continue in full force and effect in accordance with its terms, except as expressly modified by this Agreement.

5.4 Pre-Closing Legacy Asset Transactions. Tyme may, with the prior written consent by Syros (which consent shall not be unreasonably withheld, conditioned or delayed), sell, assign, license, or otherwise dispose of, in one or more transactions, some or all of Tyme's non-cash assets set forth in Section 5.4 of the Tyme Disclosure Schedule prior to or concurrent with the Closing, provided that, to the extent required under the DGCL, such transaction is approved by the stockholders of Tyme. Any proceeds of such disposition may be distributed as a dividend to Tyme's stockholders as of a record date prior to the Closing or retained and included in the calculation of Tyme Net Cash (provided that cash proceeds in excess of $5 million that are retained by Tyme as of the Closing Date shall not result in an increase to Tyme Net Cash).

ARTICLE VI

ADDITIONAL AGREEMENTS

6.1 No Solicitation

(a) No Solicitation or Negotiation. Except as expressly permitted by this Section 6.1, until the Effective Time, each of Tyme, Syros and their respective Subsidiaries shall not, and each of Tyme and Syros shall use reasonable best efforts to cause their respective directors, officers, members, employees, agents,

attorneys, consultants, contractors, accountants, financial advisors and other authorized representatives ("Representatives") not to, directly or indirectly:

(i) solicit, seek or initiate or knowingly take any action to facilitate or encourage any offers, inquiries or the making of any proposal or offer that constitutes, or would reasonably be expected to lead to, any Acquisition Proposal;

(ii) enter into, continue or otherwise participate or engage in any discussions or negotiations regarding any Acquisition Proposal, or furnish to any person any non-public information or afford any person other than Syros or Tyme, as applicable, access to such party's property, books or records (except pursuant to a request by a Governmental Authority) in connection with any offers, inquiries or the making of any proposal or offer that constitutes, or would reasonably be expected to lead to, any Acquisition Proposal;

(iii) take any action to make the provisions of any takeover statute inapplicable to any transactions contemplated by an Acquisition Proposal; or

(iv) publicly propose to do any of the foregoing described in clauses (i) through (iii).

Notwithstanding the foregoing or anything to the contrary set forth in this Agreement, subject to compliance with Section 6.1(c), prior to the Specified Time, each of Syros and Tyme may (A) furnish non-public information with respect to Syros and its Subsidiaries or Tyme and its Subsidiaries, as the case may be, to any Qualified Person (and the Representatives of such Qualified Person), or (B) engage in discussions or negotiations (including solicitation of revised Acquisition Proposals) with any Qualified Person (and the Representatives of such Qualified Person) regarding any such Acquisition Proposal; provided, (x) that either Tyme or Syros (as applicable) receives from the Qualified Person an executed confidentiality agreement on the terms not less restrictive than exist in the Confidentiality Agreement and continuing additional provisions that expressly permit such party to comply with this terms of this Section 6.1 (a copy of which shall be provided to the other party), (y) the party seeking to take the actions set forth in (A) and (B) has not otherwise materially breached this Section 6.1 with respect to such Acquisition Proposal or the person making such Acquisition Proposal, and (z) the Tyme Board or Syros Board (as applicable) has determined (after consultation with its outside financial advisors and outside legal counsel) that the failure to take such actions would be inconsistent with its fiduciary duties under applicable Law. It is understood and agreed that any violation of the restrictions in this Section 6.1 (or action that, if taken by Syros or Tyme, as applicable, would constitute such a violation) by any Representatives of Syros or Tyme shall be deemed to be a breach of this Section 6.1 by Syros or Tyme, as applicable.

(b) No Change in Recommendation or Alternative Acquisition Agreement.

Prior to the Effective Time:

(i) (A) Tyme Board shall not, except as set forth in this Section 6.1, withhold, withdraw or modify, or publicly propose to withhold, withdraw or modify, the approval or recommendation by the Tyme Board with respect to the Merger, fail to recommend against acceptance of a tender offer within ten (10) Business Days after commencement or propose publicly to approve, adopt or recommend any Acquisition Proposal (a "Tyme Board Recommendation Change") and (B) the Syros Board shall not, except as set forth in this Section 6.1, withhold, withdraw or modify, or publicly propose to withhold, withdraw or modify, the approval or recommendation by the Syros Board with respect to the Share Issuance or Syros Authorized Stock Increase, fail to recommend against acceptance of a tender offer within ten (10) Business Days after commencement or propose publicly to approve, adopt or recommend any Acquisition Proposal (a "Syros Board Recommendation Change");

(ii) each of Syros and Tyme shall not enter into any letter of intent, memorandum of understanding, agreement in principle, acquisition agreement, merger agreement or similar agreement (an

"Alternative Acquisition Agreement") providing for the consummation of a transaction contemplated by any Acquisition Proposal (other than a confidentiality agreement referred to in Section 6.1(a) entered into in the circumstances referred to in Section 6.1(a)); and

(iii) each of the Syros Board and the Tyme Board, and each committee thereof, shall not, except as set forth in this Section 6.1, adopt, approve or recommend, or publicly propose to adopt, approve or recommend, any Acquisition Proposal.

Notwithstanding the foregoing or anything to the contrary set forth in this Agreement (including the provisions of this Section 6.1), at any time prior to the Specified Time, the Syros Board or the Tyme Board, as the case may be, may effect a Syros Board Recommendation Change or Tyme Board Recommendation Change, as the case may be, (A) with respect to a Superior Proposal or (B) in response to an Intervening Event (in the case of either clause (A) or clause (B)) if: (i) such board of directors shall have determined (after consultation with its outside financial advisors and outside legal counsel) that the failure to effect such Syros Board Recommendation Change or Tyme Board Recommendation Change, as applicable, would be inconsistent with its fiduciary obligations under applicable law; (ii) such party has provided at least four Business Days prior written notice to the other party that it intends to effect a Syros Board Recommendation Change or Tyme Board Recommendation Change, as applicable, including a description in reasonable detail of the reasons for such recommendation change (and, with respect to a Superior Proposal, written copies of any relevant proposed transactions agreements with any party making such Superior Proposal (including the identity of the person making such Superior Proposal)) (a "Recommendation Change Notice") (it being understood that the Recommendation Change Notice shall not in and of itself constitute a Syros Board Recommendation Change or Tyme Board Recommendation Change for purposes of this Agreement); (iii) such party has complied in all material respects with the requirements of this Section 6.1 in connection with such potential Superior Proposal or Intervening Event (including, for the avoidance of doubt, in respect of a Superior Proposal, such proposal did not result from a material breach of this Section 6.1); and (iv) if the other party shall have delivered to such party a written, binding and irrevocable offer to alter the terms or conditions of this Agreement during the four Business Day period referred to in clause (ii) above, such party's board of directors shall have determined (after consultation with its outside financial advisors and outside legal counsel), after considering the terms of such offer by the other party, that the failure to effect a Syros Board Recommendation Change or Tyme Board Recommendation Change, as the case may be, would be inconsistent with its fiduciary duties under applicable Law. In the event of any material amendment to any Superior Proposal (including any revision in the amount, form or mix of consideration such party's stockholders would receive as a result of such potential Superior Proposal), such party shall be required to provide the other party with notice of such material amendment and there shall be a new two Business Day period following such notification during which the parties shall comply again with the requirements of this Section 6.1(b) and the board of directors of such party shall not make a Syros Board Recommendation Change or Tyme Board Recommendation Change, as applicable, prior to the end of any such period as so extended.

(c) Notices of Proposals. Each party will as promptly as reasonably practicable (and in any event within twenty four (24) hours after receipt) (i) notify the other party of its receipt of any actual or potential Acquisition Proposal and (ii) provide to the other party a copy of such Acquisition Proposal (if written), or a summary of the material terms and conditions of such Acquisition Proposal (if oral), including the identity of the person making such Acquisition Proposal, and copies of all written communications with such person with respect to such actual or potential Acquisition Proposal. Such party in receipt of an Acquisition Proposal shall notify the other party, in writing, of any decision of its board of directors as to whether to consider any Acquisition Proposal or to enter into discussions or negotiations concerning any Acquisition Proposal or to provide non-public information with respect to such to any person, which notice shall be given as promptly as practicable after such determination was reached (and in any event no later than twenty four (24) hours after such determination was reached). Such party in receipt of an Acquisition Proposal will (A) provide the other party with written notice setting forth such information as is reasonably necessary to keep such other party informed of the material terms of any such Acquisition Proposal and of any material amendments or modifications thereto, (B) keep such other party informed as promptly as practicable with respect to any changes to the material terms

of an Acquisition Proposal submitted to such party (and in any event within twenty four (24) hours following any such changes), including by providing a copy of all written proposals and a summary of all oral proposals or material oral modifications to an earlier written proposal, in each case relating to any Acquisition Proposal, (C) prior to, or substantially concurrently with, the provision of any non-public information of such party to any such person, provide such information the other party (including by posting such information to an electronic data room), to the extent such information has not previously been made available the other party, and (D) promptly (and in any event within twenty four (24) hours of such determination) notify the other party of any determination by such party's board of directors that such Acquisition Proposal constitutes a Superior Proposal.

(d) Certain Permitted Disclosure. Nothing contained in this Agreement shall prohibit Tyme or Syros or their respective Boards of Directors from complying with Rules 14d-9 and 14e-2(a) promulgated under the Exchange Act; provided, however, that any disclosure made by Tyme or Syros or their respective Boards of Directors pursuant to Rules 14d-9 and 14e-2(a) shall be limited to a statement that Tyme or Syros, as applicable, is unable to take a position with respect to the bidder's tender offer unless the applicable Board of Directors determines after consultation with its outside financial advisors and outside legal counsel, that such statement would be inconsistent with its fiduciary duties under applicable Law; provided, further, that any such disclosures (other than a "stop, look and listen" communication or similar communication of the type contemplated by Section 14d-9(f) under the Exchange Act) shall be deemed to be a Tyme Board Recommendation Change or Syros Board Recommendation Change, as applicable, unless the respective Board of Directors expressly publicly reaffirms its recommendation for the Merger and the other Contemplated Transactions within five (5) Business Days after being requested in writing to do so by the other party, it being understood that any such request in writing by the other party may only be made once by each party with respect to a particular disclosure.

(e) Cessation of Ongoing Discussions. Each of Syros and Tyme shall, and shall direct its Representatives to, cease immediately all discussions and negotiations that commenced prior to the date of this Agreement regarding any proposal that constitutes, or would reasonably be expected to lead to, an Acquisition Proposal; provided, however, that the foregoing shall not in any way limit or modify the rights of any party hereto under the other provisions of this Section 6.1. Syros and Tyme will each immediately revoke or withdraw access of any person (other than Syros, Tyme and their respective Representatives) to any data room (virtual or actual) containing any non-public information with respect to Syros and request from each third party (other than Syros, Tyme and their Representatives) the prompt return or destruction of all non-public information with respect to Syros or Tyme, as applicable, previously provided to such person.

(f) Definitions. For purposes of this Agreement, the following terms shall have the following meanings:

(i) "Acquisition Proposal" means, with respect to Syros or Tyme, (a) any inquiry, proposal or offer for a merger, consolidation, conversion, dissolution, sale of substantial assets, recapitalization, share exchange, tender offer or other business combination involving such party and its Subsidiaries (other than mergers, consolidations, conversions, recapitalizations, share exchanges or other business combinations involving solely such party and/or one or more Subsidiaries of such party), (b) any proposal for the issuance by such party of 15% or more of its equity securities or (c) any proposal or offer to acquire in any manner, directly or indirectly, 15% or more of the equity securities or consolidated total assets of such party and its Subsidiaries, in each case other than the Contemplated Transactions (including the Financing).

(ii) "Intervening Event" means a material Effect (other than any Effect resulting from a material breach of this Agreement or the Securities Purchase Agreement by the party seeking to claim an Intervening Event) that (a) was not known to or reasonably foreseeable by the Syros Board (with respect to Syros) or the Tyme Board (with respect to Tyme) (or, to the extent known or reasonably foreseeable, the consequences of which were not known or reasonably foreseeable) and (b) does not relate to an Acquisition Proposal; provided, however, the receipt, existence or terms of an Acquisition Proposal or Superior Proposal or any matter relating thereto shall not constitute an Intervening Event.

(iii) "Qualified Person" means any person making an unsolicited Acquisition Proposal that the Syros Board or the Tyme Board, as applicable, determines in good faith (after consultation with outside counsel and its financial advisors) is, or would reasonably be expected to lead to, a Superior Proposal, and such Acquisition Proposal has not resulted from a material breach by Syros or Tyme, as applicable, of its obligations under Section 6.1(a).

(iv) "Specified Time" means the earliest to occur of (a) the Effective Time, (b) either (I) in the case of Syros, the date on which the stockholders of Syros shall have approved the Required Syros Voting Proposal or (II) in the case of Tyme, the date on which the stockholders of Tyme shall have approved the Tyme Voting Proposal and (c) the time at which this Agreement is terminated in accordance with the terms hereof.

(v) "Superior Proposal" means, with respect to Syros or Tyme, any *bona fide*, unsolicited written proposal made by a third party to acquire 50% or more of the equity securities or consolidated total assets of such party and its Subsidiaries, pursuant to a tender or exchange offer, a merger, consolidation, conversion, business combination or recapitalization or a sale or exclusive license of its assets, on terms which the board of directors of such party determines in its good faith judgment to be more favorable to the holders of such party's capital stock than the Contemplated Transactions (after consultation with its financial and legal advisors), taking into account all the terms and conditions of such proposal and this Agreement (including any termination or break-up fees and conditions to consummation, as well as any written, binding offer by the other party hereto to amend the terms of this Agreement) that the board of directors of such party determines to be relevant and all financial, regulatory, legal and other aspects of such proposal that board of directors of such party determines to be relevant (including the likelihood and timing of consummation (as compared to the Contemplated Transactions)); provided, however, an upsized or modified Financing or any private placement or offering of securities for cash or similar cash-raising transaction by Syros shall not be considered a Superior Proposal.

6.2 Proxy Statement/Prospectus; Registration Statement.

(a) As promptly as practical after the execution of this Agreement, Syros and Tyme shall jointly prepare and cause to be filed with the SEC the Registration Statement, in which the Proxy Statement/Prospectus will be included as a prospectus. Each of Tyme, Merger Sub and Syros shall (i) provide to the other parties as promptly as practical all information, including financial statements and descriptions of its business and financial condition, as Syros as such other parties may reasonably request for preparation of the Registration Statement and the Proxy Statement/Prospectus and (ii) cause the timely cooperation of its independent public accountants in connection with the preparation and filing of the Registration Statement and the Proxy Statement/Prospectus, including by causing such accountants to provide a consent to the inclusion of such accountant's reports in respect of the financial statements of the applicable party in the Registration Statement and/or in the Proxy Statement/Prospectus (as applicable) and to the reference to such accountant firm as an "expert" therein. Each of Tyme, Merger Sub and Syros shall respond to any comments of the SEC and Syros shall use reasonable best efforts to have the Registration Statement declared effective under the Securities Act as promptly as practicable after such filing, and each of Tyme and Syros shall cause the Proxy Statement/Prospectus to be mailed to their respective stockholders at the earliest practicable time after the Registration Statement is declared effective under the Securities Act.

(b) Each of Tyme and Syros shall (i) inform the other promptly upon the receipt of any comments from the SEC or its staff and of any request by the SEC or its staff for amendments or supplements to the Registration Statement, the Proxy Statement/Prospectus or any filing pursuant to Section 6.2(a) or for additional information; and (ii) supply the other with copies of all correspondence between such party or any of its representatives, on the one hand, and the SEC, or its staff, on the other hand, with respect to the Registration Statement, the Proxy Statement/Prospectus, the Merger or any filing pursuant to Section 6.2(a); and (iii) use its reasonable best efforts to respond as promptly as practicable to any comments from the SEC with respect to the Registration Statement, the Proxy Statement/Prospectus or any filing pursuant to Section 6.2(a). Each of Tyme and Syros shall use commercially reasonable efforts to cause all documents that it is responsible for filing with

the SEC under this Section 6.2 to comply in all material respects with all applicable requirements of Law and the rules and regulations promulgated thereunder. Whenever either Syros or Tyme shall become aware of the occurrence of any event which is required to be set forth in an amendment or supplement to the Proxy Statement/Prospectus, the Registration Statement or any filing pursuant to Section 6.2(a), Syros or Tyme, as the case may be, shall promptly inform the other of such occurrence and cooperate in filing with the SEC or its staff, and/or mailing to stockholders of Syros and Tyme, such amendment or supplement.

(c) Notwithstanding anything to the contrary stated above, prior to filing and mailing, as applicable, the Registration Statement or Proxy Statement/Prospectus (or any amendment or supplement thereto) or responding to any comments of the SEC with respect thereto, each of Syros and Tyme shall provide the other a reasonable opportunity to review and comment on such document or response and shall consider in good faith any such comments proposed by the other party. Syros will advise Tyme, promptly after Tyme receives notice thereof, of the time when the Registration Statement has become effective or any supplement or amendment has been filed, of the issuance of any stop order or the suspension of the qualification of Syros Common Stock for offering or sale in any jurisdiction, of the initiation or threat of any proceeding for any such purpose, or of any request by the SEC for the amendment or supplement of the Registration Statement or for additional information.

(d) Syros and Tyme shall promptly make all necessary filings with respect to the Merger and the Share Issuance under the Securities Act, the Exchange Act, applicable state blue sky laws and the rules and regulations thereunder.

6.3 Nasdaq Listing. Each of Syros and Tyme shall use its commercially reasonable efforts to continue the listing of Syros Common Stock and Tyme Common Stock, respectively, on Nasdaq during the term of this Agreement. Syros shall use its commercially reasonable efforts to cause the shares of Syros Common Stock being issued in connection with the Merger to be approved for listing (subject to notice of issuance) on Nasdaq at or prior to the Effective Time, including by filing an initial listing application for the Syros Common Stock on Nasdaq with respect to the shares of Syros Common Stock to be issued pursuant to this Agreement (the "Nasdaq Listing Application"). Tyme shall cooperate with Syros to cause the Nasdaq Listing Application to be approved and shall promptly furnish to Syros all information concerning Tyme and its equityholders that may be required or reasonably requested in connection with any action contemplated by this Section 6.3.

6.4 Access to Information. Subject to compliance with applicable confidentiality obligations owed to third parties in effect as of the date of this Agreement, each of Syros and Tyme shall (and shall cause each of its Subsidiaries to) afford to the other party's officers, employees, accountants, counsel and other representatives, reasonable access, during normal business hours during the period prior to the Effective Time, to all its properties, books, contracts, commitments, personnel and records and, during such period, each of Syros and Tyme shall (and shall cause each of its Subsidiaries to) furnish promptly to the other party all information concerning its business, properties, assets and personnel as the other party may reasonably request. Each of Syros and Tyme will hold any such information which is nonpublic in confidence in accordance with the Confidentiality Agreement. No information or knowledge obtained in any investigation pursuant to this Section 6.4 or otherwise shall affect or be deemed to modify any representation or warranty contained in this Agreement or the conditions to the obligations of the parties to consummate the Merger. Without limiting the generality of the foregoing, from the date of this Agreement until the Effective Time, each of Syros and Tyme shall promptly provide the other party with copies of: (a) unaudited monthly financial statements or management accounts, when available; (b) any written materials or communications sent by or on behalf of such party to its stockholders; (c) any notice, report or other document filed with or sent to, or received from, any Governmental Authority in connection with the Merger or any of the other Contemplated Transactions; and (d) any material notice, report or other document received from any Governmental Authority.

6.5 Stockholder Approval.

(a) Tyme, acting through the Tyme Company Board, shall take all actions in accordance with applicable law, its certificate of incorporation and bylaws and Nasdaq rules to duly call, give notice of, convene

and hold as promptly as practicable, after the declaration of effectiveness of the Registration Statement, the Tyme Stockholders Meeting for the purpose of considering and voting upon the Tyme Voting Proposal. Subject to Section 6.1(b), the Tyme Board shall include in the Proxy Statement/Prospectus the recommendation of the Tyme Board in favor of approval of the Tyme Voting Proposal. Subject to Section 6.1(b), Tyme shall take all action that is both reasonable and lawful to solicit from its stockholders proxies in favor of the Tyme Voting Proposal. The Tyme Meeting shall be held as promptly as practicable after the effective date of the Registration Statement (on a date selected by Tyme in consultation with Syros) but in no event later than forty-five (45) days after the effective date of the Registration Statement and, to the extent practicable, shall be held on the same day or as close as practicable to the Syros Meeting. If sufficient votes for the approval of the Tyme Voting Proposal have not been obtained as of the close of business on the Business Day prior to the scheduled date of the Tyme Meeting or if necessary to ensure that any supplement or amendment to the joint proxy statement/prospectus is timely provided to holders of Tyme Stock, Tyme shall have the right to adjourn the Tyme Meeting to a later date or dates, such later date or dates not to exceed thirty (30) days in the aggregate from the original date that the Tyme Meeting was scheduled. Unless this Agreement is validly terminated pursuant to Section 8.1, Tyme's obligation to call, give notice of and hold the Tyme Meeting in accordance withSection 6.5(b) shall not be limited or otherwise affected by the commencement, disclosure, announcement or submission of any Acquisition Proposal, or by any Tyme Board Recommendation Change. Except in the case of a Tyme Board Recommendation Change made in compliance with Section 6.1, Tyme agrees that the Tyme Board shall recommend that the Tyme Stockholders approve the Tyme Voting Proposal and Tyme shall include such recommendation in the Proxy Statement/Prospectus. Except in the case of a Tyme Board Recommendation Change made in compliance with Section 6.1, Tyme shall use its reasonable best efforts to solicit from the Tyme Stockholders proxies in favor of the Tyme Voting Proposal and shall take all other action necessary or advisable to secure the approvals of the stockholders of Tyme. Tyme shall ensure that all proxies solicited in connection with the Tyme Meeting are solicited in material compliance with all applicable laws. Without limiting the generality of the foregoing, Tyme agrees that unless this Agreement is terminated in accordance with Section 8.1, Tyme shall not (i) cause or permit Tyme or any of its Subsidiaries to execute or enter into any definitive agreement with respect to an Acquisition Proposal or (ii) submit the approval or adoption of any Acquisition Proposal or any definitive agreement with respect to such Acquisition Proposal to a vote of its stockholders.

(b) Syros, acting through the Syros Board, shall take all actions in accordance with applicable law, its certificate of incorporation and bylaws and Nasdaq rules to duly call, give notice of, convene and hold as promptly as practicable, after the declaration of effectiveness of the Registration Statement, the Syros Stockholders Meeting for the purpose of considering and voting upon the Required Syros Voting Proposal and the Other Syros Voting Proposals. Subject to Section 6.1(b), the Syros Board shall include in the Proxy Statement/Prospectus the recommendation of the Syros Board in favor of approval of the Required Syros Voting Proposal and the Other Syros Voting Proposals. Subject to Section 6.1(b), Syros shall take all action that is both reasonable and lawful to solicit from its stockholders proxies in favor of the Required Syros Voting Proposal and the Other Syros Voting Proposals. The Syros Meeting shall be held as promptly as practicable after the effective date of the Registration Statement (on a date selected by Syros in consultation with Tyme) but in no event later than forty-five (45) days after the effective date of the Registration Statement and, to the extent practicable, shall be held on the same day or as close as practicable to the Tyme Meeting. If sufficient votes for the approval of the Required Syros Voting Proposal and the Other Syros Voting Proposals have not been obtained as of the close of business on the Business Day prior to the scheduled date of the Syros Meeting or if necessary to ensure that any supplement or amendment to the joint proxy statement/prospectus is timely provided to holders of Tyme Stock, Syros shall have the right to adjourn the Syros Meeting to a later date or dates, such later date or dates not to exceed thirty (30) days in the aggregate from the original date that the Syros Meeting was scheduled. Unless this Agreement is validly terminated pursuant to Section 8.1, Syros' obligation to call, give notice of and hold the Syros Meeting in accordance with Section 6.5(b) shall not be limited or otherwise affected by the commencement, disclosure, announcement or submission of any Acquisition Proposal, or by any Syros Board Recommendation Change. Except in the case of a Syros Board Recommendation Change made in compliance with Section 6.1, Syros agrees that the Syros Board shall recommend that the Syros Stockholders approve the Required Syros Voting Proposal and the Other Syros Voting Proposals and Syros shall include such

recommendation in the Proxy Statement/Prospectus. Except in the case of a Syros Board Recommendation Change made in compliance with Section 6.1, Syros shall use its reasonable best efforts to solicit from the Syros Stockholders proxies in favor of the Required Syros Voting Proposal and the Other Syros Voting Proposals and shall take all other action necessary or advisable to secure the approvals of the stockholders of Syros. Syros shall ensure that all proxies solicited in connection with the Syros Meeting are solicited in material compliance with all applicable laws. Syros, in its capacity as the sole stockholder of Merger Sub, shall approve the Merger. Without limiting the generality of the foregoing, Syros agrees that unless this Agreement is terminated in accordance with Section 8.1, Syros shall not (i) cause or permit Syros or any of its Subsidiaries to execute or enter into any definitive agreement with respect to an Acquisition Proposal or (ii) submit the approval or adoption of any Acquisition Proposal or any definitive agreement with respect to such Acquisition Proposal to a vote of its stockholders.

(c) Notwithstanding the foregoing, nothing herein shall limit a party's right to terminate this Agreement pursuant to Section 8.1.

6.6 Legal Conditions to Merger.

(a) Subject to the terms hereof, including Section 6.6(b), Tyme and Syros shall each use commercially reasonable efforts to (i) take, or cause to be taken, all actions, and do, or cause to be done, and to assist and cooperate with the other parties in doing, all things necessary, proper or advisable to consummate and make effective the Contemplated Transactions as promptly as practicable, (ii) as promptly as practicable, obtain from any Governmental Authority or any other third party any consents, licenses, permits, waivers, approvals, authorizations, or orders required to be obtained or made by Tyme or Syros or any of their Subsidiaries in connection with the authorization, execution and delivery of this Agreement and the consummation of the Contemplated Transactions, (iii) as promptly as practicable, make all necessary filings, and thereafter make any other required submissions, with respect to this Agreement and the Merger required under (A) the Securities Act and the Exchange Act, and any other applicable federal or state securities laws, and (B) any other applicable law and (iv) execute or deliver any additional instruments necessary to consummate the transactions contemplated by, and to fully carry out the purposes of, this Agreement. Tyme and Syros shall reasonably cooperate with each other in connection with the making of all such filings. Tyme and Syros shall use their respective commercially reasonable efforts to furnish to each other all information required for any application or other filing to be made pursuant to the rules and regulations of any applicable Law (including all information required to be included in the Proxy Statement/Prospectus and the Registration Statement) in connection with the Contemplated Transactions. For the avoidance of doubt, Syros and Tyme agree that nothing contained in this Section 6.6(a) shall modify or affect their respective rights and responsibilities under Section 6.6(b).

(b) Each of Tyme and Syros shall give (or shall cause their respective Subsidiaries to give) any notices to third parties, and use, and cause their respective Subsidiaries to use, their commercially reasonable efforts to obtain any third party consents related to or required in connection with the Merger that are (i) necessary to consummate the Contemplated Transactions, (ii) disclosed or required to be disclosed in the Tyme Disclosure Schedule or the Syros Disclosure Schedule, as the case may be, or (iii) required to prevent the occurrence of an event that may have a Tyme Material Adverse Effect or a Syros Material Adverse Effect from occurring prior to or after the Effective Time.

6.7 Public Disclosure.

(a) The initial press release with respect to the execution of this Agreement will be a joint press release in form and substance acceptable to Syros and Tyme, respectively. Thereafter, so long as this Agreement is in effect, neither Syros nor Tyme, nor any of their respective Affiliates, will issue or cause the publication of any press release or other public announcement with respect to the Merger or this Agreement without the prior consent of the other such party (such consent not to be unreasonably withheld, conditioned or delayed), unless such party determines, after consultation with outside counsel, that it is required by applicable Law or by any

listing agreement with or the listing rules of a national securities exchange to issue or cause the publication of any press release or other public announcement with respect to the Merger or this Agreement, in which event such party will endeavor, on a basis reasonable under the circumstances, to provide a meaningful opportunity to the other party to review and comment upon such press release or other announcement in advance and will give due consideration to all reasonable additions, deletions or changes suggested thereto.

(b) Notwithstanding the foregoing provisions of this Section 6.7, (1) each of Syros and Tyme may make press releases or public announcements concerning this Agreement, the Merger and the other Contemplated Transactions that consists solely of information previously disclosed in all material respects in previous press releases or announcements made by Syros and/or Tyme in compliance with this Section 6.7 and (2) each of Syros and Tyme may make public statements in response to specific questions by the press, analysts, investors or those attending industry conferences or financial analyst conference calls, and may make internal announcements to employees, so long as any such statements consist solely of information previously disclosed in all material respects in previous press releases, public disclosures or public statements made by Syros and/or Tyme in compliance with this Section 6.7 and do not reveal material, nonpublic information regarding the other parties, this Agreement, the Merger or the other Contemplated Transactions.

(c) Section 6.7 shall not apply to or limit communications with respect to any Acquisition Proposal, Superior Proposal, Recommendation Change Notice, Syros Board Recommendation Change or Tyme Board Recommendation Change.

6.8 Indemnification.

(a) From the Effective Time through the sixth anniversary of the date on which the Effective Time occurs, each of Syros and the Surviving Corporation shall, jointly and severally, indemnify and hold harmless each person who is now, or has been at any time prior to the date hereof, or who becomes prior to the Effective Time, a director or officer of Tyme, Syros or any of their respective Subsidiaries (the "Indemnified Persons"), against all claims, losses, liabilities, damages, judgments, fines and reasonable fees, costs and expenses, including attorneys' fees and disbursements, incurred in connection with any claim, action, suit, proceeding or investigation, whether civil, criminal, administrative or investigative, arising out of or pertaining to the fact that the Indemnified Person is or was an officer, director, employee or agent of Tyme, Syros or any of their respective Subsidiaries, or, while a director or officer of Tyme, Syros or any of their respective Subsidiaries, is or was serving at the request of Tyme, Syros or any of their respective Subsidiaries as a director, officer, employee or agent of another person, whether asserted or claimed prior to, at or after the Effective Time, to the fullest extent permitted by applicable law. Each Indemnified Person will be entitled to advancement of expenses (including attorneys' fees) incurred in the defense of any such claim, action, suit, proceeding or investigation from each of Syros and the Surviving Corporation following receipt by Syros or the Surviving Corporation from the Indemnified Party of a request therefor; provided that any person to whom expenses are advanced provides an undertaking, to the extent then required by the DGCL, to repay such advances if it is ultimately determined that such person is not entitled to indemnification. From the Effective Time through the sixth anniversary of the date on which the Effective Time occurs, the certificate of incorporation and bylaws of the Surviving Corporation will contain provisions at least as favorable as the provisions relating to the indemnification, advance of expenses and elimination of liability for monetary damages set forth in the certificate of incorporation and bylaws of Tyme and Syros immediately prior to the Effective Time.

(b) Syros shall either (i) maintain in force for at least six years after the Closing a policy or (ii) purchase a six-year prepaid "D&O tail policy" for the non-cancellable extension of the directors' and officers' liability coverage of Syros' existing directors' and officers' insurance policies, in each case, providing directors' and officers' liability coverage of Syros' existing directors' and officers' insurance policies for a claims reporting or discovery period of at least six years from and after the Effective Time with respect to any claim related to any period of time at or prior to the Effective Time with terms, conditions, retentions and limits of liability that are no less favorable than the coverage provided under Syros' existing policies as of the date of

this Agreement with respect to any actual or alleged error, misstatement, misleading statement, act, omission, neglect, breach of duty or any matter claimed against a director or officer of Syros by reason of him or her serving in such capacity that existed or occurred at or prior to the Effective Time (including in connection with this Agreement or the Merger).

(c) Syros shall either (i) maintain in force for at least six years after the Closing a policy or (ii) purchase a six-year prepaid "D&O tail policy" for the non-cancellable extension of Tyme's existing policy, in each case, providing directors' and officers' liability coverage of Tyme's existing directors' and officers' insurance policies for a claims reporting or discovery period of at least six years from and after the Effective Time with respect to any claim related to any period of time at or prior to the Effective Time with terms, conditions, retentions and limits of liability that are no less favorable than the coverage provided under Tyme's existing policies as of the date of this Agreement with respect to any actual or alleged error, misstatement, misleading statement, act, omission, neglect, breach of duty or any matter claimed against a director or officer of Tyme by reason of him or her serving in such capacity that existed or occurred at or prior to the Effective Time (including in connection with this Agreement or the Merger). All premiums with respect to any such insurance shall be paid or reimbursed by Syros and shall not reduce Tyme Net Cash.

(d) Syros shall pay all expenses, including reasonable attorneys' fees, that may be incurred by a person in successfully enforcing such person's rights provided in this Section 6.8.

(e) Syros and Tyme agree that all rights to exculpation, indemnification and advancement of expenses for acts or omissions occurring at or prior to the Effective Time, whether asserted or claimed prior to, at or after the Effective Time, now existing in favor of the current or former directors, officers or employees, as the case may be, of Syros, Tyme or any of their respective Subsidiaries as provided in their respective certificates of incorporation or bylaws or other organization documents or in any agreement in existence immediately prior to the Effective Time shall survive the Merger and shall continue in full force and effect. The provisions of this Section 6.8 are intended to be in addition to the rights otherwise available to the current officers and directors of Syros, Tyme or any of their respective Subsidiaries by law, charter, statute, bylaw or agreement, and shall operate for the benefit of, and shall be enforceable by, each of the Indemnified Persons, their heirs and their representatives. The obligations set forth in this Section 6.8 shall not be terminated, amended or otherwise modified in any manner that adversely affects any Indemnified Person, or any person who is a beneficiary under the policies referred to in this Section 6.8 and their heirs and representatives, without the prior written consent of such affected Indemnified Person or other person.

(f) If the Surviving Corporation or Syros or any of their respective successors or assigns shall (i) consolidate with or merge into any other person and shall not be the continuing or surviving corporation or entity of such consolidation or merger, or (ii) transfer all or substantially all of its properties and assets to any person, then, and in each such case, proper provisions shall be made so that the successors and assigns of such person shall assume all of the obligations of such person set forth in this Section 6.8.

(g) Nothing in this Agreement is intended to, shall be construed to or shall release, waive or impair any rights to directors' and officers' insurance claims under any policy that is or has been in existence with respect to Tyme, Syros or any of their respective Subsidiaries for any of their respective directors, officers or other employees, it being understood and agreed that the indemnification provided for in this Section 6.8 is not prior to or in substitution for any such claims under such policies.

6.9 Notification of Certain Matters. Syros shall give prompt notice to Tyme, and Tyme shall give prompt notice to Syros, upon becoming aware of the occurrence, or failure to occur, of any event, which occurrence or failure to occur would be reasonably likely to cause (a) (i) any representation or warranty of such party contained in this Agreement that is qualified as to materiality to be untrue or inaccurate in any respect or (ii) any other representation or warranty of such party contained in this Agreement to be untrue or inaccurate in any material respect, in each case, at any time from and after the date of this Agreement until the Effective Time, or (b) any

material failure of Syros and Merger Sub or Tyme, as the case may be, or of any officer, director, employee or agent thereof, to comply with or satisfy any covenant, condition or agreement to be complied with or satisfied by it under this Agreement.

6.10 Employee Matters.

(a) Communications. Syros and Tyme will use reasonable best efforts to consult with each other, and will consider in good faith each other's advice, prior to sending any notices or other communication materials to its employees or other individual service providers regarding this Agreement, the Merger or the effects thereof on the employment or service, compensation or benefits of its employees or other individual service providers.

(b) Severance. Prior to Closing, Tyme may enter into agreements with Tyme Associates providing for discretionary severance pay or severance benefits or short-term retention (beyond that required under existing Contracts) in an aggregate amount not to exceed $600,000 (which obligations shall be taken into account as a reduction to Tyme Net Cash). Any severance pay or severance benefits payable to Tyme Associates pursuant to any employment agreement, change in control agreement, or other separation agreement or plan in effect immediately prior to the Effective Time as a result of any separation from service occurring within 12 months of the Closing Date shall, to the maximum extent permitted by Code Section 409A, be paid in lump sum as soon as practicable following the date of such separation from service, provided that the Tyme Associate consents to the lump sum severance payment (to the extent required) and otherwise satisfies the eligibility requirements for severance pay or severance benefits under the terms of the applicable agreement, instrument or plan.

(c) Extension of Exercise Period for Certain Tyme Options. In consideration for each person set forth on Section 6.10(c) of the Tyme Disclosure Schedule entering into a cooperation agreement in form and substance satisfactory to Tyme and Syros (which cooperation agreement will include a commitment to provide cooperation and assistance in connection with the Contemplated Transactions until the date that is 90 days after Closing and include customary confidentiality and non-disparagement provisions), Tyme and Syros shall take such action as may be necessary to provide that the post-separation exercise period of any Tyme Options having an exercise price of less than $2.00 per share of Company Common Stock held by such person be extended, to the maximum extent permitted by Code Section 409A, to two years following such person's separation from service, or, if earlier, the original expiration date of such Tyme Option. Furthermore, Syros shall reasonably cooperate with Tyme to provide that any such person who is providing service to Tyme as of immediately prior to the Closing is a Continuing Service Provider.

6.11 FIRPTA Tax Certificates. On or prior to the Closing, Tyme shall deliver to Syros a properly executed certification that shares of Tyme Capital Stock are not "U.S. real property interests" in accordance with the Treasury Regulations under Sections 897 and 1445 of the Code, together with a notice to the IRS (which shall be filed by Syros with the IRS following the Closing) in accordance with the provisions of Section 1.897-2(h)(2) of the Treasury Regulations. If Syros does not receive the certification and notice described above on or before the Closing Date, Syros shall be permitted to withhold from the payments to be made pursuant to this Agreement any required withholding tax under Section 1445 of the Code.

6.12 State Takeover Laws. If any "fair price," "business combination" or "control share acquisition" statute or other similar statute or regulation is or may become applicable to any of the Contemplated Transactions, the parties hereto shall use their respective commercially reasonable efforts to (a) take such actions as are reasonably necessary so that the transactions contemplated hereunder may be consummated as promptly as practicable on the terms contemplated hereby and (b) otherwise take all such actions as are reasonably necessary to eliminate or minimize the effects of any such statute or regulation on such transactions.

6.13 Security Holder Litigation. Notwithstanding anything to the contrary herein, (a) Syros shall have the right to control the defense and settlement of any litigation related to this Agreement, the Merger or the other Contemplated Transactions brought by any stockholder or any holder of other securities of Syros against Syros

and/or its directors or officers, provided that Syros shall give Tyme the opportunity to participate in the defense of any such litigation and shall not settle any such litigation (other than any settlement not requiring the payment of any amount to any third party in excess of the retentions or deductibles under any applicable insurance policies of Syros) without the prior written consent of Tyme (which consent shall not be unreasonably withheld, conditioned or delayed), and (b) Tyme shall have the right to control the defense and settlement of any litigation related to this Agreement, the Merger or the other Contemplated Transactions brought by any stockholder or any holder of other securities of Tyme against Tyme and/or its directors or officers, provided that Tyme shall give Syros the opportunity to participate in the defense of any such litigation and shall not settle any such litigation (other than any settlement not requiring the payment of any amount to any third party in excess of the retentions or deductibles under any applicable insurance policies of Tyme) without the prior written consent of Syros (which consent shall not be unreasonably withheld, conditioned or delayed).

6.14 Section 16 Matters. Prior to the Effective Time, Syros shall take all such steps as may be required to cause any acquisitions of Syros Common Stock (and any options to purchase the same) in connection with this Agreement and the Contemplated Transactions, by each individual who is reasonably expected to become subject to the reporting requirements of Section 16(a) of the Exchange Act with respect to Syros following the Merger, to be exempt under Rule 16b-3 promulgated under the Exchange Act.

6.15 Calculation of Tyme Net Cash.

(a) Not less than five (but no more than seven) calendar days prior to the anticipated date for the Tyme Meeting (the "Anticipated Closing Date"), Tyme will deliver to Syros a schedule (the "Tyme Net Cash Schedule") setting forth, in reasonable detail, Tyme's good faith, estimated calculation of its Net Cash ("Tyme Net Cash") prepared and certified by Tyme's Chief Financial Officer or Chief Accounting Officer (or if there is no Chief Financial Officer or Chief Accounting Officer, the Chief Executive Officer of Tyme). Tyme shall make available to Syros, as requested by Syros, the work papers and back-up materials used or useful in preparing the Tyme Net Cash Schedule and, if requested by Syros, Tyme's accountants and counsel at reasonable times and upon reasonable notice.

(b) On the fourth calendar day following the delivery of the Tyme Net Cash Schedule pursuant to Section 6.15(a), the Tyme Net Cash Schedule shall become final and binding on all parties to this agreement unless on or prior to the third calendar day following such delivery Syros disputes such Net Cash Schedule by delivering, in good faith, a written notice to Tyme describing in reasonable detail each item in dispute and Syros' proposed revisions to such Net Cash Schedule (a "Dispute Notice").

(c) If representatives of Syros and Tyme are unable to negotiate an agreed-upon determination of any items timely disputed in a Dispute Notice within three days after delivery of such Dispute Notice, then any such disputed items shall be referred to an independent auditor of recognized national standing jointly selected by Syros and Tyme (the "Accounting Firm"), each acting reasonably and as quickly as possible. Syros shall promptly deliver to the Accounting Firm the work papers and back-up materials used in preparing the relevant Net Cash Schedule(s), and Syros and Tyme shall use reasonable best efforts to cause the Accounting Firm to make its determination as soon as possible and within seven (7) calendar days of accepting its selection. Tyme and Syros shall be afforded the opportunity to present to the Accounting Firm any material related to the unresolved disputes and to discuss the issues with the Accounting Firm; provided, however, that no such presentation or discussion shall occur without the presence of a representative of each of Tyme and Syros. The determination of the Accounting Firm shall be limited to the items in dispute submitted to the Accounting Firm and limited to applying the definition of Net Cash as set forth herein. Any determination of the amount of Tyme Net Cash made by the Accounting Firm shall be made in writing delivered to each of Syros and Tyme, shall be final and binding on the parties hereto and shall be deemed to have been finally determined for purposes of this Agreement and to represent the Tyme Net Cash, as applicable, for all purposes of this Agreement. The parties shall delay the Closing until the resolution of the matters described in this Section 6.15(c). The fees and expenses of the Accounting Firm shall be allocated between Syros and Tyme in the same proportion that the disputed

amount of Tyme Net Cash that was unsuccessfully disputed by such party (as finally determined by the Accounting Firm) bears to the total disputed amount of Tyme Net Cash. If this Section 6.15(c) applies as to the determination of Tyme Net Cash, upon resolution of the matter in accordance with this Section 6.15(c), the parties shall not be required to determine Tyme Net Cash again even though the Closing Date may occur later than the Anticipated Closing Date, except that either Tyme or Syros may request a redetermination of Tyme Net Cash if the Closing Date is more than thirty calendar days after the Anticipated Closing Date (provided, that, Syros may not request such a redetermination if such delay is due to (x) Syros' material breach of this Agreement or (y) if such delay is due to the application of this Section 6.15(c) and more than 75% of the items in the Dispute Notice were resolved in Tyme's favor).

(d) For purposes of this Agreement:

(i) "Cash Determination Time" means the close of business as of the Business Day immediately prior to the anticipated Closing Date (the "Anticipated Closing Date").

(ii) "Indebtedness" means, with respect to any person, any liabilities of such person or its Subsidiaries (A) for borrowed money, (B) evidenced by bonds, debentures, notes or similar instruments, (C) upon which interest charges are customarily paid (other than obligations accepted in connection with the purchase of products or services in the ordinary course of business), (D) in respect of liabilities of others that are secured by (or which the holder of such liabilities has an existing right, contingent or otherwise, to be secured by) any Lien or security interest on property owned or acquired by the person in question whether or not the obligations secured thereby have been assumed, (E) under leases required to be accounted for as capital leases under GAAP (but excluding, for the avoidance of doubt, obligations under the Tyme Real Estate Leases), (F) for any "applicable employment taxes" (as defined in Section 2302(d)(1) of the CARES Act) elected to be deferred pursuant to Section 2302 of the CARES Act, or (G) guarantees relating to any such liabilities.

(iii) "Net Cash" means, as of the Cash Determination Time and without duplication, (a) Tyme's unrestricted free cash, cash equivalents and marketable securities, minus (b) the sum (without duplication) of: (i) all accounts payable, accrued expenses (including accrued tax liabilities) and Tyme's other short- and long-term liabilities payable in cash (except to the extent such liabilities are with respect to employees that Syros intends to retain and realize the benefit of after Closing (disregarding any cooperation provided pursuant to Section 6.10(b))); (ii) any Transaction Expenses of Tyme or for which Tyme is liable; and (iii) any indebtedness of Tyme; minus (c) any projected liabilities payable in cash associated with the shut-down of any on-going clinical trials of Tyme that will not be continued after the Closing; plus (d) all prepaid Tyme expenses of a type identified on Annex B that may be refunded in cash or used toward satisfying liabilities of Syros or the Surviving Corporation payable in cash; plus (e) the aggregate amount of any costs or expenses, including attorneys' fees or settlement costs (collectively, "Litigation Losses"), incurred and paid by Tyme prior to the Closing in successfully defending or enforcing its rights with respect to any potential or actual transaction litigation. Each component of Net Cash shall be determined in accordance with GAAP applied on a basis consistent with the application of GAAP in the preparation of Tyme's most recent audited financial statements. A sample calculation of Tyme Net Cash and its components is set forth in Annex B for illustrative purposes only.

(iv) "Transaction Expenses" means, as of the Cash Determination Time and without duplication, the sum of (a) the cash cost (including a reasonable estimate of payment or reimbursement for continued coverage under any employee benefit plan) of any change of control, bonus, severance (voluntary or otherwise), retention or similar payments (whether "single trigger" or "double trigger") that are or become due in connection with the consummation of the Contemplated Transactions and that are unpaid as of the Closing (taking into account any employment separations actually intended to be effected upon Closing, but excluding liabilities with respect to employees that Syros intends to retain and realize the benefit of after Closing (disregarding any cooperation provided pursuant to Section 6.10(b)), (b) the cash equivalent value of any retention payments that are or become due to any employee of such Person and its Subsidiaries in connection with the consummation of the Contemplated Transactions and that are unpaid as of the Closing; (c) any costs, fees and expenses incurred by

such Person and its Subsidiaries, or for which such Person and its Subsidiaries is liable, in connection with the negotiation, preparation and execution of this Agreement or any agreements, documents, certificates, opinions or other items contemplated hereby and the consummation of the Contemplated Transactions (including the solicitation of proxies) and that are unpaid as of the Closing, including filing fees, brokerage fees and commissions, finders' fees or financial advisory fees, or any fees and expenses of proxy solicitors, counsel or accountants payable by such Person and its Subsidiaries; and (d) the cash cost to purchase any warrant that is outstanding as of immediately prior to the Effective Time that, pursuant to its terms, is required to be repurchased upon the consummation of the Contemplated Transactions.

6.16 Corporate Governance. Prior to the Effective Time, Syros shall take all actions necessary to cause one (1) director on the Syros Board as of the Effective Time shall be a designee of Tyme (subject to approval of the Nominating and Governance Committee of Syros in accordance with the Corporate Guidelines of Syros as in effect on the date hereof, such approval not to be unreasonably withheld, conditioned or delayed). Tyme shall identify a nominee that is eligible under the Corporate Guidelines of Syros as in effect on the date hereof and notify Syros of its proposed nominee at least thirty days prior to the Anticipated Closing Date

6.17 Intended Tax Treatment. The parties agree that the transactions described hereunder are intended to qualify for the Intended Tax Treatment. Notwithstanding the foregoing, except for Syros' representation in Section 4.16(i), Syros makes no representations or warranties to Tyme, any stockholders of Tyme, or any other person regarding the Tax treatment of the Merger or the other transactions contemplated by this Agreement. Tyme acknowledges that it is the responsibility of Tyme and its stockholders to seek Tax advice from their own Tax advisors regarding the Tax treatment to Tyme and its stockholders of the Merger and the other transactions contemplated by this Agreement.

6.18 SM-88 Program. To the extent Tyme's SM-88 assets are not sold or out-licensed prior to Closing, Syros shall explore and consider in good faith the viability of continuing to develop SM-88 in parallel with Syros' other drug candidates or the sale or out-license of SM-88, in each case with a view toward maximizing shareholder value.

6.19 Financing.

(a) Syros shall use its reasonable best efforts to finalize and consummate the Financing, including (i) negotiating any further instruments or agreements necessary to effect to the Financing (the "Financing Agreements"); (ii) satisfying on a timely basis all conditions in the Securities Purchase Agreement that are to be satisfied by Syros; and (iii) enforcing its rights under the Securities Purchase Agreement and any other documents related to the Financing. Syros shall keep Tyme informed on a reasonably current basis in reasonable detail of the status of its efforts to complete the Financing.

(b) Syros shall not terminate any commitment in the Securities Purchase Agreement or amend or waive any material provisions thereof without the prior written consent of Tyme. Syros shall give Tyme notice immediately following any breach or threatened breach of or any termination or threatened termination by any party of the Securities Purchase Agreement or other documents related to the Financing.

(c) For the sake of clarity, the obligations of Syros under this Agreement are not contingent upon the availability of the Financing or any other financing.

ARTICLE VII

CONDITIONS TO MERGER

7.1 Conditions to Each Party's Obligation to Effect the Merger. The respective obligations of each party to this Agreement to effect the Merger shall be subject to the satisfaction prior to the Closing Date of the following conditions:

(a) Stockholder Approvals. The Required Tyme Voting Proposal shall have been approved at the Tyme Meeting by the requisite vote of the stockholders of Tyme under applicable Law and Tyme's certificate of incorporation. The Required Syros Voting Proposal shall have been approved at the Syros Meeting, at which a quorum is present, by the requisite vote of the stockholders of Syros under applicable Law and stock market regulations.

(b) Governmental Approvals. Other than the filing of the Certificate of Merger, all authorizations, consents, orders or approvals of, or declarations or filings with, or expirations of waiting periods imposed by, any Governmental Authority in connection with the Merger and the consummation of the other Contemplated Transactions, the failure of which to file, obtain or occur is reasonably likely to have a Syros Material Adverse Effect or a Tyme Material Adverse Effect, shall have been filed, been obtained or occurred on terms and conditions that would not reasonably be likely to have a Syros Material Adverse Effect or a Tyme Material Adverse Effect.

(c) Registration Statement; Proxy Statement/Prospectus. The Registration Statement shall have become effective under the Securities Act and no stop order suspending the effectiveness of the Registration Statement shall have been issued and no proceeding for that purpose, and no similar proceeding with respect to the Proxy Statement/Prospectus, shall have been initiated or threatened in writing by the SEC or its staff.

(d) No Injunctions. No Governmental Authority of competent jurisdiction shall have enacted, issued, promulgated, enforced or entered any order, executive order, stay, decree, judgment or injunction (preliminary or permanent) or statute, rule or regulation which is in effect and which has the effect of making the Merger illegal or otherwise prohibiting consummation of the Merger.

(e) Nasdaq Notification. (i) The Nasdaq Listing Application shall have been approved, and (ii) the shares of the Syros Common Stock to be issued pursuant to the Share Issuance shall have been approved for listing (subject to official notice of issuance) on Nasdaq.

(f) Net Cash. The Tyme Net Cash shall have been finally determined in accordance withSection 6.15, and such Tyme Net Cash as finally determined shall exceed $50 million as of the Closing Date (excluding, solely for the purpose of this condition, the amount by which such Tyme Net Cash was increased for any Litigation Losses).

7.2 Additional Conditions to the Obligations of Syros and Merger Sub. The obligations of Syros and Merger Sub to effect the Merger shall be subject to the satisfaction on or prior to the Closing Date of each of the following additional conditions, any of which may be waived in writing exclusively by Syros and Merger Sub:

(a) Representations and Warranties. The representations and warranties of Tyme set forth in this Agreement and in any certificate or other writing delivered by Tyme pursuant hereto shall be true and correct (i) as of the date of this Agreement (except in the case of this clause (i), (A) to the extent such representations and warranties are specifically made as of a particular date, in which case such representations and warranties shall be true and correct as of such date and (B) where the failure to be true and correct (without regard to any materiality or Tyme Material Adverse Effect qualifications contained therein), individually or in the aggregate, has not had, and is not reasonably likely to have, a Tyme Material Adverse Effect) and (ii) as of the Closing Date

as though made on and as of the Closing Date (except in the case of this clause (ii), (A) to the extent such representations and warranties are specifically made as of a particular date, in which case such representations and warranties shall be true and correct as of such date, (B) for changes expressly provided for in this Agreement and (C) where the failure to be true and correct (without regard to any materiality or Tyme Material Adverse Effect qualifications contained therein), individually or in the aggregate, has not had, and is not reasonably likely to have, a Tyme Material Adverse Effect); provided, however, that the representations and warranties made by Tyme in Sections 3.1, 3.2, 3.3, 3.4, 3.5, 3.6 and 3.8(a) shall not be subject to the qualifications set forth in clauses (i)(B) and (ii)(C) above; provided, further, that the representations and warranties set forth inSection 3.6(a) and 3.6(c) shall be true and correct except for such inaccuracies as are in the aggregate de minimis.

(b) Performance of Obligations of Tyme. Tyme shall have performed in all material respects all obligations required to be performed by it under this Agreement on or prior to the Closing Date.

(c) No Tyme Material Adverse Effect. No Tyme Material Adverse Effect shall have occurred since the date of this Agreement and be continuing.

(d) Officers' Certificate. Syros shall have received an officers' certificate duly executed by each of the Chief Executive Officer and Chief Financial Officer of Tyme to the effect that the conditions of Sections 7.2(a), (b) and (c) have been satisfied.

7.3 Additional Conditions to the Obligations of Tyme. The obligation of Tyme to effect the Merger shall be subject to the satisfaction on or prior to the Closing Date of each of the following additional conditions, any of which may be waived, in writing, exclusively by Tyme:

(a) Representations and Warranties. The representations and warranties of Syros and Merger Sub set forth in this Agreement and in any certificate or other writing delivered by Syros or Merger Sub pursuant hereto shall be true and correct (i) as of the date of this Agreement (except in the case of this clause (i), (A) to the extent such representations and warranties are specifically made as of a particular date, in which case such representations and warranties shall be true and correct as of such date and (B) where the failure to be true and correct (without regard to any materiality or Syros Material Adverse Effect qualifications contained therein), individually or in the aggregate, has not had, and is not reasonably likely to have, a Syros Material Adverse Effect) and (ii) as of the Closing Date as though made on and as of the Closing Date (except in the case of this clause (ii), (A) to the extent such representations and warranties are specifically made as of a particular date, in which case such representations and warranties shall be true and correct as of such date, (B) for changes contemplated by this Agreement and (C) where the failure to be true and correct (without regard to any materiality or Syros Material Adverse Effect qualifications contained therein), individually or in the aggregate, has not had, and is not reasonably likely to have, a Syros Material Adverse Effect); provided, however, that the representations and warranties made by Syros and Merger Sub inSections 4.1, 4.2, 4.3, 4.4, 4.5, 4.6 and 4.8(a) shall not be subject to the qualifications set forth in clauses (i)(B) and (ii)(C) above;provided, further, that the representations and warranties set forth in Section 4.6(a) and 4.6(c) shall be true and correct except for such inaccuracies as are in the aggregatede minimis.

(b) Performance of Obligations of Syros and Merger Sub. Syros and Merger Sub shall have performed in all material respects all obligations required to be performed by them under this Agreement on or prior to the Closing Date.

(c) No Syros Material Adverse Effect. No Syros Material Adverse Effect shall have occurred since the date of this Agreement and be continuing.

(d) Financing. The Securities Purchase Agreement shall be in full force and effect and all conditions precedent to the Financing shall have been completed in accordance with the terms thereof, except for such conditions as shall have been waived in accordance with the provisions of the Securities Purchase Agreement,

and the Financing shall be completed substantially concurrently with the Merger with gross proceeds to Syros of at least $100,000,000.

(e) Director Nominee. Subject to Tyme's compliance with the requirements set forth in Section 6.16, a Tyme director nominee shall have been appointed to Syros' board of directors in accordance with Section 6.16, effective as of Closing.

(f) Officers' Certificate. Tyme shall have received an officers' certificate duly executed by each of the Chief Executive Officer and Chief Financial Officer of Syros to the effect that the conditions of Sections 7.3(a), (b), (c), and (d) have been satisfied.

7.4 Frustration of Closing Conditions. A party may not rely on the failure of a condition to be satisfied to avoid the Closing if such party's material breach of this Agreement was a cause of the failure of such condition to be satisfied.

ARTICLE VIII

TERMINATION AND AMENDMENT

8.1 Termination. This Agreement may be terminated at any time prior to the Effective Time (with respect to Sections 8.1(b) through 8.1(i), by written notice by the terminating party to the other party), whether before or, subject to the terms hereof, after approval of the Required Tyme Voting Proposal by the stockholders of Tyme or approval of the Required Syros Voting Proposal by the stockholders of Syros:

(a) by mutual written consent of Syros and Tyme;

(b) by either Syros or Tyme if the Merger shall not have been consummated by December 31, 2022 (the "Outside Date") (provided that the right to terminate this Agreement under this Section 8.1(b) shall not be available to any party whose failure to fulfill any obligation under this Agreement has been a principal cause of or resulted in the failure of the Merger to occur on or before the Outside Date); provided, that, if as of such date all conditions set forth in Article VII (other than the condition set forth in Section 7.1(g)) have been satisfied or waived, the Outside Date shall automatically be extended until the date that is two (2) Business Days following the final determination of Tyme Net Cash in accordance with Section 6.15;

(c) by either Syros or Tyme if a Governmental Authority of competent jurisdiction shall have issued a nonappealable final order, decree or ruling or taken any other nonappealable final action, in each case having the effect of permanently restraining, enjoining or otherwise prohibiting the Merger; provided, however, that a party hereto shall not be permitted to terminate this Agreement pursuant to this Section 8.1(c) if the issuance of any such order, decree, ruling or other action is attributable to the failure of such party (or any Affiliate of such party) to perform in any material respect any covenant in this Agreement required to be performed by such party (or any Affiliate of such party) at or prior to the Effective Time;

(d) by either Syros or Tyme if at the Syros Meeting (including any adjournment or postponement), at which a vote on the Required Syros Voting Proposal is taken, the requisite vote of the stockholders of Syros in favor of the Required Syros Voting Proposal shall not have been obtained;

(e) by Syros, if at any time prior to the receipt of the Tyme Stockholder Approval: (i) the Tyme Board shall have failed to include its recommendation to the approval of the Required Tyme Voting Proposal in the Proxy Statement/Prospectus or shall have withdrawn or modified in a manner adverse to Syros its recommendation of the Required Tyme Voting Proposal; (ii) after the receipt by Tyme of an Acquisition Proposal, Syros requests in writing that the Tyme Board publicly reconfirm its recommendation of the Required

Tyme Voting Proposal and the Tyme Board fails to do so within ten Business Days after its receipt of Syros' request; (iii) the Tyme Board (or any committee thereof) shall have approved or recommended to the stockholders of Tyme an Acquisition Proposal (and not withdrawn such approval or recommendation); (iv) a tender offer or exchange offer for outstanding shares of Tyme Capital Stock is commenced (other than by Syros or an Affiliate of Syros), and Tyme Board (or any committee thereof) recommends that the stockholders of Tyme tender their shares in such tender or exchange offer or, within ten Business Days after the commencement of such tender offer or exchange offer, Tyme Board fails to recommend against acceptance of such offer; or (v) Tyme shall have materially and willfully breached its obligations under Section 6.1 or Section 6.5(a) of this Agreement and such breach, if curable, has not been cured as of the effectiveness of such termination and at least five Business Days following delivery of written notice from Syros to Tyme of such breach.

(f) by Tyme, if at any time prior to the receipt of the Required Syros Stockholder Approval: (i) Syros Board shall have failed to include its recommendation to the approval of the Required Syros Voting Proposal and the Other Syros Voting Proposals in the Proxy Statement/Prospectus or shall have withdrawn or modified in a manner adverse to Tyme its recommendation of the Required Syros Voting Proposal and the Other Syros Voting Proposals; (ii) after the receipt by Syros of an Acquisition Proposal, Tyme requests in writing that the Syros Board publicly reconfirm its recommendation of the Required Syros Voting Proposal and the Other Syros Voting Proposals and the Syros Board fails to do so within ten Business Days after its receipt of Tyme's request; (iii) the Syros Board (or any committee thereof) shall have approved or recommended to the stockholders of Syros an Acquisition Proposal (and has not withdrawn such approval or recommendation); (iv) a tender offer or exchange offer for outstanding shares of Syros Common Stock is commenced (other than by Tyme or an Affiliate of Tyme), and Syros Board (or any committee thereof) recommends that the stockholders of Syros tender their shares in such tender or exchange offer or, within ten Business Days after the commencement of such tender offer or exchange offer, Syros Board fails to recommend against acceptance of such offer; or (v) Syros shall have materially and willfully breached its obligations under Section 6.1 or Section 6.5(b) of this Agreement and such breach, if curable, has not been cured as of the effectiveness of such termination and at least five Business Days following delivery of written notice from Tyme to Syros of such breach;

(g) by Syros, if there has been a breach of or failure to perform any representation, warranty, covenant or agreement set forth in this Agreement (other than those referred to elsewhere in this Section 8.1) on the part of Tyme, which breach would cause the conditions set forth in Section 7.2(a) or (b) not to be satisfied; provided that neither Syros nor Merger Sub is then in material breach of any representation, warranty or covenant under this Agreement and provided, further, that if such breach or failure to perform is curable by Tyme, as applicable, then this Agreement shall not terminate pursuant to this Section 8.1(g) as a result of such particular breach or failure until the expiration of a thirty (30) day period commencing upon delivery of written notice from Syros to Tyme of such breach or failure and it being understood that this Agreement shall not terminate pursuant to this Section 8.1(g) as a result of such particular breach or failure if such breach or failure is cured prior to such termination becoming effective;

(h) by Tyme, if there has been a breach of or failure to perform any representation, warranty, covenant or agreement set forth in this Agreement (other than those referred to elsewhere in this Section 8.1) on the part of Syros, which breach would cause the conditions set forth in Section 7.3(a) or (b) not to be satisfied; provided that Tyme is not then in material breach of any representation, warranty or covenant under this Agreement and provided, further, that if such breach or failure to perform is curable by Syros, then this Agreement shall not terminate pursuant to this Section 8.1(h) as a result of such particular breach or failure until the expiration of a thirty (30) day period commencing upon delivery of written notice from Tyme to Syros of such breach or failure and it being understood that this Agreement shall not terminate pursuant to this Section 8.1(h) as a result of such particular breach or failure if such breach or failure is cured prior to such termination becoming effective; or

(i) by either Syros or Tyme if at the Tyme Meeting (including any adjournment or postponement), at which a vote on the Required Tyme Voting Proposal is taken, the requisite vote of the stockholders of Tyme in favor of the Required Tyme Voting Proposal shall not have been obtained.

8.2 Effect of Termination. In the event of termination of this Agreement as provided in Section 8.1, this Agreement shall immediately become void and there shall be no liability or obligation on the part of Syros, Tyme, Merger Sub or their respective officers, directors, stockholders or Affiliates; provided that (a) any such termination shall not relieve any party from liability for any knowing and intentional breach of this Agreement, fraud or intentional misconduct and (b) the provisions of Section 5.3 (Confidentiality), this Section 8.2 (Effect of Termination), Section 8.3 (Fees and Expenses) and Article IX (Miscellaneous) of this Agreement and the Confidentiality Agreement shall remain in full force and effect and survive any termination of this Agreement.

8.3 Fees and Expenses.

(a) Except as set forth in this Section 8.3, all fees and expenses incurred in connection with this Agreement and the Contemplated Transactions shall be paid by the party incurring such expenses, whether or not the Merger is consummated; provided, however, that Tyme and Syros shall share equally (i) all fees and expenses of the Exchange Agent, and (ii) all fees and expenses, other than accountant's and attorneys' fees, incurred with respect to the printing, filing and mailing of the Proxy Statement/Prospectus (including any related preliminary materials) and the Registration Statement and any amendments or supplements thereto.

(b) Tyme shall pay Syros a termination fee of $2,443,000 (the "Tyme Termination Fee") in the event of the termination of this Agreement:

(i) by Syros pursuant to Sections 8.1(e); or

(ii) by Syros or Tyme, as applicable, pursuant to Sections 8.1(b) or 8.1(g), so long as (A) prior to the Specified Time, any person makes an Acquisition Proposal or amends an Acquisition Proposal made prior to the date of this Agreement with respect to Tyme and has not withdrawn such Acquisition Proposal; and (B) within 12 months after such termination Tyme enters into a definitive agreement to consummate (which is consummated, whether or not within or after the 12 month period), or consummates, any Acquisition Proposal (regardless of whether made before or after the termination of this Agreement); provided that for purposes of this Section 8.3(b)(iii), the references to 15% in the definition of Acquisition Proposal shall be deemed to be 50%.

(c) Syros shall pay Tyme a termination fee of $2,068,000 (the "Syros Termination Fee") in the event of the termination of this Agreement:

(i) by Tyme pursuant to Section 8.1(f); or

(ii) by Syros or Tyme, as applicable, pursuant to Sections 8.1(b) or 8.1(h), so long as (A) prior to the Specified Time, any person makes an Acquisition Proposal or amends an Acquisition Proposal made prior to the date of this Agreement with respect to Syros and has not withdrawn such Acquisition Proposal; and (B) within 12 months after such termination Syros enters into a definitive agreement to consummate, or consummates, any Acquisition Proposal (regardless of whether made before or after the termination of this Agreement); provided that for purposes of this Section 8.3(c)(iii), the references to 15% in the definition of Acquisition Proposal shall be deemed to be 50%.

(d) Any fee due under Section 8.3(b)(i) or 8.3(c)(i) shall be paid by wire transfer of same day funds within one Business Day of the date of termination of this Agreement. Any fee due under Section 8.3(b)(ii) or Section 8.3(c)(ii) shall be paid by wire transfer of same-day funds within two Business Days after the date on which the transaction referenced in clause (B) of such Section 8.3(b)(ii) or Section 8.3(c)(ii), as applicable, is consummated. If one party fails to promptly pay to the other any expense reimbursement or fee due pursuant to this Section 8.3, the defaulting party shall pay the costs and expenses (including legal fees and expenses) in connection with any action, including the filing of any lawsuit or other legal action, taken to collect payment, together with interest on the amount of any unpaid fee at the prime rate published in the Wall Street Journal for the relevant period, plus five percent per annum, compounded quarterly, from the date such expense reimbursement or fee was required to be paid.

(e) The parties hereto acknowledge that the agreements contained in this Section 8.3 are an integral part of the Contemplated Transactions, and that, without these agreements, the parties hereto would not enter into this Agreement. Notwithstanding Section 8.2 or any other provision of this Agreement, payment of the termination fees described in, and under the circumstances provided for in, this Section 8.3 shall constitute the sole and exclusive remedy of Syros or Tyme, as applicable in connection with any termination of this Agreement in the circumstances in which such fees became payable. In the event that Syros or Tyme shall receive the payment of a termination fee under the circumstances provided for in this Section 8.3, the receipt of such fee shall be deemed to be liquidated damages for any and all losses or damages suffered or incurred by Syros and any of its Affiliates or Tyme and any of its Affiliates, as applicable, or any other person in connection with this Agreement (and the termination hereof), the Contemplated Transactions (and the abandonment thereof) or any matter forming the basis for such termination, and none of the Syros, Merger Sub any of their respective Affiliates or Tyme or any of its Affiliates, as applicable, or any other person, shall be entitled to bring or maintain any other claim, action or proceeding against Syros or Tyme, as applicable, or any of their respective Affiliates arising out of this Agreement, any of the Contemplated Transactions or any matters forming the basis for such termination; provided, however, this Section 8.3(e) shall not relieve either party of any liability for a knowing and intentional breach of this Agreement, fraud or intentional misconduct prior to such termination. For the avoidance of doubt, this Section 8.3(e) shall not limit the right of any party to equitable remedies (including specific performance) prior to the termination of this Agreement.

(f) The parties hereto acknowledge and agree that (i) in no event shall Tyme be required to pay Tyme Termination Fee on more than one occasion, nor shall Syros be required to pay Syros Termination Fee on more than one occasion and (ii) in each case whether or not such fee may be payable under more than one provision of this Agreement at the same or at different times and the occurrence of different events.

8.4 Amendment. This Agreement may be amended by the parties hereto, by action taken or authorized by their respective Boards of Directors, at any time before or after approval of the matters presented in connection with the Merger by the stockholders of any of the parties, but, after any such approval, no amendment shall be made which by Law requires further approval by such stockholders without such further approval. This Agreement may not be amended except by an instrument in writing signed on behalf of each of the parties hereto.

8.5 Extension; Waiver. At any time prior to the Effective Time, the parties hereto, by action taken or authorized by their respective Boards of Directors, may, to the extent legally allowed, (a) extend the time for the performance of any of the obligations or other acts of the other parties hereto, (b) waive any inaccuracies in the representations and warranties contained herein or in any document delivered pursuant hereto and (c) waive compliance with any of the agreements or conditions contained herein. Any agreement on the part of a party hereto to any such extension or waiver shall be valid only if set forth in a written instrument signed on behalf of such party. Such extension or waiver shall not be deemed to apply to any time for performance, inaccuracy in any representation or warranty, or noncompliance with any agreement or condition, as the case may be, other than that which is specified in the extension or waiver. The failure of any party to this Agreement to assert any of its rights under this Agreement or otherwise shall not constitute a waiver of such rights.

8.6 Procedure for Termination, Amendment, Extension or Waiver. A termination of this Agreement pursuant to Section 8.1, an amendment, modification or supplement of this Agreement pursuant to Section 8.4 or an extension or waiver of this Agreement pursuant to Section 8.5 shall, in order to be effective, require action by the respective boards of directors of the applicable parties.

ARTICLE IX

MISCELLANEOUS

9.1 Nonsurvival of Representations, Warranties and Agreements. None of the representations, warranties, covenants and agreements in this Agreement shall survive the Effective Time, except for the agreements

contained in Article I, Article II, Section 6.10, 6.16, 6.17, and 6.18 and this Article IX. This Section 9.1 shall have no effect upon any other obligations of the parties hereto, whether to be performed before or after the consummation of the Merger.

9.2 Notices. All notices and other communications hereunder shall be in writing and shall be deemed duly delivered (i) three Business Days after being sent by registered or certified mail, return receipt requested, postage prepaid, or (ii) one Business Day after being sent for next Business Day delivery, fees prepaid, via a reputable overnight courier service, in each case to the intended recipient as set forth below:

(a) if to Syros or Merger Sub, to

Syros Pharmaceuticals, Inc.
35 CambridgePark Drive, 4th Floor
Cambridge, MA 02140
Attention: Nancy Simonian

with a copy (which shall not constitute notice) to:

Wilmer Cutler Pickering Hale and Dorr LLP
60 State Street
Boston, MA 02109
Attention: Cynthia T. Mazareas, Esq.
Joseph B. Conahan, Esq.
Eric P. Hanson, Esq.
Email: cynthia.mazareas@wilmerhale.com
joseph.conahan@wilmerhale.com
eric.hanson@wilmerhale.com
Fax: (617) 526-5000

(b) if to Tyme, to

Tyme Technologies, Inc.
1 Pluckemin Way – Suite 103
Bedminster, New Jersey 07921
Attention: James Biehl
Email: jim.biehl@tymeinc.com

with a copy (which shall not constitute notice) to:

Faegre Drinker Biddle & Reath LLP
One Logan Square, Suite 2000
Philadelphia, Pennsylvania 19103
Attention: Elizabeth A. Diffley, Esq.
Brandon C. Mason, Esq.
Email: elizabeth.diffley@faegredrinker.com
brandon.mason@faegredrinker.com
Fax: +1 215 988 2757

Any party to this Agreement may give any notice or other communication hereunder using any other means (including personal delivery, messenger service, telecopy, ordinary mail or electronic mail), but no such notice or other communication shall be deemed to have been duly given unless and until it actually is received by the party for whom it is intended. Any party to this Agreement may change the address to which notices and other

communications hereunder are to be delivered by giving the other parties to this Agreement notice in the manner herein set forth.

9.3 Entire Agreement. This Agreement (including the Schedules, Annexes and Exhibits hereto and the documents and instruments referred to herein that are to be delivered at the Closing) constitutes the entire agreement among the parties to this Agreement and supersedes any prior understandings, agreements or representations by or among the parties hereto, or any of them, written or oral, with respect to the subject matter hereof and the parties hereto expressly disclaim reliance on any such prior understandings, agreements or representations to the extent not embodied in this Agreement. Notwithstanding the foregoing, the Confidentiality Agreement shall remain in effect in accordance with its terms.

9.4 No Third-Party Beneficiaries. This Agreement is not intended to, and shall not, confer upon any other person any rights or remedies hereunder, except (a) as set forth in or contemplated by the terms and provisions of Section 6.8 and Section 6.10, and (b) from and after the Effective Time, the rights of the holders of Tyme Common Stock, Tyme Options or Tyme Warrants to receive the consideration due to them pursuant to and in accordance with Article II.

9.5 Assignment. No party may assign any of its rights or delegate any of its performance obligations under this Agreement, in whole or in part, by operation of Law or otherwise without the prior written consent of the other parties, and any such assignment without such prior written consent shall be null and void. Subject to the preceding sentence, this Agreement shall be binding upon, inure to the benefit of, and be enforceable by, the parties hereto and their respective successors and permitted assigns. Any purported assignment of rights or delegation of performance obligations in violation of this Section 9.5 is void.

9.6 Severability. Any term or provision of this Agreement that is invalid or unenforceable in any situation in any jurisdiction shall not affect the validity or enforceability of the remaining terms and provisions hereof or the validity or enforceability of the offending term or provision in any other situation or in any other jurisdiction. If the final judgment of a court of competent jurisdiction declares that any term or provision hereof is invalid or unenforceable, the parties hereto agree that the court making such determination shall have the power to limit the term or provision, to delete specific words or phrases, or to replace any invalid or unenforceable term or provision with a term or provision that is valid and enforceable and that comes closest to expressing the intention of the invalid or unenforceable term or provision, and this Agreement shall be enforceable as so modified. In the event such court does not exercise the power granted to it in the prior sentence, the parties hereto agree to replace such invalid or unenforceable term or provision with a valid and enforceable term or provision that will achieve, to the extent possible, the economic, business and other purposes of such invalid or unenforceable term.

9.7 Counterparts and Signature. This Agreement may be executed in two or more counterparts (including by facsimile or by an electronic scan delivered by electronic mail), each of which shall be deemed an original but all of which together shall be considered one and the same agreement and shall become effective when counterparts have been signed by each of the parties hereto and delivered to the other parties, it being understood that all parties need not sign the same counterpart. This Agreement may be executed and delivered by facsimile or by an electronic scan delivered by electronic mail.

9.8 Interpretation. When reference is made in this Agreement to an Article or a Section, such reference shall be to an Article or Section of this Agreement, unless otherwise indicated. The table of contents, table of defined terms and headings contained in this Agreement are for convenience of reference only and shall not affect in any way the meaning or interpretation of this Agreement. The language used in this Agreement shall be deemed to be the language chosen by the parties hereto to express their mutual intent, and no rule of strict construction shall be applied against any party. Whenever the context may require, any pronouns used in this Agreement shall include the corresponding masculine, feminine or neuter forms, and the singular form of nouns and pronouns shall include the plural, and vice versa. Any reference to any federal, state, local or foreign statute or Law shall be deemed also to refer to all rules and regulations promulgated thereunder, unless the context

requires otherwise, in each case as amended, modified, re-enacted thereof, substituted, from time to time. References to any agreement or Contract are to that agreement or Contract as amended, modified or supplemented from time to time in accordance with the terms hereof and thereof. References to "$" and "dollars" are to the currency of the United States. The words "hereof," "herein" and "hereunder" and words of like import used in this Agreement shall refer to this Agreement as a whole and not to any particular provision of this Agreement. Whenever the words "include," "includes" or "including" are used in this Agreement, they shall be deemed to be followed by the words "without limitation." The word "or" is not exclusive. "Writing," "written" and comparable terms refer to printing, typing and other means of reproducing words (including electronic media) in a visible form. All accounting terms used herein will be interpreted, and all accounting determinations hereunder will be made, in accordance with GAAP unless otherwise expressly specified. References from or through any date shall mean, unless otherwise specified, from and including or through and including, respectively. Where this Agreement refers to information that was "made available" or "delivered", that means that such information was either (i) provided directly to Syros or Tyme, as applicable, by the other party, (ii) included in the virtual data rooms established by Syros and Tyme created for the purposes of providing information to the other party in connection with this Agreement at least 24 hours prior to the execution and delivery of this Agreement or (iii) filed with and publicly available on the SEC's EDGAR system prior to the date of this Agreement. When used in the agreement, (a) "Entity" means any corporation (including any non-profit corporation), partnership (including any general partnership, limited partnership or limited liability partnership), joint venture, estate, trust, company (including any company limited by shares, limited liability company or joint stock company), firm, society or other enterprise, association, organization or entity, and each of its successors; (b) "Governmental Authority" means any (i) nation, state, commonwealth, province, territory, county, municipality, district or other jurisdiction of any nature, (ii) federal, state, local, municipal, foreign or other government, (iii) governmental or quasi-governmental authority of any nature (including any governmental division, department, agency, commission, bureau, instrumentality, official, ministry, fund, foundation, center, organization, unit, body or Entity and any court, arbitrator or other tribunal), or (iv) self-regulatory organization (including Nasdaq); (c) "Knowledge" means the actual knowledge (and any knowledge that such person would reasonably be expected to know in the ordinary course of the performance of their employment responsibilities or by making a reasonable inquiry of their direct reports) of any of (i) with respect to Tyme, Richie Cunningham and Frank Porfido or (ii) with respect to Syros, Nancy Simonian and Jason Haas; and (d) "person" means any natural person or Entity, including a Governmental Authority, as applicable. No summary of this Agreement prepared by any party shall affect the meaning or interpretation of this Agreement.

9.9 Governing Law. All matters arising out of or relating to this Agreement and the Contemplated Transactions (including its interpretation, construction, performance and enforcement) shall be governed by and construed in accordance with the internal laws of the State of Delaware without giving effect to any choice or conflict of Law provision or rule (whether of the State of Delaware or any other jurisdiction) that would cause the application of laws of any jurisdictions other than those of the State of Delaware.

9.10 Remedies. Except as otherwise provided herein, any and all remedies herein expressly conferred upon a party will be deemed cumulative with and not exclusive of any other remedy conferred hereby, or by Law or equity upon such party, and the exercise by a party of any one remedy will not preclude the exercise of any other remedy. The parties hereto agree that irreparable damage would occur in the event that any of the provisions of this Agreement were not performed in accordance with their specific terms or were otherwise breached. It is accordingly agreed that the parties shall be entitled to an injunction or injunctions to prevent breaches of this Agreement and to enforce specifically the terms and provisions of this Agreement, this being in addition to any other remedy to which they are entitled at Law or in equity.

9.11 Submission to Jurisdiction. Each of the parties to this Agreement (a) consents to submit itself to the exclusive personal jurisdiction of the Court of Chancery of the State of Delaware, New Castle County, or, if that court does not have jurisdiction, a federal court sitting in Wilmington, Delaware in any action or proceeding arising out of or relating to this Agreement or any of the Contemplated Transactions, (b) agrees that all claims in respect of such action or proceeding shall be heard and determined in any such court, (c) agrees that it shall not

attempt to deny or defeat such personal jurisdiction by motion or other request for leave from any such court and (d) agrees not to bring any action or proceeding arising out of or relating to this Agreement or any of the transaction contemplated by this Agreement in any other court. Each of the parties hereto waives any defense of inconvenient forum to the maintenance of any action or proceeding so brought and waives any bond, surety or other security that might be required of any other party with respect thereto. Any party may make service on another party by sending or delivering a copy of the process to the party to be served at the address and in the manner provided for the giving of notices in Section 9.2. Nothing in this Section 9.11, however, shall affect the right of any party to serve legal process in any other manner permitted by law.

9.12 WAIVER OF JURY TRIAL. EACH OF SYROS, THE MERGER SUB AND TYME HEREBY IRREVOCABLY WAIVES ALL RIGHT TO TRIAL BY JURY IN ANY ACTION, PROCEEDING OR COUNTERCLAIM (WHETHER BASED ON CONTRACT, TORT OR OTHERWISE) ARISING OUT OF OR RELATING TO THIS AGREEMENT OR THE TRANSACTIONS CONTEMPLATED HEREBY OR THE ACTIONS OF SYROS, THE MERGER SUB OR TYME IN THE NEGOTIATION, ADMINISTRATION, PERFORMANCE AND ENFORCEMENT OF THIS AGREEMENT.

9.13 Disclosure Schedule. Each of the Tyme Disclosure Schedule and the Syros Disclosure Schedule shall be arranged in sections corresponding to the numbered sections contained in this Agreement, and the disclosure in any section shall qualify only (a) the corresponding section of this Agreement and (b) the other sections of this Agreement, to the extent that it is reasonably apparent from a reading of such disclosure that it also qualifies or applies to such other sections. The inclusion of any information in the Tyme Disclosure Schedule or the Syros Disclosure Schedule, as applicable, shall not be deemed to be an admission or acknowledgment, in and of itself, that such information is required by the terms hereof to be disclosed, is material, has resulted in or would result in a Tyme Material Adverse Effect or a Syros Material Adverse Effect, as applicable, or is outside the Ordinary Course of Business.

[Remainder of Page Intentionally Left Blank]

IN WITNESS WHEREOF, the parties have executed this Agreement as of the date first written above.

SYROS PHARMACEUTICALS, INC.

By: /s/ Nancy Simonian
Name: Nancy Simonian, M.D.
Title: President and Chief Executive Officer

TACK ACQUISITION CORP.

By: /s/ Nancy Simonian
Name: Nancy Simonian, M.D.
Title: President

TYME TECHNOLOGIES, INC.

By: /s/ Richard Cunningham
Name: Richard Cunningham
Title: Chief Executive Officer

PIPER | SANDLER

1251 Avenue of the Americas, 7th Floor, New York, NY 10020
Tel: 212-284-9300 | Fax: 212-284-9334
Piper Sandler & Co. Since 1895. Member SIPC and FINRA

Board of Directors
Syros Pharmaceuticals, Inc.
35 CambridgePark Drive, 4th Floor
Cambridge, Massachusetts 02140

July 1, 2022

Members of the Board:

You have requested our opinion as to the fairness, from a financial point of view, to Syros Pharmaceuticals, Inc., a Delaware corporation ("Syros") of the Exchange Ratio (as defined in the Agreement) to be paid by Syros to each holder of common stock, par value $0.001 per share ("Tyme Common Stock"), of Tyme Technologies, Inc., a Delaware corporation ("Tyme"), other than certain shares held by Syros or Tyme, pursuant to the Agreement and Plan of Merger, dated as of July 1, 2022 (the "Agreement"}, to be entered into among Tyme, Syros and Tack Acquisition Corp., a Delaware corporation and a newly formed wholly owned subsidiary of Syros ("Merger Sub"). The Agreement provides for, among other things, the merger (the "Merger") of the Merger Sub with and into Tyme, as a result of which Tyme will survive the Merger and become a wholly owned subsidiary of Syros. The terms and conditions of the Merger are more fully set forth in the Agreement.

In connection with our review of the Merger, and in arriving at our opinion, we have: (i) reviewed and analyzed the financial terms of a draft of the Agreement dated June 29, 2022; (ii) reviewed and analyzed certain financial and other data with respect to Syros and Tyme which was publicly available, (iii) reviewed and analyzed certain information, including financial forecasts, relating to the business, earnings, cash flow, assets, liabilities and prospects of Syros and Tyme, on a stand-alone basis, that were publicly available, as well as those that were furnished to us by Syros; (iv) conducted discussions with members of senior management and representatives of Syros and Tyme concerning the matters described in clauses (ii) and (iii) above, as well as their respective businesses and prospects before and after giving effect to the Merger; (v) reviewed the current and historical reported prices and trading activity of Syros common stock, par value $0.0001 per share ("Syres Common Stock"), and similar information for certain other companies deemed by us to be comparable to Syres; (vi) compared the financial performance of Syros with that of certain other publicly-traded companies that we deemed relevant; (vii) performed a discounted cash flow analysis with respect to Syros' projections; and (viii) reviewed the financial terms, to the extent publicly available, of certain business combination transactions that we deemed relevant. In addition, we have conducted such other analyses, examinations and inquiries and considered such other financial, economic and market criteria as we have deemed necessary in arriving at our opinion.

We have relied upon and assumed, without assuming liability or responsibility for independent verification, the accuracy and completeness of all information that was publicly available or was furnished, or otherwise made available, to us or discussed with or reviewed by us. We have further relied upon the assurances of the management of Syros that the financial information provided has been prepared on a reasonable basis in accordance with industry practice, and that they are not aware of any information or facts that would make any information provided to us incomplete or misleading. Without limiting the generality of the foregoing, for the purpose of this opinion, we have assumed that with respect to financial forecasts, estimates and other forward-looking information reviewed by us, that such information has been reasonably prepared based on assumptions reflecting the best currently available estimates and judgments of the management of Syros and Tyme as to the expected future results of operations and financial condition of Syros and Tyme, respectively. We express no opinion as to any such financial forecasts, estimates or forward-looking information or the assumptions on which they were based. We have relied, with your consent, on advice of the outside counsel and the independent accountants to Syros, and on the assumptions of the management of Syros as to all accounting, legal, tax and financial reporting matters with respect to Syros, Tyme and the Agreement.

In arriving at our opinion, we have assumed that the executed Agreement will be in all material respects identical to the last draft reviewed by us. We have relied upon and assumed, without independent verification, that (i) the representations and warranties of all parties to the Agreement and all other related documents and instruments that are referred to therein are true and correct, (ii) each party to such agreements will fully and timely perform all of the covenants and agreements required to be performed by such party, (iii) the Merger will be consummated pursuant to the terms of the Agreement without amendments thereto, including the Merger Partner Net Cash (as defined in the Agreement) closing condition, and (iv) all conditions to the consummation of the Merger will be satisfied without waiver by any party of any conditions or obligations thereunder. Additionally, we have assumed that all the necessary regulatory approvals and consents required for the Merger will be obtained in a manner that will not adversely affect Syros, Tyme or the contemplated benefits of the Merger.

In arriving at our opinion, we have not performed any appraisals or valuations of any specific assets or liabilities (fixed, contingent or other) of Syros or Tyme, and have not been furnished or provided with any such appraisals or valuations, nor have we evaluated the solvency of Syros or Tyme under any state or federal law relating to bankruptcy, insolvency or similar matters. The analyses performed by us in connection with this opinion were going concern analyses, subject to the assumption to which you have consented that Tyme's assets are substantially cash deposits. We express no opinion regarding the liquidation value of Syros, Tyme or any other entity. Without limiting the generality of the foregoing, we have undertaken no independent analysis of any pending or threatened litigation, regulatory action, possible unasserted claims or other contingent liabilities, to which Syros or Tyme or any of their affiliates is a party or may be subject, and at the direction of Syros and with its consent, our opinion makes no assumption concerning, and therefore does not consider, the possible assertion of claims, outcomes or damages arising out of any such matters. We have also assumed that neither Syros nor Tyme is party to any material pending transaction, including without limitation any financing (other than the private placement of Syros Common Stock expected to occur concurrently with the Merger), recapitalization, acquisition or merger, divestiture or spin-off, other than the Merger.

No company or transaction used in any analysis for purposes of comparison is identical to Syros or the Merger. Accordingly, an analysis of the results of the comparisons is not mathematical; rather, it involves complex considerations and judgments about differences in the companies and transactions to which Syros and the Merger were compared and other factors that could affect the public trading value or transaction value of the companies.

This opinion is necessarily based upon the information available to us and facts and circumstances as they exist and are subject to evaluation on the date hereof; events occurring after the date hereof could materially affect the assumptions used in preparing this opinion. We are not expressing any opinion herein as to the price at which shares of Syros Common Stock or Tyme Common Stock may trade following announcement of the Merger or at any future time. We have not undertaken to reaffirm or revise this opinion or otherwise comment upon any events occurring after the date hereof and do not have any obligation to update, revise or reaffirm this opinion.

We have been engaged by Syros to act as its financial advisor in connection with the Merger and we will receive a fee from Syros for providing our services, a portion of which is contingent upon the consummation of the Merger. We will also receive a fee for rendering this opinion. Our opinion fee is not contingent upon the consummation of the Merger or the conclusions reached in our opinion. In addition, we are acting as co -agent to Syros in connection with the private placement of Syros Common Stock that is expected to occur concurrently with the Merger, for which we will receive a fee. In connection with our roles as financial advisor and co-agent, Syros has agreed to indemnify us against certain liabilities and reimburse us for certain expenses in connection with our services. We have, in the past, provided financing services to Syros; more specifically, we acted as an underwriter on Syros' (i) June 2016 initial public offering, (ii) January 2018 follow-on offering, (iii) March 2019 follow-on offering, and (iv) January 2021 follow-on offering. Moreover, we may continue to provide investment banking or brokerage services to Syros and its affiliates, for which we would expect to receive fees. In the ordinary course of our business, we and our affiliates may actively trade securities of Syros and Tyme for our

own account or the account of our customers and, accordingly, may at any time hold a long or short position in such securities. We may also, in the future, provide investment banking and financial advisory services to the Syros, Tyme or entities that are affiliated with Syros or Tyme, for which we would expect to receive compensation.

Consistent with applicable legal and regulatory requirements, Piper Sandler has adopted policies and procedures to establish and maintain the independence of Piper Sandler's Research Department and personnel. As a result, Piper Sandler's research analysts may hold opinions, make statements or recommendations, and/or publish research reports with respect to Syros or Tyme and other participants in the Merger that differ from the views of Piper Sandler's investment banking personnel.

This opinion is provided solely to the Board of Directors of Syros in connection with its consideration of the Merger and is not intended to be and does not constitute a recommendation to any stockholder of Syros as to how such stockholder should act or vote with respect to the Merger or any other matter. Except with respect to the use of this opinion in connection with the proxy statement relating to the Merger in accordance with our engagement letter with Syros, this opinion shall not be disclosed, referred to, published or otherwise used (in whole or in part), nor shall any public references to us be made, without our prior written approval. This opinion has been approved for issuance by the Piper Sandler Opinion Committee.

This opinion addresses solely the fairness, from a financial point of view, to Syros of the proposed Exchange Ratio set forth in the Agreement and does not address any other terms or agreement relating to the Merger or any other terms of the Agreement. We were not requested to opine as to, and this opinion does not address: (i) the basic business decision to proceed with or effect the Merger; (ii) the merits of the Merger relative to any alternative transaction or business strategy that may be available to Syros;(iii) any other terms contemplated by the Agreement or the fairness of the Merger to, or any consideration received in connection therewith by, any creditor or other constituency of Syros: or (iv) the solvency or financial viability of Syros or Tyme at the date hereof, upon consummation of the Merger, or at any future time. Furthermore, we express no opinion with respect to the amount or nature of compensation to any officer, director or employee of any party to the Merger, or any class of such persons, to be paid by Syros in the Merger or with respect to the fairness of any such compensation.

Based upon and subject to the foregoing and based upon such other factors as we consider relevant, it is our opinion that the Exchange Ratio pursuant to the Agreement is fair, from a financial point of view, to Syros as of the date hereof.

Sincerely,

PIPER SANDLER & CO.

MOELIS & COMPANY

July 2, 2022

Board of Directors
Tyme Technologies, Inc.
1 Pluckemin Way
Bedminster, NJ 07921

Members of the Board:

You have requested our opinion as to the fairness, from a financial point of view, to the holders of common stock, par value $0.0001 per share ("Company Common Stock"), of Tyme Technologies, Inc. (the "Company"), of the Exchange Ratio (as defined below) set forth in the Agreement and Plan of Merger (the "Agreement") to be entered into by and among Syros Pharmaceuticals, Inc. (the "Acquiror"), Tack Acquisition Corp., a wholly owned subsidiary of the Acquiror ("Merger Sub"), and the Company. As more fully described in the Agreement, Merger Sub will be merged with and into the Company (the "Transaction") and each issued and outstanding share of Company Common Stock, other than shares held in treasury or by any subsidiary of the Company or owned by the Acquiror, Merger Sub or any other subsidiary of the Acquiror, will be automatically converted into the right to receive a number (the "Exchange Ratio") of shares of common stock, par value $0.001 per share ("Acquiror Common Stock"), of the Acquiror equal to the quotient determined by dividing (x) the quotient determined by dividing the sum of $7.5 million plus the Tyme Net Cash (as defined, and subject to adjustment as provided, in the Agreement) by the number of shares of Company Common Stock outstanding immediately prior to the closing of the Transaction by (y) the Syros Per Share Price (as defined below). In connection with the Transaction and as contemplated by the Agreement, the Acquiror has also entered into a securities purchase agreement with investors providing for, subject to the terms described therein, the issuance of (x) shares of Acquiror Common Stock (or pre-funded warrants to purchase shares of Acquiror Common Stock, "Pre-Funded Warrants"), together with (y) warrants to purchase either Acquiror Common Stock or Pre-Funded Warrants for aggregate gross proceeds of approximately $130,000,000 (the "Private Placement"). For purposes of this opinion, the term "Syros Per Share Price" means $0.94.

In arriving at our opinion, we have, among other things: (i) reviewed certain publicly available business and financial information relating to the Company and the Acquiror; (ii) reviewed certain internal information relating to the business, earnings, cash flow, assets (including estimates of Tyme Net Cash), liabilities and prospects of the Company furnished to us by the Company, including financial forecasts and estimates provided to or discussed with us by the management of the Company under a dissolution scenario (the "Company Dissolution Projections") and an alternative operating plan scenario (the "Company Development Plan Projections"); (iii) reviewed certain internal information relating to the business, earnings, cash flow, assets, liabilities and prospects of the Acquiror furnished to us by the Acquiror and the Company, including financial forecasts and estimates provided to or discussed with us by the Acquiror, as adjusted by the management of the Company (the "Company Projections for the Acquiror"); (iv) reviewed certain information relating to the capitalization of the Company and the Acquiror furnished to us by the Company and the Acquiror; (v) reviewed estimates prepared and provided to us by the management of the Company as to (1) the Company's projected utilization on a standalone basis of net operating losses to achieve future tax savings and (2) the Acquiror's projected utilization on a standalone basis of net operating losses to achieve future tax savings; (vi) considered certain potential pro forma impacts of the Transaction on the combined company resulting from the Transaction, including estimates prepared and provided to us by the management of the Company as to the combined company's projected utilization of net operating losses to achieve future tax savings (the "Combined Company NOL Utilization Estimates"); (vii) conducted discussions with members of the senior management and representatives of the Company and the Acquiror concerning the information described in clauses (i) through (vi) of this paragraph, as well as the business and prospects of the Company and the Acquiror, generally;

(viii) reviewed publicly available financial and stock market data of certain other companies in lines of business that we deemed relevant; (ix) considered the results of efforts by or on behalf of the Company, including by us at the Company's direction, to solicit indications of interest from third parties with respect to a possible acquisition of all or a portion of the Company; (x) reviewed an execution version of the Agreement made available to us on July 2, 2022; (xi) participated in certain discussions and negotiations among representatives of each of the Company and the Acquiror and their respective advisors; and (xi) conducted such other financial studies and analyses and took into account such other information as we deemed appropriate.

In connection with our review, we have, with your consent, relied on the information supplied to, discussed with or reviewed by us for purposes of this opinion being complete and accurate in all material respects. We have not assumed any responsibility for independent verification of, and we did not independently verify, any of such information. With your consent, we have relied upon, without independent verification, the assessment of the Company and its legal, tax, regulatory and accounting advisors with respect to legal, tax, regulatory and accounting matters. In light of the Company's management's views regarding the achievability of, and financing needed to successfully pursue, the Company Development Plan Projections, you have directed us to use and rely on the Company Dissolution Projections for purposes of our analyses and this opinion. With respect to the Company Dissolution Projections and the Company Projections for the Acquiror, we have assumed, at your direction, that they have been reasonably prepared on a basis reflecting the best currently available estimates and judgments of the management of the Company as to the future performance of the Company and the Acquiror, respectively. With respect to the Combined Company NOL Utilization Estimates referred to above, we have assumed, at your direction, that they have been reasonably prepared on a basis reflecting the best currently available estimates and judgments of the management of the Company as to the matters covered thereby. At your direction, we have assumed that the Company Dissolution Projections, the Company Projections for the Acquiror and the Combined Company NOL Utilization Estimates are a reasonable basis upon which to evaluate the Company, the Acquiror and the Transaction and at your direction we have relied upon these financial forecasts for purposes of our analyses and this opinion. We express no views as to the reasonableness of any such financial forecasts or other information or the assumptions on which they are based. We also have relied, without independent verification, upon the assessment of the management of the Company as to (i) the validity and marketability of, and risks associated with, the existing and future technology and products of the Company and the Acquiror and (ii) the probabilities of success used to develop financial forecasts attributable to existing and future technology and products of the Company and the Acquiror. In addition, with your consent, we have not made any independent evaluation or appraisal of any of the assets or liabilities (contingent, derivative, off-balance-sheet, or otherwise) of the Company or the Acquiror, nor have we been furnished with any such evaluation or appraisal. With your consent, we have assumed that any adjustment to be made to the Exchange Ratio pursuant to the Agreement or otherwise would not be material to our analyses or this opinion.

Our opinion does not address the Company's underlying business decision to effect the Transaction or the relative merits of the Transaction as compared to any alternative business strategies or transactions that might be available to the Company and does not address any legal, regulatory, tax or accounting matters (including any tax implications to the Company's stockholders). At your direction, we have not been asked to, nor do we, offer any opinion as to any terms of the Agreement or any aspect or implication of the Transaction or the Private Placement (but our analysis of the Exchange Ratio reflects the consummation of the Private Placement), except for the fairness of the Exchange Ratio from a financial point of view to the holders of Company Common Stock. Our opinion does not address any aspect or implication of any voting agreement previously entered into, or any voting, support or lock-up agreement entered into or to be entered into in connection with the Transaction, by any holder of Company Common Stock. We are not expressing any opinion as to fair value or the solvency of the Company or the Acquiror following the closing of the Transaction or at any time. We understand that the Agreement also permits the Company, with the consent of the Acquiror and subject to the terms thereof, to sell, assign, license or otherwise dispose of some or all of its non-cash assets prior to or concurrent with the closing of the Transaction, with the proceeds of any such disposition to be distributed to holders of Company Common

Stock or included in the calculation of Tyme Net Cash. We express no views as to the fairness or value of any such disposition or any such proceeds. We are also not expressing any opinion as to what the value of shares of Acquiror Common Stock actually will be when issued in the Transaction or the prices at which shares of Company Common Stock or Acquiror Common Stock may trade at any time. We have assumed that the shares of Acquiror Common Stock to be issued in the Transaction will be approved for trading on the Nasdaq Stock Market. In rendering this opinion, we have assumed, with your consent, that the final executed form of the Agreement will not differ in any material respect from the draft that we have reviewed, that the Transaction and the Private Placement will each be consummated in accordance with its respective terms without any waiver or modification that could be material to our analysis, and that the parties to the Agreement will comply with all the material terms of the Agreement. We have assumed, with your consent, that all governmental, regulatory or other consents or approvals necessary for the completion of the Transaction will be obtained, except to the extent that could not be material to our analysis.

Our opinion is necessarily based on economic, monetary, market and other conditions as in effect on, and the information made available to us as of, the date hereof, and we assume no responsibility to update this opinion for developments occurring or coming to our attention after the date hereof. For purposes of our opinion and analysis, we have evaluated the Exchange Ratio by comparing the range of values indicated by our discounted cash flow analysis for a share of Acquiror Common Stock (after giving effect to (x) the consummation of the Transaction and the Private Placement and (y) the Exchange Ratio) to the range of values indicated by our discounted cash flow analysis for a share of Company Common Stock on a standalone basis using the Company Dissolution Projections.

We have acted as your financial advisor in connection with the Transaction and will receive a fee for our services, a substantial portion of which is contingent upon the consummation of the Transaction. We will also receive a fee upon delivery of this opinion. Our affiliates, employees, officers and partners may at any time own securities (long or short) of the Company and the Acquiror. In the future, we may provide investment banking and other services to the Company and the Acquiror and may receive compensation for such services.

This opinion is for the use and benefit of the Board of Directors of the Company (solely in its capacity as such) in its evaluation of the Transaction. This opinion does not constitute a recommendation as to how any holder of securities should vote or act with respect to the Transaction or any other matter. This opinion does not address the fairness of the Transaction or any aspect or implication thereof to, or any other consideration of or relating to, the holders of any class of securities, creditors or other constituencies of the Company, other than the fairness of the Exchange Ratio provided in the Transaction pursuant to the Agreement from a financial point of view to the holders of Company Common Stock. In addition, we do not express any opinion as to the fairness of the amount or nature of any compensation to be received by any officers, directors or employees of any parties to the Transaction, or any class of such persons, relative to the Exchange Ratio or otherwise. This opinion was approved by a Moelis & Company LLC fairness opinion committee.

Based upon and subject to the foregoing, it is our opinion that, as the date hereof, the Exchange Ratio provided in the Transaction pursuant to the Agreement is fair from a financial point of view to the holders of Company Common Stock.

Very truly yours,

/s/ Moelis & Company LLC

MOELIS & COMPANY LLC

SYROS PHARMACEUTICALS, INC.

[FORM OF] SUPPORT AGREEMENT

This Support Agreement (this "Agreement") is made and entered into as of [•], 2022, by and among Tyme Technologies, Inc. a Delaware corporation ("Tyme"), Syros Pharmaceuticals, Inc., a Delaware corporation ("Syros"), and the undersigned stockholder (the "Stockholder") of Syros.

RECITALS

WHEREAS, concurrently with the execution and delivery hereof, Syros, Tyme and Tack Acquisition Corp., a Delaware corporation and a wholly owned subsidiary of Syros (the "Merger Sub"), have entered into an agreement and plan of merger (as such agreement may be amended or supplemented from time to time pursuant to the terms thereof, the "Merger Agreement"), pursuant to which Merger Sub will merge with and into Tyme, with Tyme surviving the merger as the surviving corporation and a wholly owned subsidiary of Syros (the "Merger").

WHEREAS, the Stockholder is the beneficial owner (as defined in Rule13d-1 under the Exchange Act) of such number of shares of Syros Common Stock as indicated in the signature page of the Stockholder.

WHEREAS, as an inducement to the willingness of Tyme to enter into the Merger Agreement, Tyme has required that Stockholder enter into this Agreement.

NOW, THEREFORE, intending to be legally bound, the parties hereby agree as follows:

1. Certain Definitions. Capitalized terms used but not otherwise defined herein shall have the meanings ascribed thereto in the Merger Agreement. For all purposes of this Agreement, the following terms shall have the following respective meanings:

(a) "Constructive Sale" means, with respect to any security, a short sale with respect to such security, entering into or acquiring a derivative contract with respect to such security, entering into or acquiring a futures or forward contract to deliver such security or entering into any other hedging or other derivative transaction that has the effect of either directly or indirectly materially changing the economic benefits or risks of ownership of such security.

(b) "Shares" means (i) all shares of Syros Common Stock owned, beneficially or of record, by the Stockholder as of the date hereof, and (ii) all additional shares of Syros Common Stock acquired by the Stockholder, beneficially or of record, during the period commencing with the execution and delivery of this Agreement and expiring on the Closing Date.

(c) "Transfer" or "Transferred" means, with respect to any security, the direct or indirect assignment, sale, transfer, tender, exchange, pledge or hypothecation, or the grant, creation or suffrage of a lien, security interest or encumbrance in or upon, or the gift, grant or placement in trust, or the Constructive Sale or other disposition of such security (including transfers by testamentary or intestate succession, by domestic relations order or other court order, or otherwise by operation of law) or any right, title or interest therein (including any right or power to vote to which the holder thereof may be entitled, whether such right or power is granted by proxy or otherwise), or the record or beneficial ownership thereof, the offer to make such a sale, transfer, Constructive Sale or other disposition, and each agreement, arrangement or understanding, whether or not in writing, to effect any of the foregoing.

2. Transfer and Voting Restrictions. The Stockholder covenants to Syros and Tyme as follows:

(a) During the period commencing with the execution and delivery of this Agreement and expiring on the Expiration Date (as defined below), the Stockholder shall not Transfer any of the Stockholder's Shares, or publicly announce its intention to Transfer any of its Shares.

(b) Except as otherwise permitted by this Agreement or by order of a court of competent jurisdiction, the Stockholder will not commit any act that would restrict the Stockholder's legal power, authority and right to vote all of the Shares held by the Stockholder or otherwise prevent or disable the Stockholder from performing any of his, her or its obligations under this Agreement. Without limiting the generality of the foregoing, except for this Agreement and as otherwise permitted by this Agreement, the Stockholder shall not enter into any voting agreement with any person or entity with respect to any of the Stockholder's Shares, grant any person or entity any proxy (revocable or irrevocable) or power of attorney with respect to any of the Shares, deposit any Shares in a voting trust or otherwise enter into any agreement or arrangement with any person or entity limiting or affecting the Stockholder's legal power, authority or right to vote the Stockholder's Shares in favor of the Syros Voting Proposals.

(c) Notwithstanding anything else herein to the contrary, the Stockholder may, at any time, Transfer Shares (i) by will or other testamentary document or by intestacy, (ii) to any investment fund or other entity controlled or managed by the Stockholder, (iii) to any member of the Stockholder's immediate family or (iv) to any trust for the direct or indirect benefit of the Stockholder or the immediate family of the Stockholder or otherwise for estate planning purposes; provided, that (x) such Transferred Shares shall continue to be bound by this Agreement and (y) the applicable transferee shall have executed and delivered to Syros and Tyme a support agreement substantially identical to this Agreement upon consummation of such Transfer.

3. Agreement to Vote Shares. The Stockholder covenants to Syros and Tyme as follows:

(a) Until the Expiration Date (as defined below), at any meeting of the stockholders of Syros, however called, and at every adjournment or postponement thereof, and on every action or approval by written consent of the stockholders of Syros, the Stockholder shall be present (in person or by proxy) and vote, or exercise its right to consent with respect to, all Shares held by the Stockholder (A) in favor of the Syros Voting Proposals and (B) against any Acquisition Proposal.

(b) If the Stockholder is the beneficial owner, but not the record holder, of Shares, the Stockholder shall cause the record holder and any nominees to be present (in person or by proxy) and vote all the Stockholder's Shares in accordance with this Section 3.

(c) In the event of a stock split, stock dividend or distribution, or any change in the capital stock of Syros by reason of anysplit-up, reverse stock split, recapitalization, combination, reclassification, reincorporation, exchange of shares or the like, the term "Shares" shall be deemed to refer to and include such shares as well as all such stock dividends and distributions and any securities into which or for which any or all of such shares may be changed or exchanged or which are received in such transaction.

4. Action in Stockholder Capacity Only. The Stockholder is entering into this Agreement solely in the Stockholder's capacity as a record holder and beneficial owner, as applicable, of its Shares and not in the Stockholder's capacity as a director or officer of Syros. Nothing herein shall limit or affect the Stockholder's ability to act as an officer or director of Syros, including exercising rights of Syros under the Merger Agreement, or to exercise Stockholder's fiduciary duties as an officer director.

5. Documentation and Information. The Stockholder shall permit and hereby authorizes Syros and Tyme to publish and disclose in all documents and schedules filed with the SEC, and any press release or other disclosure document that Syros or Tyme reasonably determines to be necessary in connection with the transactions contemplated by the Merger Agreement, such Stockholder's identity and ownership of the Share and the nature of such Stockholder's commitments and obligations under this Agreement.

6. Irrevocable Proxy. The Stockholder hereby revokes (or agrees to cause to be revoked) any proxies that the Stockholder has heretofore granted with respect to its Shares. In the event and to the extent that the Stockholder fails to vote the Shares in accordance with Section 3 at any applicable meeting of the stockholders of Syros, the Stockholder shall be deemed to have irrevocably granted to, and appointed, Tyme, and any individual designated in writing by Tyme, and each of them individually, as his, her or its proxy and attorney-in-fact (with full power of substitution), for and in its name, place and stead, to vote his, her or its Shares at any meeting of the Syros stockholders called with respect to any of the matters specified in, and in accordance and consistent with, Section 3 of this Agreement. Tyme agrees not to exercise the proxy granted herein for any purpose other than the purposes described in this Agreement. Except as otherwise provided for herein, the Stockholder hereby affirms that the irrevocable proxy is coupled with an interest and may under no circumstances be revoked and that such irrevocable proxy is executed and intended to be irrevocable. Notwithstanding any other provisions of this Agreement, the irrevocable proxy granted hereunder shall automatically terminate upon the termination of this Agreement.

7. No Solicitation. Subject to Section 4, the Stockholder agrees not to, directly or indirectly, including through any of its officers, directors or agents, (a) solicit, seek or initiate or knowingly take any action to facilitate or encourage, any offers, inquiries or the making of any proposal or offer that constitutes, or could reasonably be expected to lead to, any Acquisition Proposal or (b) enter into, continue or otherwise participate or engage in any discussions or negotiations regarding any Acquisition Proposal, or furnish to any person any non-public information or afford any person, other than Syros or Tyme, as applicable, access to such party's property, books or records (except pursuant to a request by a Governmental Entity) in connection with, any Acquisition Proposal; provided, however, that nothing in this Section 7 shall prevent the Stockholder from referring a person to this Section 7 or to the Merger Agreement.

8. Representations and Warranties of the Stockholder. The Stockholder hereby represents and warrants to Syros and Tyme as follows:

(a) (i) The Stockholder is the beneficial or record owner of the number of shares of Syros Common Stock indicated on the signature page of the Stockholder (which shall be deemed to be "held" by the Stockholder for purposes of Section 3 unless otherwise expressly stated with respect to any shares in); and (ii) the Stockholder does not beneficially own any securities of Syros other than the shares of Syros Common Stock and rights to purchase shares of Syros Common Stock set forth on the signature page of the Stockholder.

(b) Except as otherwise provided in this Agreement, the Stockholder has full power and authority to (i) make, enter into and carry out the terms of this Agreement and (ii) vote all of its Shares in the manner set forth in this Agreement without the consent or approval of, or any other action on the part of, any other person or entity (including any Governmental Entity). Without limiting the generality of the foregoing, the Stockholder has not entered into any voting agreement (other than this Agreement) with any person with respect to any of the Stockholder's Shares, granted any person any proxy (revocable or irrevocable) or power of attorney with respect to any of the Stockholder's Shares, deposited any of the Stockholder's Shares in a voting trust or entered into any arrangement or agreement with any person limiting or affecting the Stockholder's legal power, authority or right to vote the Stockholder's Shares on any matter, in each case that conflicts with this Agreement.

(c) This Agreement has been duly and validly executed and delivered by the Stockholder and (assuming the due authorization, execution and delivery by the other parties hereto) constitutes a valid and binding agreement of the Stockholder enforceable against the Stockholder in accordance with its terms, subject to the Enforceability Exceptions. The execution and delivery of this Agreement by the Stockholder and the performance by the Stockholder of the agreements and obligations hereunder will not result in any breach or violation of or be in conflict with or constitute a default under any term of any Contract or if applicable any provision of an organizational document (including a certificate of incorporation) to or by which the Stockholder is a party or bound, or any applicable law to which the Stockholder (or any of the Stockholder's assets) is subject or bound, except for any such breach, violation, conflict or default which, individually or in the aggregate, would

not reasonably be expected to materially impair or adversely affect the Stockholder's ability to perform its obligations under this Agreement.

(d) The Stockholder has had the opportunity to review the Merger Agreement and this Agreement with the Stockholder's legal counsel. The Stockholder understands and acknowledges that Tyme is entering into the Merger Agreement in reliance upon the Stockholder's execution, delivery and performance of this Agreement.

(e) The execution, delivery and performance of this Agreement by the Stockholder do not and will not require any consent, approval, authorization or permit of, action by, filing with or notification to, any Governmental Authority, except for any such consent, approval, authorization, permit, action, filing or notification the failure of which to make or obtain, individually or in the aggregate, has not and would not materially impair the Stockholder's ability to perform its obligations under this Agreement.

(f) With respect to the Stockholder, as of the date hereof, there is no action, suit, investigation or proceeding pending against, or, to the knowledge of the Stockholder, threatened against, the Stockholder or any of the Stockholder's properties or assets (including the Shares) that would reasonably be expected to prevent or materially delay or impair the ability of the Stockholder to perform its obligations hereunder or to consummate the transactions contemplated hereby.

(g) Neither the Stockholder nor any of its Representatives or Affiliates has employed or made any agreement with any broker, finder or similar agent or any Person which will result in the obligation of such Stockholder, Syros, Tyme, or any of their respective Affiliates to pay any finder's fee, brokerage fees or commission or similar payment in connection with the transactions contemplated hereby.

9. Termination. This Agreement shall terminate and shall cease to be of any further force or effect as of the earlier of (a) such date and time as the Merger Agreement shall have been terminated pursuant to the terms thereof, (b) the Closing, or (c) the date on which the Syros Voting Proposals shall have been approved by the requisite holders of Syros Common Stock (the "***Expiration Date***"); provided, however, that (i) Section 10 shall survive the termination of this Agreement, and (ii) the termination of this Agreement shall not relieve any party hereto from any liability for any material and willful breach of this Agreement prior to the Expiration Date.

10. Miscellaneous Provisions.

(a) Amendments. No amendment of this Agreement shall be effective against any party unless it shall be in writing and signed by each of the parties hereto.

(b) Entire Agreement. This Agreement (including the documents and instruments referred to herein that are to be delivered at the Closing) constitutes the entire agreement among the parties to this Agreement and supersedes any prior understandings, agreements or representations by or among the parties hereto, or any of them, written or oral, with respect to the subject matter hereof and the parties hereto expressly disclaim reliance on any such prior understandings, agreements or representations to the extent not embodied in this Agreement.

(c) Governing Law. All matters arising out of or relating to this Agreement (including its interpretation, construction, performance and enforcement) shall be governed by and construed in accordance with the internal laws of the State of Delaware without giving effect to any choice or conflict of Law provision or rule (whether of the State of Delaware or any other jurisdiction) that would cause the application of laws of any jurisdictions other than those of the State of Delaware.

(d) Submission to Jurisdiction. Each of the parties to this Agreement (a) consents to submit itself to the exclusive personal jurisdiction of the Court of Chancery of the State of Delaware, New Castle County, or, if that court does not have jurisdiction, a federal court sitting in Wilmington, Delaware in any action or proceeding arising out of or relating to this Agreement or any of the Contemplated Transactions, (b) agrees that all claims in respect of such action or proceeding shall be heard and determined in any such court, (c) agrees that it shall not

attempt to deny or defeat such personal jurisdiction by motion or other request for leave from any such court and (d) agrees not to bring any action or proceeding arising out of or relating to this Agreement or any of the transaction contemplated by this Agreement in any other court. Each of the parties hereto waives any defense of inconvenient forum to the maintenance of any action or proceeding so brought and waives any bond, surety or other security that might be required of any other party with respect thereto. Any party may make service on another party by sending or delivering a copy of the process to the party to be served at the address and in the manner provided for the giving of notices in Section 10(j). Nothing in this Section 10(d), however, shall affect the right of any party to serve legal process in any other manner permitted by law.

(e) WAIVER OF JURY TRIAL. EACH OF SYROS, TYME AND THE STOCKHOLDER HEREBY IRREVOCABLY WAIVES ALL RIGHT TO TRIAL BY JURY IN ANY ACTION, PROCEEDING OR COUNTERCLAIM (WHETHER BASED ON CONTRACT, TORT OR OTHERWISE) ARISING OUT OF OR RELATING TO THIS AGREEMENT OR THE TRANSACTIONS CONTEMPLATED HEREBY OR THE ACTIONS OF SYROS, TYME OR THE STOCKHOLDER IN THE NEGOTIATION, ADMINISTRATION, PERFORMANCE AND ENFORCEMENT OF THIS AGREEMENT.

(f) Assignment. No party may assign any of its rights or delegate any of its performance obligations under this Agreement, in whole or in part, by operation of Law or otherwise without the prior written consent of the other parties, and any such assignment without such prior written consent shall be null and void. Subject to the preceding sentence, this Agreement shall be binding upon, inure to the benefit of, and be enforceable by, the parties hereto and their respective successors and permitted assigns. Any purported assignment of rights or delegation of performance obligations in violation of this Section 10(f) is void.

(g) No Third Party Rights. This Agreement is not intended to, and shall not, confer upon any other person any rights or remedies hereunder, except as set forth in or contemplated by the terms and provisions set forth herein.

(h) Severability. Any term or provision of this Agreement that is invalid or unenforceable in any situation in any jurisdiction shall not affect the validity or enforceability of the remaining terms and provisions hereof or the validity or enforceability of the offending term or provision in any other situation or in any other jurisdiction. If the final judgment of a court of competent jurisdiction declares that any term or provision hereof is invalid or unenforceable, the parties hereto agree that the court making such determination shall have the power to limit the term or provision, to delete specific words or phrases, or to replace any invalid or unenforceable term or provision with a term or provision that is valid and enforceable and that comes closest to expressing the intention of the invalid or unenforceable term or provision, and this Agreement shall be enforceable as so modified. In the event such court does not exercise the power granted to it in the prior sentence, the parties hereto agree to replace such invalid or unenforceable term or provision with a valid and enforceable term or provision that will achieve, to the extent possible, the economic, business and other purposes of such invalid or unenforceable term.

(i) Specific Performance. The parties hereto agree that irreparable damage would occur in the event that any of the provisions of this Agreement were not performed in accordance with their specific terms or were otherwise breached. It is accordingly agreed that the parties shall be entitled to an injunction or injunctions to prevent breaches of this Agreement and to enforce specifically the terms and provisions of this Agreement, this being in addition to any other remedy to which they are entitled at law or in equity.

(j) Notices. All notices and other communications hereunder shall be in writing and shall be deemed duly delivered (i) three Business Days after being sent by registered or certified mail, return receipt requested, postage prepaid, or (ii) one Business Day after being sent for next Business Day delivery, fees prepaid, via a reputable overnight courier service, in each case to the intended recipient as set forth below:

(a) if to Syros, to

Syros Pharmaceuticals, Inc.
35 CambridgePark Drive, 4th Floor
Cambridge, MA 02140
Attention: Nancy Simonian

with a copy (which shall not constitute notice) to:

Wilmer Cutler Pickering Hale and Dorr LLP
60 State Street
Boston, MA 02109
Attention: Cynthia T. Mazareas, Esq.
Joseph B. Conahan,
Esq. Eric P. Hanson, Esq.
Email: cynthia.mazareas@wilmerhale.com
joseph.conahan@wilmerhale.com
eric.hanson@wilmerhale.com
Fax: (617) 526-5000

(b) if to Tyme, to

Tyme Technologies, Inc.
1 Pluckemin Way – Suite 103
Bedminster, NJ 07921
Attention: James Biehl

with a copy (which shall not constitute notice) to:

Faegre Drinker Biddle & Reath LLP
One Logan Square, Suite 2000
Philadelphia, Pennsylvania 19103
Attention: Elizabeth A. Diffley, Esq.
Brandon C. Mason, Esq.
Email: elizabeth.diffley@faegredrinker.com
brandon.mason@faegredrinker.com

(c) if to the Stockholder, to the Stockholder's address, electronic mail address or facsimile shown below Stockholder's signature to this Agreement.

Any party to this Agreement may give any notice or other communication hereunder using any other means (including personal delivery, messenger service, telecopy, ordinary mail or electronic mail), but no such notice or other communication shall be deemed to have been duly given unless and until it actually is received by the party for whom it is intended. Any party to this Agreement may change the address to which notices and other communications hereunder are to be delivered by giving the other parties to this Agreement notice in the manner herein set forth.

(k) Counterparts. This Agreement may be executed in two or more counterparts (including by facsimile, by an electronic scan delivered by electronic mail or any electronic signature), each of which shall be deemed an original but all of which together shall be considered one and the same agreement and shall become effective when counterparts have been signed by each of the parties hereto and delivered to the other parties, it being understood that all parties need not sign the same counterpart. This Agreement may be executed and delivered by facsimile, by an electronic scan delivered by electronic mail or by delivery of any electronic signature.

(l) Interpretation. When reference is made in this Agreement to a Section, such reference shall be to a Section of this Agreement, unless otherwise indicated. The language used in this Agreement shall be deemed to be the language chosen by the parties hereto to express their mutual intent, and no rule of strict construction shall

be applied against any party. Whenever the context may require, any pronouns used in this Agreement shall include the corresponding masculine, feminine or neuter forms, and the singular form of nouns and pronouns shall include the plural, and vice versa. Any reference to any federal, state, local or foreign statute or Law shall be deemed also to refer to all rules and regulations promulgated thereunder, unless the context requires otherwise, in each case as amended, modified, re-enacted thereof, substituted, from time to time. References to any agreement or Contract are to that agreement or Contract as amended, modified or supplemented from time to time in accordance with the terms hereof and thereof. The words "hereof," "herein" and "hereunder" and words of like import used in this Agreement shall refer to this Agreement as a whole and not to any particular provision of this Agreement. Whenever the words "include," "includes" or "including" are used in this Agreement, they shall be deemed to be followed by the words "without limitation." The word "or" is not exclusive. "Writing," "written" and comparable terms refer to printing, typing and other means of reproducing words (including electronic media) in a visible form. References from or through any date shall mean, unless otherwise specified, from and including or through and including, respectively. When used in Agreement, "person" means any natural person or entity, including a governmental authority, as applicable. No summary of this Agreement prepared by any party shall affect the meaning or interpretation of this Agreement.

[Remainder of Page Left Intentionally Blank]

IN WITNESS WHEREOF, the undersigned have caused this Agreement to be duly executed as of the date first above written.

TYME:

TYME TECHNOLOGIES, INC.

By: _____
Name: _____
Title: _____

SIGNATURE PAGE TO SUPPORT AGREEMENT

SYROS:

SYROS PHARMACEUTICALS, INC.

By: _____
Name: _____
Title: _____

SIGNATURE PAGE TO SUPPORT AGREEMENT

[STOCKHOLDER], in his/her capacity as the Stockholder:

Signature: _____

Address:

_____

_____

_____

Outstanding shares of the Syros Common Stock beneficially owned by the Stockholder:_____

Other shares of Syros Common Stock deemed beneficially owned by the Stockholder by virtue of outstanding derivative securities: _____

TYME TECHNOLOGIES, INC.

[FORM OF] SUPPORT AGREEMENT

This Support Agreement (this "Agreement") is made and entered into as of [•], 2022, by and among Syros Pharmaceuticals, Inc. a Delaware corporation ("Syros"), Tyme Technologies, Inc., a Delaware corporation ("Tyme"), and the undersigned stockholder (the "Stockholder") of Tyme.

RECITALS

WHEREAS, concurrently with the execution and delivery hereof, Tyme, Syros and Tack Acquisition Corp., a Delaware corporation and a wholly owned subsidiary of Syros (the "Merger Sub"), have entered into an agreement and plan of merger (as such agreement may be amended or supplemented from time to time pursuant to the terms thereof, the "Merger Agreement"), pursuant to which Merger Sub will merge with and into Tyme, with Tyme surviving the merger as the surviving corporation and a wholly owned subsidiary of Syros (the "Merger").

WHEREAS, the Stockholder is the beneficial owner (as defined in Rule13d-1 under the Exchange Act) of such number of shares of Tyme Common Stock as indicated in the signature page of the Stockholder.

WHEREAS, as an inducement to the willingness of Syros to enter into the Merger Agreement, Syros has required that Stockholder enter into this Agreement.

NOW, THEREFORE, intending to be legally bound, the parties hereby agree as follows:

1. Certain Definitions. Capitalized terms used but not otherwise defined herein shall have the meanings ascribed thereto in the Merger Agreement. For all purposes of this Agreement, the following terms shall have the following respective meanings:

(a) "Constructive Sale" means, with respect to any security, a short sale with respect to such security, entering into or acquiring a derivative contract with respect to such security, entering into or acquiring a futures or forward contract to deliver such security or entering into any other hedging or other derivative transaction that has the effect of either directly or indirectly materially changing the economic benefits or risks of ownership of such security.

(b) "Shares" means (i) all shares of Tyme Common Stock owned, beneficially or of record, by the Stockholder as of the date hereof, and (ii) all additional shares of Tyme Common Stock acquired by the Stockholder, beneficially or of record, during the period commencing with the execution and delivery of this Agreement and expiring on the Closing Date.

(c) "Transfer" or "Transferred" means, with respect to any security, the direct or indirect assignment, sale, transfer, tender, exchange, pledge or hypothecation, or the grant, creation or suffrage of a lien, security interest or encumbrance in or upon, or the gift, grant or placement in trust, or the Constructive Sale or other disposition of such security (including transfers by testamentary or intestate succession, by domestic relations order or other court order, or otherwise by operation of law) or any right, title or interest therein (including any right or power to vote to which the holder thereof may be entitled, whether such right or power is granted by proxy or otherwise), or the record or beneficial ownership thereof, the offer to make such a sale, transfer, Constructive Sale or other disposition, and each agreement, arrangement or understanding, whether or not in writing, to effect any of the foregoing.

2. Transfer and Voting Restrictions. The Stockholder covenants to Tyme and Syros as follows:

(a) During the period commencing with the execution and delivery of this Agreement and expiring on the Expiration Date (as defined below), the Stockholder shall not Transfer any of the Stockholder's Shares, or publicly announce its intention to Transfer any of its Shares.

(b) Except as otherwise permitted by this Agreement or by order of a court of competent jurisdiction, the Stockholder will not commit any act that would restrict the Stockholder's legal power, authority and right to vote all of the Shares held by the Stockholder or otherwise prevent or disable the Stockholder from performing any of his, her or its obligations under this Agreement. Without limiting the generality of the foregoing, except for this Agreement and as otherwise permitted by this Agreement, the Stockholder shall not enter into any voting agreement with any person or entity with respect to any of the Stockholder's Shares, grant any person or entity any proxy (revocable or irrevocable) or power of attorney with respect to any of the Shares, deposit any Shares in a voting trust or otherwise enter into any agreement or arrangement with any person or entity limiting or affecting the Stockholder's legal power, authority or right to vote the Stockholder's Shares in favor of the Tyme Voting Proposals.

(c) Notwithstanding anything else herein to the contrary, the Stockholder may, at any time, Transfer Shares (i) by will or other testamentary document or by intestacy, (ii) to any investment fund or other entity controlled or managed by the Stockholder, (iii) to any member of the Stockholder's immediate family or (iv) to any trust for the direct or indirect benefit of the Stockholder or the immediate family of the Stockholder or otherwise for estate planning purposes; provided, that (x) such Transferred Shares shall continue to be bound by this Agreement and (y) the applicable transferee shall have executed and delivered to Tyme and Syros a support agreement substantially identical to this Agreement upon consummation of such Transfer.

3. Agreement to Vote Shares. The Stockholder covenants to Tyme and Syros as follows:

(a) Until the Expiration Date (as defined below), at any meeting of the stockholders of Tyme, however called, and at every adjournment or postponement thereof, and on every action or approval by written consent of the stockholders of Tyme, the Stockholder shall be present (in person or by proxy) and vote, or exercise its right to consent with respect to, all Shares held by the Stockholder (A) in favor of the Required Tyme Voting Proposal and (B) against any Acquisition Proposal.

(b) If the Stockholder is the beneficial owner, but not the record holder, of Shares, the Stockholder shall cause the record holder and any nominees to be present (in person or by proxy) and vote all the Stockholder's Shares in accordance with this Section 3.

(c) In the event of a stock split, stock dividend or distribution, or any change in the capital stock of Tyme by reason of anysplit-up, reverse stock split, recapitalization, combination, reclassification, reincorporation, exchange of shares or the like, the term "Shares" shall be deemed to refer to and include such shares as well as all such stock dividends and distributions and any securities into which or for which any or all of such shares may be changed or exchanged or which are received in such transaction.

4. Action in Stockholder Capacity Only. The Stockholder is entering into this Agreement solely in the Stockholder's capacity as a record holder and beneficial owner, as applicable, of its Shares and not in the Stockholder's capacity as a director or officer of Tyme. Nothing herein shall limit or affect the Stockholder's ability to act as an officer or director of Tyme, including exercising rights of Tyme under the Merger Agreement, or to exercise Stockholder's fiduciary duties as an officer director.

5. Documentation and Information. The Stockholder shall permit and hereby authorizes Tyme and Syros to publish and disclose in all documents and schedules filed with the SEC, and any press release or other disclosure document that Tyme or Syros reasonably determines to be necessary in connection with the transactions contemplated by the Merger Agreement, such Stockholder's identity and ownership of the Share and the nature of such Stockholder's commitments and obligations under this Agreement.

6. Irrevocable Proxy. The Stockholder hereby revokes (or agrees to cause to be revoked) any proxies that the Stockholder has heretofore granted with respect to its Shares. In the event and to the extent that the Stockholder fails to vote the Shares in accordance with Section 3 at any applicable meeting of the stockholders of Tyme, the Stockholder shall be deemed to have irrevocably granted to, and appointed, Syros, and any individual designated in writing by Syros, and each of them individually, as his, her or its proxy and attorney-in-fact (with full power of substitution), for and in its name, place and stead, to vote his, her or its Shares at any meeting of the Tyme stockholders called with respect to any of the matters specified in, and in accordance and consistent with, Section 3 of this Agreement. Syros agrees not to exercise the proxy granted herein for any purpose other than the purposes described in this Agreement. Except as otherwise provided for herein, the Stockholder hereby affirms that the irrevocable proxy is coupled with an interest and may under no circumstances be revoked and that such irrevocable proxy is executed and intended to be irrevocable. Notwithstanding any other provisions of this Agreement, the irrevocable proxy granted hereunder shall automatically terminate upon the termination of this Agreement.

7. No Solicitation. Subject to Section 4, the Stockholder agrees not to, directly or indirectly, including through any of its officers, directors or agents, (a) solicit, seek or initiate or knowingly take any action to facilitate or encourage, any offers, inquiries or the making of any proposal or offer that constitutes, or could reasonably be expected to lead to, any Acquisition Proposal or (b) enter into, continue or otherwise participate or engage in any discussions or negotiations regarding any Acquisition Proposal, or furnish to any person any non-public information or afford any person, other than Tyme or Syros, as applicable, access to such party's property, books or records (except pursuant to a request by a Governmental Entity) in connection with, any Acquisition Proposal; provided, however, that nothing in this Section 7 shall prevent the Stockholder from referring a person to this Section 7 or to the Merger Agreement.

8. Representations and Warranties of the Stockholder. The Stockholder hereby represents and warrants to Tyme and Syros as follows:

(a) (i) The Stockholder is the beneficial or record owner of the number of shares of Tyme Common Stock indicated on the signature page of the Stockholder (which shall be deemed to be "held" by the Stockholder for purposes of Section 3 unless otherwise expressly stated with respect to any shares in); and (ii) the Stockholder does not beneficially own any securities of Tyme other than the shares of Tyme Common Stock and rights to purchase shares of Tyme Common Stock set forth on the signature page of the Stockholder.

(b) Except as otherwise provided in this Agreement, the Stockholder has full power and authority to (i) make, enter into and carry out the terms of this Agreement and (ii) vote all of its Shares in the manner set forth in this Agreement without the consent or approval of, or any other action on the part of, any other person or entity (including any Governmental Entity). Without limiting the generality of the foregoing, the Stockholder has not entered into any voting agreement (other than this Agreement) with any person with respect to any of the Stockholder's Shares, granted any person any proxy (revocable or irrevocable) or power of attorney with respect to any of the Stockholder's Shares, deposited any of the Stockholder's Shares in a voting trust or entered into any arrangement or agreement with any person limiting or affecting the Stockholder's legal power, authority or right to vote the Stockholder's Shares on any matter, in each case that conflicts with this Agreement.

(c) This Agreement has been duly and validly executed and delivered by the Stockholder and (assuming the due authorization, execution and delivery by the other parties hereto) constitutes a valid and binding agreement of the Stockholder enforceable against the Stockholder in accordance with its terms, subject to the Enforceability Exceptions. The execution and delivery of this Agreement by the Stockholder and the performance by the Stockholder of the agreements and obligations hereunder will not result in any breach or violation of or be in conflict with or constitute a default under any term of any Contract or if applicable any provision of an organizational document (including a certificate of incorporation) to or by which the Stockholder is a party or bound, or any applicable law to which the Stockholder (or any of the Stockholder's assets) is subject or bound, except for any such breach, violation, conflict or default which, individually or in the aggregate, would

not reasonably be expected to materially impair or adversely affect the Stockholder's ability to perform its obligations under this Agreement.

(d) The Stockholder has had the opportunity to review the Merger Agreement and this Agreement with the Stockholder's legal counsel. The Stockholder understands and acknowledges that Syros is entering into the Merger Agreement in reliance upon the Stockholder's execution, delivery and performance of this Agreement.

(e) The execution, delivery and performance of this Agreement by the Stockholder do not and will not require any consent, approval, authorization or permit of, action by, filing with or notification to, any Governmental Authority, except for any such consent, approval, authorization, permit, action, filing or notification the failure of which to make or obtain, individually or in the aggregate, has not and would not materially impair the Stockholder's ability to perform its obligations under this Agreement.

(f) With respect to the Stockholder, as of the date hereof, there is no action, suit, investigation or proceeding pending against, or, to the knowledge of the Stockholder, threatened against, the Stockholder or any of the Stockholder's properties or assets (including the Shares) that would reasonably be expected to prevent or materially delay or impair the ability of the Stockholder to perform its obligations hereunder or to consummate the transactions contemplated hereby.

(g) Neither the Stockholder nor any of its Representatives or Affiliates has employed or made any agreement with any broker, finder or similar agent or any Person which will result in the obligation of such Stockholder, Tyme, Syros, or any of their respective Affiliates to pay any finder's fee, brokerage fees or commission or similar payment in connection with the transactions contemplated hereby.

9. Termination. This Agreement shall terminate and shall cease to be of any further force or effect as of the earlier of (a) such date and time as the Merger Agreement shall have been terminated pursuant to the terms thereof, (b) the Closing, or (c) the date on which the Tyme Voting Proposals shall have been approved by the requisite holders of Tyme Common Stock (the "***Expiration Date***"); provided, however, that (i) Section 10 shall survive the termination of this Agreement, and (ii) the termination of this Agreement shall not relieve any party hereto from any liability for any material and willful breach of this Agreement prior to the Expiration Date.

10. Miscellaneous Provisions.

(a) Amendments. No amendment of this Agreement shall be effective against any party unless it shall be in writing and signed by each of the parties hereto.

(b) Entire Agreement. This Agreement (including the documents and instruments referred to herein that are to be delivered at the Closing) constitutes the entire agreement among the parties to this Agreement and supersedes any prior understandings, agreements or representations by or among the parties hereto, or any of them, written or oral, with respect to the subject matter hereof and the parties hereto expressly disclaim reliance on any such prior understandings, agreements or representations to the extent not embodied in this Agreement.

(c) Governing Law. All matters arising out of or relating to this Agreement (including its interpretation, construction, performance and enforcement) shall be governed by and construed in accordance with the internal laws of the State of Delaware without giving effect to any choice or conflict of Law provision or rule (whether of the State of Delaware or any other jurisdiction) that would cause the application of laws of any jurisdictions other than those of the State of Delaware.

(d) Submission to Jurisdiction. Each of the parties to this Agreement (a) consents to submit itself to the exclusive personal jurisdiction of the Court of Chancery of the State of Delaware, New Castle County, or, if that court does not have jurisdiction, a federal court sitting in Wilmington, Delaware in any action or proceeding arising out of or relating to this Agreement or any of the Contemplated Transactions, (b) agrees that all claims in respect of such action or proceeding shall be heard and determined in any such court, (c) agrees that it shall not

attempt to deny or defeat such personal jurisdiction by motion or other request for leave from any such court and (d) agrees not to bring any action or proceeding arising out of or relating to this Agreement or any of the transaction contemplated by this Agreement in any other court. Each of the parties hereto waives any defense of inconvenient forum to the maintenance of any action or proceeding so brought and waives any bond, surety or other security that might be required of any other party with respect thereto. Any party may make service on another party by sending or delivering a copy of the process to the party to be served at the address and in the manner provided for the giving of notices in Section 10(j). Nothing in this Section 10(d), however, shall affect the right of any party to serve legal process in any other manner permitted by law.

(e) WAIVER OF JURY TRIAL. EACH OF TYME, SYROS AND THE STOCKHOLDER HEREBY IRREVOCABLY WAIVES ALL RIGHT TO TRIAL BY JURY IN ANY ACTION, PROCEEDING OR COUNTERCLAIM (WHETHER BASED ON CONTRACT, TORT OR OTHERWISE) ARISING OUT OF OR RELATING TO THIS AGREEMENT OR THE TRANSACTIONS CONTEMPLATED HEREBY OR THE ACTIONS OF TYME, SYROS OR THE STOCKHOLDER IN THE NEGOTIATION, ADMINISTRATION, PERFORMANCE AND ENFORCEMENT OF THIS AGREEMENT.

(f) Assignment. No party may assign any of its rights or delegate any of its performance obligations under this Agreement, in whole or in part, by operation of Law or otherwise without the prior written consent of the other parties, and any such assignment without such prior written consent shall be null and void. Subject to the preceding sentence, this Agreement shall be binding upon, inure to the benefit of, and be enforceable by, the parties hereto and their respective successors and permitted assigns. Any purported assignment of rights or delegation of performance obligations in violation of this Section 10(f) is void.

(g) No Third Party Rights. This Agreement is not intended to, and shall not, confer upon any other person any rights or remedies hereunder, except as set forth in or contemplated by the terms and provisions set forth herein.

(h) Severability. Any term or provision of this Agreement that is invalid or unenforceable in any situation in any jurisdiction shall not affect the validity or enforceability of the remaining terms and provisions hereof or the validity or enforceability of the offending term or provision in any other situation or in any other jurisdiction. If the final judgment of a court of competent jurisdiction declares that any term or provision hereof is invalid or unenforceable, the parties hereto agree that the court making such determination shall have the power to limit the term or provision, to delete specific words or phrases, or to replace any invalid or unenforceable term or provision with a term or provision that is valid and enforceable and that comes closest to expressing the intention of the invalid or unenforceable term or provision, and this Agreement shall be enforceable as so modified. In the event such court does not exercise the power granted to it in the prior sentence, the parties hereto agree to replace such invalid or unenforceable term or provision with a valid and enforceable term or provision that will achieve, to the extent possible, the economic, business and other purposes of such invalid or unenforceable term.

(i) Specific Performance. The parties hereto agree that irreparable damage would occur in the event that any of the provisions of this Agreement were not performed in accordance with their specific terms or were otherwise breached. It is accordingly agreed that the parties shall be entitled to an injunction or injunctions to prevent breaches of this Agreement and to enforce specifically the terms and provisions of this Agreement, this being in addition to any other remedy to which they are entitled at law or in equity.

(j) Notices. All notices and other communications hereunder shall be in writing and shall be deemed duly delivered (i) three Business Days after being sent by registered or certified mail, return receipt requested, postage prepaid, or (ii) one Business Day after being sent for next Business Day delivery, fees prepaid, via a reputable overnight courier service, in each case to the intended recipient as set forth below:

(a) if to Syros, to

Syros Pharmaceuticals, Inc.
35 CambridgePark Drive, 4th Floor
Cambridge, MA 02140
Attention: Nancy Simonian

with a copy (which shall not constitute notice) to:

Wilmer Cutler Pickering Hale and Dorr LLP
60 State Street
Boston, MA 02109
Attention: Cynthia T. Mazareas, Esq.
Joseph B. Conahan,
Esq. Eric P. Hanson, Esq.
Email: cynthia.mazareas@wilmerhale.com
joseph.conahan@wilmerhale.com
eric.hanson@wilmerhale.com
Fax: (617) 526-5000

(b) if to Tyme, to

Tyme Technologies, Inc.
1 Pluckemin Way – Suite 103
Bedminster, NJ 07921
Attention: James Biehl

with a copy (which shall not constitute notice) to:

Faegre Drinker Biddle & Reath LLP
One Logan Square, Suite 2000
Philadelphia, Pennsylvania 19103
Attention: Elizabeth A. Diffley, Esq.
Brandon C. Mason, Esq.
Email: elizabeth.diffley@faegredrinker.com
brandon.mason@faegredrinker.com

(c) if to the Stockholder, to the Stockholder's address, electronic mail address or facsimile shown below Stockholder's signature to this Agreement.

Any party to this Agreement may give any notice or other communication hereunder using any other means (including personal delivery, messenger service, telecopy, ordinary mail or electronic mail), but no such notice or other communication shall be deemed to have been duly given unless and until it actually is received by the party for whom it is intended. Any party to this Agreement may change the address to which notices and other communications hereunder are to be delivered by giving the other parties to this Agreement notice in the manner herein set forth.

(k) Counterparts. This Agreement may be executed in two or more counterparts (including by facsimile, by an electronic scan delivered by electronic mail or any electronic signature), each of which shall be deemed an original but all of which together shall be considered one and the same agreement and shall become effective when counterparts have been signed by each of the parties hereto and delivered to the other parties, it being understood that all parties need not sign the same counterpart. This Agreement may be executed and delivered by facsimile, by an electronic scan delivered by electronic mail or by delivery of any electronic signature.

(l) Interpretation. When reference is made in this Agreement to a Section, such reference shall be to a Section of this Agreement, unless otherwise indicated. The language used in this Agreement shall be deemed to be the language chosen by the parties hereto to express their mutual intent, and no rule of strict construction shall

be applied against any party. Whenever the context may require, any pronouns used in this Agreement shall include the corresponding masculine, feminine or neuter forms, and the singular form of nouns and pronouns shall include the plural, and vice versa. Any reference to any federal, state, local or foreign statute or Law shall be deemed also to refer to all rules and regulations promulgated thereunder, unless the context requires otherwise, in each case as amended, modified, re-enacted thereof, substituted, from time to time. References to any agreement or Contract are to that agreement or Contract as amended, modified or supplemented from time to time in accordance with the terms hereof and thereof. The words "hereof," "herein" and "hereunder" and words of like import used in this Agreement shall refer to this Agreement as a whole and not to any particular provision of this Agreement. Whenever the words "include," "includes" or "including" are used in this Agreement, they shall be deemed to be followed by the words "without limitation." The word "or" is not exclusive. "Writing," "written" and comparable terms refer to printing, typing and other means of reproducing words (including electronic media) in a visible form. References from or through any date shall mean, unless otherwise specified, from and including or through and including, respectively. When used in Agreement, "person" means any natural person or entity, including a governmental authority, as applicable. No summary of this Agreement prepared by any party shall affect the meaning or interpretation of this Agreement.

[Remainder of Page Left Intentionally Blank]

IN WITNESS WHEREOF, the undersigned have caused this Agreement to be duly executed as of the date first above written.

TYME:
TYME TECHNOLOGIES, INC.

By: _____
Name: _____
Title: _____

SIGNATURE PAGE TO SUPPORT AGREEMENT

SYROS:

SYROS PHARMACEUTICALS, INC.

By: _____

Name: _____

Title: _____

SIGNATURE PAGE TO SUPPORT AGREEMENT

[STOCKHOLDER],
in his/her capacity as the Stockholder:

Signature: _____

Address:

_____

_____

_____

Outstanding shares of the Tyme Common Stock beneficially
owned by the Stockholder:_____

Other shares of Tyme Common Stock deemed beneficially owned by the Stockholder by virtue of outstanding derivative securities: _____

SECURITIES PURCHASE AGREEMENT

This SECURITIES PURCHASE AGREEMENT (this "**Agreement**") is made and entered into as of July 3, 2022 (the "**Execution Date**") by and among Syros Pharmaceuticals, Inc., a Delaware corporation (the "**Company**"), and the Investors identified on **Exhibit A** attached hereto (each an "**Investor**" and collectively the "**Investors**").

RECITALS

A. On or prior to the date hereof, (i) the Company has entered into that certain Agreement and Plan of Merger (as in effect as of the date hereof, the "**Merger Agreement**"), with Tack Acquisition Corp., a Delaware corporation and wholly-owned subsidiary of the Company ("**Merger Sub**"), and Tyme Technologies, Inc., a Delaware corporation (the "**Target**"), in substantially the form provided to the Investors prior to the date hereof, pursuant to which, prior to the Closing (as defined below), the Merger Sub shall merge with and into the Target and, at the Closing, Target, as the surviving entity, shall be a wholly-owned subsidiary of the Company (the "**Merger**").

B. The Company and the Investors are executing and delivering this Agreement in reliance upon the exemption from securities registration afforded by the provisions of Section 4(a)(2) of the 1933 Act (as defined below), and Rule 506 of Regulation D ("**Regulation D**") as promulgated by the SEC (as defined below) under the 1933 Act;

C. In connection with and contingent on the closing of the Merger (the "**Merger Closing**"), as contemplated by the Merger Agreement, the Investors wish to purchase from the Company, and the Company wishes to sell and issue to the Investors, upon the terms and subject to the conditions stated in this Agreement, (A) shares (the "**Shares**") of the Company's Common Stock, par value $0.001 per share (the "**Common Stock**") and/or pre-funded warrants to purchase Common Stock in the form attached hereto as **Exhibit B** (the "**Pre-Funded Warrants**") and (B) warrants to purchase either Common Stock or Pre-Funded Warrants, at the election of the holder, in the form attached hereto as **Exhibit C** (the "**Warrants**"); and

D. Contemporaneously with the sale of the Shares, the Pre-Funded Warrants and the Warrants, the parties hereto will execute and deliver a Registration Rights Agreement, in the form attached hereto as **Exhibit D** (the "**Registration Rights Agreement**"), pursuant to which the Company will agree to provide certain registration rights in respect of the Shares and the Warrant Shares (as defined below) under the 1933 Act and applicable state securities laws.

In consideration of the mutual promises made herein and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the parties hereto agree as follows:

1. **Definitions**. For the purposes of this Agreement, the following terms shall have the meanings set forth below:

"**Affiliate**" means, with respect to any Person, any other Person which directly or indirectly through one or more intermediaries Controls, is controlled by, or is under common Control with such Person.

"**Business Day**" means a day, other than a Saturday or Sunday, on which banks in New York City are open for the general transaction of business.

"**Bylaws**" means the Company's Second Amended and Restated By-Laws.

"**Certificate of Incorporation**" means the Company's Restated Certificate of Incorporation.

"**Closing**" has the meaning set forth in Section 3.1.

"**Closing Date**" has the meaning set forth in Section 3.1.

"**Closing Securities**" means the Shares, the Pre-Funded Warrants and the Warrants sold at Closing.

"**Common Stock**" has the meaning set forth in the recitals to this Agreement.

"**Company Covered Person**" means, with respect to the Company as an "issuer" for purposes of Rule 506 promulgated under the 1933 Act, any Person listed in the first paragraph of Rule 506(d)(1).

"**Company's Knowledge**" means the actual knowledge of the executive officers (as defined in Rule 405 under the 1933 Act) of the Company.

"**Control**" (including the terms "controlling," "controlled by" or "under common control with") means the possession, direct or indirect, of the power to direct or cause the direction of the management and policies of a Person, whether through the ownership of voting securities, by contract or otherwise.

"**Disqualification Event**" has the meaning set forth in Section 4.33.

"**EDGAR system**" has the meaning set forth in Section 4.9.

"**Environmental Laws**" has the meaning set forth in Section 4.15.

"**GAAP**" has the meaning set forth in Section 4.17.

"**Governmental Entity**" means any national, federal, state, municipal, local, territorial, foreign or other government or any department, commission, board, bureau, agency, regulatory authority or instrumentality thereof, or any court, judicial, administrative or arbitral body or public or private tribunal.

"**HSR Act**" has the meaning set forth in Section 7.9.

"**Intellectual Property**" has the meaning set forth in Section 4.14.

"**Investor Questionnaire**" has the meaning set forth in Section 5.8.

"**Material Adverse Effect**" means a material adverse effect on (i) the assets, liabilities, results of operations, financial condition or business of the Company and its subsidiaries taken as a whole, (ii) the legality or enforceability of any of the Transaction Documents or (iii) the ability of the Company to perform its obligations under the Transaction Documents, except that for purposes of Section 6.1(i) of this Agreement, in no event shall a change in the market price of the Common Stock alone constitute a "Material Adverse Effect".

"**Material Contract**" means any contract, instrument or other agreement to which the Company is a party or by which it is bound that has been filed or was required to have been filed as an exhibit to the SEC Filings pursuant to Item 601(b)(4) or Item 601(b)(10) of Regulation S-K.

"**Nasdaq**" means the Nasdaq Global Select Market.

"**Person**" means an individual, corporation, partnership, limited liability company, trust, business trust, association, joint stock company, joint venture, sole proprietorship, unincorporated organization, governmental authority or any other form of entity not specifically listed herein.

"**Placement Agents**" means Cowen and Company, LLC and Piper Sandler & Co.

"**Pre-Funded Warrants**" has the meaning set forth in the recitals to this Agreement.

"**Press Release**" has the meaning set forth in Section 9.8.

"**Principal Trading Market**" means the Trading Market on which the Common Stock is primarily listed on and quoted for trading, which, as of the date of this Agreement and the Closing Date, shall be the Nasdaq Global Select Market.

"**Prior Registration Rights Agreement**" means that certain Registration Rights Agreement, dated December 4, 2020, by and among the Company and the other parties thereto.

"**Registration Rights Agreement**" has the meaning set forth in the recitals to this Agreement.

"**Regulation D**" has the meaning set forth in the recitals to this Agreement.

"**Regulatory Authorities**" has the meaning set forth in Section 4.30.

"**Required Investors**" has the meaning set forth in the Registration Rights Agreement.

"**Sanctions**" has the meaning set forth in Section 4.25.

"**Sanctioned Country**" has the meaning set forth in Section 4.25.

"**SEC**" means the U.S. Securities and Exchange Commission.

"**SEC Filings**" has the meaning set forth in Section 4.8.

"**Securities**" means the Shares, the Pre-Funded Warrants, the Warrants, and the Warrant Shares.

"**Shares**" has the meaning set forth in the recitals to this Agreement.

"**Short Sales**" means all "short sales" as defined in Rule 200 of Regulation SHO under the 1934 Act (but shall not be deemed to include the location and/or reservation of borrowable shares of Common Stock).

"**Stockholder Approval**" has the meaning set forth in Section 7.2.

"**Trading Day**" means (i) a day on which the Common Stock is listed or quoted and traded on its Principal Trading Market (other than the OTC Bulletin Board), or (ii) if the Common Stock is not listed on a Trading Market (other than the OTC Bulletin Board), a day on which the Common Stock is traded in the over-the-counter market, as reported by the OTC Bulletin Board, or (iii) if the Common Stock is not quoted on any Trading Market, a day on which the Common Stock is quoted in the over-the-counter market as reported in the "pink sheets" by OTC Markets Group Inc. (or any similar organization or agency succeeding to its functions of reporting prices); provided, that in the event that the Common Stock is not listed or quoted as set forth in (i), (ii) or (iii) hereof, then Trading Day shall mean a Business Day.

"**Trading Market**" means whichever of the New York Stock Exchange, the NYSE American, the Nasdaq Global Select Market, the Nasdaq Global Market, the Nasdaq Capital Market or the OTC Bulletin Board on which the Common Stock is listed or quoted for trading on the date in question.

"**Transfer Agent**" has the meaning set forth in Section 7.2(a).

"**Transaction Documents**" means this Agreement, the Pre-Funded Warrants, the Warrants and the Registration Rights Agreement.

"**Warrants**" has the meaning set forth in the recitals to this Agreement.

"**Warrant Shares**" means the shares of Common Stock issuable upon exercise of the Warrants and the Pre-Funded Warrants.

"**1933 Act**" means the Securities Act of 1933, as amended, or any successor statute, and the rules and regulations promulgated thereunder.

"**1934 Act**" means the Securities Exchange Act of 1934, as amended, or any successor statute, and the rules and regulations promulgated thereunder.

2. **Purchase and Sale of the Securities**. On the Closing Date, upon the terms and subject to the conditions set forth herein, the Company will issue and sell, and each Investor will purchase, severally and not jointly, (A) the number of Shares set forth opposite the name of such Investor under the heading "Number of Shares" on **Exhibit A** attached hereto, (B) a Pre-Funded Warrant to purchase the number of Warrant Shares set forth opposite the name of such Investor under the heading "Number of Warrant Shares Underlying Pre-Funded Warrant" on **Exhibit A** attached hereto, if any, and (C) a Warrant to purchase the number of Warrant Shares set forth opposite the name of such Investor under the heading "Number of Warrant Shares Underlying Warrant" on **Exhibit A** attached hereto. The Shares and Pre-Funded Warrants will be sold in fixed combinations with the Warrants, with each Investor receiving a Warrant to purchase one share of Common Stock per each Share or Warrant Share underlying a Pre-Funded Warrant purchased by such Investor. The purchase price per Share and accompanying Warrant shall be $0.94. The purchase price per Pre-Funded Warrant and accompanying Warrant shall be $0.9399. The Pre-Funded Warrants shall have an exercise price equal to $0.0001 per Warrant Share. The Warrants shall have an exercise price equal to $1.034 per Warrant Share.

3. **Closing.**

3.1 Upon the satisfaction of the conditions set forth in Section 6, the completion of the purchase and sale of the Closing Securities (the "**Closing**") shall occur remotely via exchange of documents and signatures on the date of, and substantially concurrently with (but contingent upon), the consummation of the Merger (the date of the Closing, the "**Closing Date**").

3.2 Upon delivery of written notice from (or on behalf of) the Company to each Investor (the "**Closing Notice**") that the Company reasonably expects all conditions to the closing of the Merger to be satisfied or waived on a date that is not less than five (5) business days from the date on which the Closing Notice is delivered to each such Investor, each Investor, on the Closing Date, shall deliver or cause to be delivered to the Company, via wire transfer of immediately available funds pursuant to the wire instructions specified by the Company in the Closing Notice, an amount equal to the purchase price to be paid by the Investor for the Closing Securities to be acquired by it as set forth opposite the name of such Investor under the heading "Aggregate Purchase Price of Securities" on **Exhibit A** attached hereto.

3.3 At the Closing, the Company shall deliver or cause to be delivered to each Investor (A) a number of Shares, registered in the name of the Investor (or its nominee in accordance with its delivery instructions), equal to the number of Shares set forth opposite the name of such Investor under the heading "Number of Shares" on **Exhibit A** attached hereto, (B) a Pre-Funded Warrant, registered in the name of the Investor (or its nominee in accordance with its delivery instructions), to purchase up to the number of Warrant Shares set forth opposite the name of such Investor under the heading "Number of Warrant Shares Underlying Pre-Funded Warrant" on **Exhibit A** attached hereto, if any, and (C) a Warrant, registered in the name of the Investor (or its nominee in accordance with its delivery instructions), to purchase the number of Warrant Shares set forth opposite the name of such Investor under the heading "Number of Warrant Shares Underlying Warrant". The Shares shall be delivered via a book-entry record through the Transfer Agent. Unless the Company and an Investor otherwise mutually agree with respect to such Investor's Shares, at Closing settlement shall occur on a "delivery versus payment" basis.

4. **Representations and Warranties of the Company**. The Company hereby represents and warrants to the Investors that, except (a) as described in the Company's SEC Filings filed at least one Trading Day prior to the Execution Date and (b) as set forth on the disclosure schedule delivered herewith (which is arranged in numbered and lettered sections corresponding to the numbered and lettered sections contained in this Section 4) (the "**Disclosure Schedule**"), each of which qualify these representations and warranties in their entirety:

4.1 **Organization, Good Standing and Qualification**. The Company is a corporation duly organized, validly existing and in good standing under the laws of the jurisdiction of its incorporation and has all requisite corporate power and authority to carry on its business as now conducted and to own or lease its properties. The Company is duly qualified to do business as a foreign corporation and is in good standing in each jurisdiction in which the conduct of its business or its ownership or leasing of property makes such qualification or leasing necessary unless the failure to so qualify has not had and would not reasonably be expected to have a Material Adverse Effect. Syros Securities Corporation, a Massachusetts corporation, and Syros Pharmaceuticals (Ireland) Limited, an Irish limited liability company, are the only subsidiaries of the Company and are wholly-owned by the Company. Each subsidiary of the Company has been duly incorporated or organized and is validly existing and in good standing (or such equivalent concepts to the extent they exist under the law of such jurisdiction) under the laws of the jurisdiction of its incorporation or organization, and have all requisite power and authority to carry on their business as now conducted and to own or lease their properties. The Company's subsidiaries are duly qualified to do business and are in good standing (or such equivalent concept to the extent it exists under the law of such jurisdiction) in each jurisdiction in which the conduct of their business or their ownership or leasing of property makes such qualification necessary unless the failure to so qualify has not had and would not reasonably be expected to have a Material Adverse Effect.

4.2 **Authorization**. The Company has the requisite corporate power and authority and has taken all requisite corporate action necessary for, and no further action on the part of the Company, its officers, directors and stockholders is necessary for, (i) the authorization, execution and delivery of the Transaction Documents, (ii) the authorization of the performance of all obligations of the Company hereunder or thereunder, and (iii) the authorization, issuance (or reservation for issuance) and delivery of the Securities, subject to obtaining Stockholder Approval. The Transaction Documents constitute the legal, valid and binding obligations of the Company, enforceable against the Company in accordance with their terms, subject to bankruptcy, insolvency, fraudulent transfer, reorganization, moratorium and similar laws of general applicability, relating to or affecting creditors' rights generally and to general equitable principles.

4.3 **Capitalization**. The Company is authorized under its Certificate of Incorporation to issue 200,000,000 shares of Common Stock. The Company's disclosure of its issued and outstanding capital stock in its most recent SEC Filing containing such disclosure was accurate in all material respects as of the date indicated in such SEC Filing. Since the date indicated in such SEC Filing, there has not been any change the Company's capital stock, other than as a result of the exercise of stock options or the award of stock options or restricted stock units in the ordinary course of business pursuant to the Company's stock-based compensation plans described in the SEC Filings. All of the issued and outstanding shares of the Company's capital stock have been duly authorized and validly issued and are fully paid and nonassessable; none of such shares were issued in violation of any preemptive rights; and such shares were issued in compliance in all material respects with applicable state and federal securities law and any rights of third parties. No Person is entitled to preemptive or similar statutory or contractual rights with respect to the issuance by the Company of any securities of the Company, including, without limitation, the Securities. Except for stock options and restricted stock units approved pursuant to Company stock-based compensation plans described in the SEC Filings and warrants described in the SEC Filings, there are no outstanding warrants, options, convertible securities or other rights, agreements or arrangements of any character under which the Company is or may be obligated to issue any equity securities of any kind, except as contemplated by this Agreement and the Merger Agreement. Except (a) for the Registration Rights Agreement and the Prior Registration Rights Agreement and (b) as set forth on the Disclosure Schedule, there are no voting agreements, buy-sell agreements, option or right of first purchase agreements or other agreements of any kind among the Company and any of the securityholders of the Company relating to the

securities of the Company held by them. Except (a) as provided in the Registration Rights Agreement and the Prior Registration Rights Agreement and (b) as set forth on the Disclosure Schedule, no Person has the right to require the Company to register any securities of the Company under the 1933 Act, whether on a demand basis or in connection with the registration of securities of the Company for its own account or for the account of any other Person.

The issuance and sale of the Securities hereunder will not obligate the Company to issue shares of Common Stock or other securities to any other Person (other than the Investors) and will not result in the adjustment of the exercise, conversion, exchange or reset price of any outstanding security.

The Company does not have outstanding stockholder purchase rights or "poison pill" or any similar arrangement in effect giving any Person the right to purchase any equity interest in the Company upon the occurrence of certain events.

4.4 **Valid Issuance**. Subject to receipt of the Stockholder Approval, the Shares will be duly and validly authorized and, when issued and paid for pursuant to this Agreement, will be validly issued, fully paid and nonassessable, and shall be free and clear of all encumbrances and restrictions (other than those created by the Investors), except for restrictions on transfer set forth in the Transaction Documents or imposed by applicable securities laws. Subject to receipt of the Stockholder Approval, the Warrant Shares will be duly and validly authorized and reserved for issuance and, upon exercise of the Pre-Funded Warrants or Warrants, as applicable, in accordance with their respective terms, including the payment of any exercise price therefor, will be validly issued, fully paid and nonassessable and will be free and clear of all encumbrances and restrictions (other than those created by the Investors), except for restrictions on transfer set forth in the Transaction Documents or imposed by applicable securities laws. Assuming the accuracy of the representations and warranties of each Investor in Section 5 hereof, the Warrant Shares will be issued in compliance with all applicable federal and state securities laws.

4.5 **Consents**. Subject to the accuracy of the representations and warranties of each Investor set forth in Section 5 hereof, the execution, delivery and performance by the Company of the Transaction Documents and the offer, issuance and sale of the Securities require no consent of, action by or in respect of, or filing with, any Person, governmental body, agency, or official other than (a) the Stockholder Approval, (b) filings that have been made pursuant to applicable state securities laws, (c) post-sale filings pursuant to applicable state and federal securities laws, (d) filings pursuant to the rules and regulations of Nasdaq, including with respect to obtaining Stockholder Approval, (e) filing of the registration statement required to be filed by the Registration Rights Agreement, (f) filings required by the 1933 Act, 1934 Act, and the rules of the SEC, including the registration statement on Form S-4 with respect to the Merger and the proxy statement/prospectus included therein, and (g) filings required to consummate the Merger as provided under the Merger Agreement, each of which the Company has filed or undertakes to file within the applicable time. Subject to the accuracy of the representations and warranties of each Investor set forth in Section 5 hereof, the Company has taken all action necessary to exempt (i) the issuance and sale of the Securities and (ii) the other transactions contemplated by the Transaction Documents from the provisions of any stockholder rights plan or other "poison pill" arrangement, any anti-takeover, business combination or control share law or statute binding on the Company or to which the Company or any of its assets and properties is subject that is or could reasonably be expected to become applicable to the Investors as a result of the transactions contemplated hereby, including without limitation, the issuance of the Securities and the ownership, disposition or voting of the Shares or the Warrant Shares by the Investors or the exercise of any right granted to the Investors pursuant to this Agreement or the other Transaction Documents.

4.6 **Use of Proceeds**. The net proceeds of the sale of the Securities hereunder shall be used by the Company for advancement of the Company's clinical development pipeline, business development activities, working capital and general corporate purposes.

4.7 **No Material Adverse Change**. Since March 31, 2022, except as identified and described in the SEC Filings filed at least one Trading Day prior to the date hereof, there has not been:

(i) any change in the consolidated assets, liabilities, financial condition or operating results of the Company from that reflected in the financial statements included in the Company's Quarterly Report on Form 10-Q for the quarter ended March 31, 2022, except for changes in the ordinary course of business which have not had and would not reasonably be expected to have a Material Adverse Effect, individually or in the aggregate;

(ii) any declaration or payment by the Company of any dividend, or any authorization or payment by the Company of any distribution, on any of the capital stock of the Company, or any redemption or repurchase by the Company of any securities of the Company;

(iii) any material damage, destruction or loss, whether or not covered by insurance, to any assets or properties of the Company;

(iv) any waiver, not in the ordinary course of business, by the Company of a material right or of a material debt owed to it;

(v) any satisfaction or discharge of any lien, claim or encumbrance or payment of any obligation by the Company, except in the ordinary course of business and which is not material to the assets, properties, financial condition, operating results or business of the Company (as such business is presently conducted);

(vi) any change or amendment to the Company's Certificate of Incorporation or Bylaws, or material change to any Material Contract or arrangement by which the Company is bound or to which any of its assets or properties is subject;

(vii) any material labor difficulties or, to the Company's Knowledge, labor union organizing activities with respect to employees of the Company;

(viii) any material transaction entered into by the Company other than in the ordinary course of business;

(ix) the loss of the services of any key employee, or material change in the composition or duties of the senior management of the Company; or

(x) any other event or condition of any character that has had or would reasonably be expected to have a Material Adverse Effect.

4.8 **SEC Filings**. The Company has timely filed all reports, schedules, forms, statements and other documents required to be filed by the Company under the 1933 Act and the 1934 Act, including pursuant to Section 13(a) or 15(d) thereof, for the one year period preceding the date hereof (collectively, the "**SEC Filings**"). At the time of filing thereof, the SEC Filings complied in all material respects with the requirements of the 1933 Act or the 1934 Act, as applicable, and the rules and regulations of the SEC thereunder.

4.9 **No Conflict, Breach, Violation or Default**. The execution, delivery and performance of the Transaction Documents by the Company and the issuance and sale of the Securities in accordance with the provisions thereof will not, except (solely in the case of clause (i)(b) and clause (ii)) for such violations, conflicts or defaults as would not reasonably be expected, individually or in the aggregate, to have a Material Adverse Effect, (i) conflict with or result in a breach or violation of (a) any of the terms and provisions of, or constitute a default under, the Company's Certificate of Incorporation or the Company's Bylaws, both as in effect on the date hereof (true and complete copies of which have been made available to the Investors through the Electronic Data Gathering, Analysis, and Retrieval system (the "**EDGAR system**")), or (b) assuming the accuracy of the representations and warranties in Section 5 and subject to the Stockholder Approval, any applicable statute, rule, regulation or order

of any governmental agency or body or any court, domestic or foreign, having jurisdiction over the Company or its subsidiaries, or any of their assets or properties, or (ii) conflict with, or constitute a default (or an event that with notice or lapse of time or both would become a default) under, result in the creation of any lien, encumbrance or other adverse claim upon any of the properties or assets of the Company or its subsidiaries or give to others any rights of termination, amendment, acceleration or cancellation (with or without notice, lapse of time or both) of, any Material Contract. This Section 4.9 does not relate to matters with respect to tax status, which are the subject of Section 4.10, employee relations and labor matters, which are the subject of Section 4.13, or environmental laws, which are the subject of Section 4.15.

4.10 **Tax Matters**. The Company and its subsidiaries have timely prepared and filed all material tax returns required to have been filed by them with all appropriate governmental agencies and timely paid all material taxes shown thereon or otherwise owed by them. There are no material unpaid assessments against the Company nor, to the Company's Knowledge, any audits by any federal, state or local taxing authority. All material taxes that the Company is required to withhold or to collect for payment have been duly withheld and collected and paid to the proper governmental entity or third party when due. There are no tax liens pending or, to the Company's Knowledge, threatened against the Company or any of its assets or property. With the exception of agreements or other arrangements that are not primarily related to taxes entered into in the ordinary course of business, there are no outstanding tax sharing agreements or other such arrangements between the Company and any other corporation or entity (other than a subsidiary of the Company).

4.11 **Title to Properties**. The Company and its subsidiaries have good and marketable title to all real properties and all other material properties and assets owned by them, in each case free from liens, encumbrances and defects, except such as would not reasonably be expected, individually or in the aggregate, to have a Material Adverse Effect; and the Company and its subsidiaries hold any leased real or personal property under valid and enforceable leases with no exceptions, except such as would not reasonably be expected, individually or in the aggregate, to have a Material Adverse Effect.

4.12 **Certificates, Authorities and Permits**. The Company possesses adequate certificates, authorities or permits issued by appropriate governmental agencies or bodies necessary to conduct the business now operated by it, except where failure to so possess would not reasonably be expected, individually or in the aggregate, to result in a Material Adverse Effect. The Company has not received any written notice of proceedings relating to the revocation or modification of any such certificate, authority or permit that would reasonably be expected to have a Material Adverse Effect, individually or in the aggregate, on the Company.

4.13 **Labor Matters**.

(a) Neither the Company nor any of its subsidiaries is a party to or bound by any collective bargaining agreements or other agreements with labor organizations. To the Company's Knowledge, neither the Company nor any of its subsidiaries has violated in any material respect any laws, regulations, orders or contract terms affecting the collective bargaining rights of employees or labor organizations, or any laws, regulations or orders affecting employment discrimination, equal opportunity employment, or employees' health, safety, welfare, wages and hours.

(b) No material labor dispute with the employees of the Company or any of its subsidiaries, or with the employees of any principal supplier, manufacturer, customer or contractor of the Company or any of its subsidiaries, exists or, to the Company's Knowledge, is threatened or imminent.

4.14 **Intellectual Property**. The Company and its subsidiaries own, possess, license or have other rights to use, all patents, patent applications, trade and service marks, trade and service mark registrations, trade names, copyrights, licenses, inventions, trade secrets, technology, know-how and other intellectual property (collectively, the "**Intellectual Property**") necessary for the conduct of the Company's business in all material respects as now conducted or as proposed in the SEC Filings to be conducted; and (a) there are no rights of third

parties to any such Intellectual Property, including no liens, security interests or other encumbrances; (b) to the Company's Knowledge, there is no material infringement by third parties of any such Intellectual Property; (c) there is no pending or, to the Company's Knowledge, threatened action, suit, proceeding or claim by others challenging the Company's rights in or to any such Intellectual Property; (d) such Intellectual Property that is described in the SEC Filings has not been adjudged by a court of competent jurisdiction invalid or unenforceable, in whole or in part; (e) there is no pending or, to the Company's Knowledge, threatened action, suit, proceeding or claim by others challenging the validity or scope of any such Intellectual Property that is owned or licensed by the Company, including interferences, oppositions, reexaminations or government proceedings; (f) there is no pending or, to the Company's Knowledge, threatened action, suit, proceeding or claim by others that the Company infringes, misappropriates, or otherwise violates any patent, trademark, copyright, trade secret or other proprietary rights of others; and (g) each key employee of the Company and each Company employee involved with the development of Intellectual Property has entered into an invention assignment agreement with the Company.

4.15 **Environmental Matters**. Neither the Company nor any of its subsidiaries is in violation of any statute, rule, regulation, decision or order of any governmental agency or body or any court, domestic or foreign, relating to the use, disposal or release of hazardous or toxic substances or relating to the protection or restoration of the environment or human exposure to hazardous or toxic substances (collectively, "**Environmental Laws**"), nor has the Company or any of its subsidiaries released any hazardous substances regulated by Environmental Law onto any real property that it owns or operates, and has not received any written notice or claim it is liable for any off-site disposal or contamination pursuant to any Environmental Laws, which violation, release, notice, claim, or liability would reasonably be expected, individually or in the aggregate, to have a Material Adverse Effect, and to the Company's Knowledge, there is no pending or threatened investigation that would reasonably be expected to lead to such a claim.

4.16 **Legal Proceedings**. There are no legal, governmental or regulatory investigations, actions, suits or proceedings pending, or to the Company's Knowledge, threatened to which the Company or its subsidiaries are a party or to which any property of the Company or its subsidiaries are the subject that, individually or in the aggregate, would reasonably be expected to have a Material Adverse Effect.

4.17 **Financial Statements**. The financial statements included in each SEC Filing comply in all material respects with applicable accounting requirements and the rules and regulations of the SEC with respect thereto as in effect at the time of filing (or to the extent corrected by a subsequent restatement) and present fairly, in all material respects, the consolidated financial position of the Company as of the dates shown and its consolidated results of operations and cash flows for the periods shown, subject in the case of unaudited financial statements to normal, immaterial year-end audit adjustments, and such consolidated financial statements have been prepared in conformity with United States generally accepted accounting principles applied on a consistent basis during the periods involved ("**GAAP**") (except as may be disclosed therein or in the notes thereto, and except that the unaudited financial statements may not contain all footnotes required by GAAP, and, in the case of quarterly financial statements, except as permitted by Form 10-Q under the 1934 Act). Except as set forth in the financial statements of the Company included in the SEC Filings filed prior to the date hereof, the Company has not incurred any liabilities, contingent or otherwise, except those incurred in the ordinary course of business, consistent (as to amount and nature) with past practices since the date of such financial statements, none of which, individually or in the aggregate, have had or would reasonably be expected to have a Material Adverse Effect.

4.18 **Insurance Coverage**. The Company maintains in full force and effect insurance coverage that is customary for comparably situated companies for the business being conducted and properties owned or leased by the Company, and the Company reasonably believes such insurance coverage to be adequate against all liabilities, claims and risks against which it is customary for comparably situated companies to insure.

4.19 **Compliance with Nasdaq Continued Listing Requirements**. The Company is in compliance with applicable Nasdaq continued listing requirements. There are no proceedings pending or, to the Company's

Knowledge, threatened against the Company relating to the continued listing of the Common Stock on Nasdaq and the Company has not received any notice of, nor to the Company's Knowledge is there any reasonable basis for, the delisting of the Common Stock from Nasdaq.

4.20 **Brokers and Finders**. Other than the Placement Agents, no Person will have, as a result of the transactions contemplated by the Transaction Documents, any valid right, interest or claim against or upon the Company or an Investor for any commission, fee or other compensation pursuant to any agreement, arrangement or understanding entered into by or on behalf of the Company. No Investor shall have any obligation with respect to any fees, or with respect to any claims made by or on behalf of other Persons for fees, in each case of the type contemplated by this Section 4.20 that may be due in connection with the transactions contemplated by this Agreement or the Transaction Documents.

4.21 **No Directed Selling Efforts or General Solicitation**. Neither the Company nor any Person acting on its behalf has conducted any general solicitation or general advertising (as those terms are used in Regulation D) in connection with the offer or sale of any of the Securities.

4.22 **No Integrated Offering**. Neither the Company nor its subsidiaries nor any Person acting on their behalf has, directly or indirectly, made any offers or sales of any Company security or solicited any offers to buy any Company security, under circumstances that would (i) adversely affect reliance by the Company on Section 4(a)(2) and Rule 506(b) of Regulation D for the exemption from registration for the transactions contemplated hereby or would require registration of the Securities under the 1933 Act or (ii) cause the offer and sale of the Securities pursuant to this Agreement to be integrated with prior offerings by the Company for purposes of any applicable law, regulation or stockholder approval provisions.

4.23 **Private Placement**. Assuming the accuracy of the representations and warranties of the Investors set forth in Section 5, the offer and sale of the Closing Securities to the Investors and the exercise of the Pre-Funded Warrants and Warrants as contemplated hereby are exempt from the registration requirements of the 1933 Act. The issuance and sale of the Closing Securities and the exercise of the Pre-Funded Warrants and Warrants do not contravene the rules and regulations of Nasdaq.

4.24 **Questionable Payments**. Neither the Company nor its subsidiaries nor, to the Company's Knowledge, any of their current or former directors, officers, employees, agents or other Persons acting on behalf of the Company or its subsidiaries, has on behalf of the Company or its subsidiaries in connection with their business: (a) used any corporate funds for unlawful contributions, gifts, entertainment or other unlawful expenses relating to political activity; (b) made any direct or indirect unlawful payments to any governmental officials or employees from corporate funds; (c) established or maintained any unlawful or unrecorded fund of corporate monies or other assets which is in violation of law; (d) made any false or fictitious entries on the books and records of the Company; (e) made any unlawful bribe, rebate, payoff, influence payment, kickback or other unlawful payment of any nature or (f) violated or is in violation of any provision of the Foreign Corrupt Practices Act of 1977, as amended.

4.25 **No Conflicts with Sanctions Laws**. Neither the Company nor any of its subsidiaries, directors, officers or employees, nor, to the Company's Knowledge, any agent, affiliate or other person associated with or acting on behalf of the Company or any of its subsidiaries is currently the subject or the target of any sanctions administered or enforced by the U.S. government (including, without limitation, the Office of Foreign Assets Control of the U.S. Department of the Treasury or the U.S. Department of State and including, without limitation, the designation as a "specially designated national" or "blocked person"), the United Nations Security Council, the European Union, Her Majesty's Treasury or other relevant sanctions authority (collectively, "**Sanctions**"), nor is the Company or any of its subsidiaries located, organized or resident in a country or territory that is the subject or target of Sanctions, including, without limitation, Cuba, Iran, North Korea, Syria, the Crimea region of Ukraine, the so-called Donetsk People's Republic, and the so-called Luhansk People's Republic (each, a "**Sanctioned Country**"); and the Company and its subsidiaries will not directly or indirectly use the proceeds of

the offering of the Securities hereunder, or lend, contribute or otherwise make available such proceeds to any subsidiary, joint venture partner or other person or entity (i) to fund or facilitate any activities of or business with any person that, at the time of such funding or facilitation, is the subject or target of Sanctions, (ii) to fund or facilitate any activities of or business in any Sanctioned Country or (iii) in any other manner that will result in a violation by any person (including any person participating in the transaction, whether as underwriter, advisor, investor or otherwise) of Sanctions. For the past five years, the Company and its subsidiaries have not knowingly engaged in and are not now knowingly engaged in any dealings or transactions with any person that at the time of the dealing or transaction is or was the subject or the target of Sanctions or with any Sanctioned Country.

4.26 **Transactions with Affiliates**. None of the executive officers or directors of the Company and, to the Company's Knowledge, none of the employees of the Company is presently a party to any transaction with the Company (other than as holders of stock options, restricted stock units, warrants and/or restricted stock, and for services as employees, officers and directors), including any contract, agreement or other arrangement providing for the furnishing of services to or by, providing for rental of real or personal property to or from, or otherwise requiring payments to or from any officer, director or such employee or, to the Company's Knowledge, any entity in which any officer, director, or any such employee has a substantial interest or is an officer, director, trustee or partner.

4.27 **Internal Controls**. The Company has established and maintains disclosure controls and procedures (as defined in Rules 13a-15 and 15d-15 under the 1934 Act), which (a) are designed to ensure that material information relating to the Company, including its subsidiaries, is made known to the Company's principal executive officer and its principal financial officer by others within those entities; (b) have been evaluated by management of the Company for effectiveness as of the end of the Company's most recent fiscal quarter; and (c) are effective in all material respects to perform the functions for which they were established. Since the end of the Company's most recent audited fiscal year, there have been no material weaknesses in the Company's internal control over financial reporting (whether or not remediated) and no change in the Company's internal control over financial reporting that has materially affected, or would reasonably be expected to materially affect, the Company's internal control over financial reporting. The Company is not aware of any change in its internal controls over financial reporting that has occurred during its most recent fiscal quarter that has materially affected, or would reasonably be expected to materially affect, the Company's internal control over financial reporting.

4.28 **Disclosures**. Neither the Company nor any Person acting on its behalf has provided the Investors or their agents or counsel with any information that constitutes or would reasonably be expected to constitute material nonpublic information concerning the Company or its subsidiaries, other than with respect to the transactions contemplated hereby, which will be disclosed in the Press Release (as defined below) or in a Form 8-K filed with the SEC no later than the Business Day immediately following the date this Agreement is executed. The SEC Filings do not contain any untrue statement of a material fact or omit to state a material fact required to be stated therein or necessary in order to make the statements contained therein, in light of the circumstances under which they were made, not misleading. The Company understands and confirms that the Investors will rely on the foregoing representations in effecting transactions in securities of the Company.

4.29 **Required Filings**. Except for the transactions contemplated by this Agreement, including the acquisition of the Securities contemplated hereby, no event or circumstance has occurred or information exists with respect to the Company or its business, properties, operations or financial condition, which, under applicable law, rule or regulation, requires public disclosure or announcement by the Company but which has not been so publicly announced or disclosed (assuming for this purpose that the SEC Filings are being incorporated by reference into an effective registration statement filed by the Company under the 1933 Act).

4.30 **Investment Company**. The Company is not required to be registered as, and immediately following the Closing will not be required to register as, an "investment company" within the meaning of the Investment Company Act of 1940, as amended.

4.31 **Tests and Preclinical and Clinical Trials**. (i) The preclinical studies and clinical trials conducted by or on behalf of or sponsored by the Company or its subsidiaries, or in which the Company or its subsidiaries have participated, that are described in the SEC Filings, or the results of which are referred to in the SEC Filings, as applicable, were, and if still pending are, being conducted in all material respects in accordance with standard medical and scientific research standards and procedures for products or product candidates comparable to those being developed by the Company and all applicable statutes and all applicable rules and regulations of the U.S. Food and Drug Administration and comparable regulatory agencies outside of the United States to which they are subject, including the European Medicines Agency (collectively, the "**Regulatory Authorities**") and Good Clinical Practice and Good Laboratory Practice requirements; (ii) the descriptions in the SEC Filings of the results of such studies and trials are accurate and complete descriptions in all material respects and fairly present the data derived therefrom; (iii) to the Company's Knowledge, there are no other studies or trials not described in the SEC Filings, the results of which the Company believes are inconsistent with or reasonably call into question the results described or referred to in the SEC Filings; (iv) the Company and its subsidiaries have operated at all times and are currently in compliance with all applicable statutes, rules and regulations of the Regulatory Authorities, except where such non-compliance would not, individually or in the aggregate, have a Material Adverse Effect; and (v) neither the Company nor any of its subsidiaries have received any written notices, correspondence or other communications from the Regulatory Authorities or any other governmental agency requiring or threatening the termination, material modification or suspension of any preclinical studies or clinical trials that are described in the SEC Filings or the results of which are referred to in the SEC Filings, other than ordinary course communications with respect to modifications in connection with the design and implementation of such studies or trials.

4.32 **Manipulation of Price**. The Company has not taken, and, to the Company's Knowledge, no Person acting on its behalf has taken, directly or indirectly, any action designed to cause or to result in the stabilization or manipulation of the price of any security of the Company to facilitate the sale or resale of any of the Securities.

4.33 **Anti-Bribery and Anti-Money Laundering Laws**. Each of the Company, its subsidiaries and any of their respective officers, directors, supervisors, managers, agents, or employees, are and have at all times been in compliance with and its participation in the offering will not violate: (A) anti-bribery laws, including but not limited to, any applicable law, rule, or regulation of any locality, including but not limited to any law, rule, or regulation promulgated to implement the OECD Convention on Combating Bribery of Foreign Public Officials in International Business Transactions, signed December 17, 1997, including the U.S. Foreign Corrupt Practices Act of 1977, as amended, the U.K. Bribery Act 2010, or any other law, rule or regulation of similar purposes and scope or (B) anti-money laundering laws, including, but not limited to, applicable federal, state, international, foreign or other laws, regulations or government guidance regarding anti-money laundering, including, without limitation, Title 18 US. Code sections 1956 and 1957, the Patriot Act, the Bank Secrecy Act, and international anti-money laundering principles or procedures by an intergovernmental group or organization, such as the Financial Action Task Force on Money Laundering, of which the United States is a member and with which designation the United States representative to the group or organization continues to concur, all as amended, and any Executive order, directive, or regulation pursuant to the authority of any of the foregoing, or any orders or licenses issued thereunder.

4.34 **No Bad Actors**. No "bad actor" disqualifying event described in Rule 506(d)(1)(i)-(viii) of the 1933 Act (a "**Disqualification Event**") is applicable to the Company or, to the Company's Knowledge, any Company Covered Person, except for a Disqualification Event as to which Rule 506(d)(2)(ii–iv) or (d)(3) is applicable.

4.35 **No Additional Agreements**. Except as set forth on the Disclosure Schedule, the Company has no other agreements or understandings (including, without limitation, side letters) with any Investor or any other party to purchase Securities or any other equity or equity-linked securities of the Company on terms more favorable to such Investor or other party than as set forth herein.

4.36 **Shell Company Status**. The Company is not, and has never been, an issuer identified in Rule 144(i)(1).

4.37 **Compliance**. The Company is not (i) in default under or in violation of (and no event has occurred that has not been waived that, with notice or lapse of time or both, would result in a default by the Company under), nor has the Company received notice of a claim that it is in default under or that it is in violation of, any indenture, loan or credit agreement or any other agreement or instrument to which it is a party or by which it or any of its properties is bound (whether or not such default or violation has been waived) or (ii) in violation of any judgment, decree or order of any court, arbitrator or governmental body, except in each case as could not have or reasonably be expected to result in a Material Adverse Effect.

4.38 **Authorization of Merger Agreement**. All necessary corporate action has been duly and validly taken by the Company and the Merger Sub to authorize the execution, delivery and performance of the Merger Agreement. The Merger Agreement has been duly and validly authorized by all necessary corporate action on the part of the Company and the Merger Sub, executed and delivered by the Company and the Merger Sub and constitutes legal, valid and binding obligations of the Company and the Merger Sub enforceable against the Company and the Merger Sub in accordance with its terms, except as the enforceability thereof may be limited by bankruptcy, insolvency, reorganization, fraudulent conveyance, moratorium or other similar laws relating to or affecting the enforcement of creditors' rights generally and by general principles of equity or public policy (regardless of whether enforcement is sought in a proceeding at law or in equity). To the knowledge of the Company, the representations and warranties of the Target contained in Article III of the Merger Agreement (as qualified therein and in the disclosure schedules thereto) were, as of the date of the Merger Agreement, and are, as of the date hereof (except to the extent such representations and warranties are made as of another date, in which case such representations and warranties are true and correct as of that date), true and accurate in all material respects (or, if any such representations or warranties are qualified by materiality, material adverse effect or similar language, true and correct in all respects). The Company has furnished or otherwise made available to each Investor a true and substantially complete copy of the Merger Agreement as in effect as of the date hereof.

5. **Representations and Warranties of the Investors**. Each of the Investors hereby severally, and not jointly, represents and warrants to the Company that:

5.1 **Organization and Existence**. Such Investor is a duly incorporated or organized and validly existing corporation, limited partnership, limited liability company or other legal entity, has all requisite corporate, partnership or limited liability company power and authority to enter into and consummate the transactions contemplated by the Transaction Documents and to carry out its obligations hereunder and thereunder, and to invest in the Securities pursuant to this Agreement, and is in good standing under the laws of the jurisdiction of its incorporation or organization.

5.2 **Authorization**. The execution, delivery and performance by such Investor of the Transaction Documents to which such Investor is a party have been duly authorized and each has been duly executed and when delivered will constitute the valid and legally binding obligation of such Investor, enforceable against such Investor in accordance with their respective terms, subject to bankruptcy, insolvency, fraudulent transfer, reorganization, moratorium and similar laws of general applicability, relating to or affecting creditors' rights generally, and general principles of equity.

5.3 **Purchase Entirely for Own Account**. The Securities to be received by such Investor hereunder will be acquired for such Investor's own account, not as nominee or agent, for the purpose of investment and not with a view to the resale or distribution of any part thereof in violation of the 1933 Act, and such Investor has no present intention of selling, granting any participation in, or otherwise distributing the same in violation of the 1933 Act without prejudice, however, to such Investor's right at all times to sell or otherwise dispose of all or any part of such Securities in compliance with applicable federal and state securities laws. The Securities are being purchased by such Investor in the ordinary course of its business. Nothing contained herein shall be deemed a representation or warranty by such Investor to hold the Securities for any period of time. Such Investor is not a broker-dealer registered with the SEC under the 1934 Act or an entity engaged in a business that would require it to be so registered.

5.4 **Investment Experience**. Such Investor acknowledges that it can bear the economic risk and complete loss of its investment in the Securities and has such knowledge and experience in financial or business matters that it is capable of evaluating the merits and risks of the investment contemplated hereby.

5.5 **Disclosure of Information**. Such Investor has had an opportunity to receive, review and understand all information related to the Company requested by it and to ask questions of and receive answers from the Company regarding the Company, its business and the terms and conditions of the offering of the Securities, and has conducted and completed its own independent due diligence. Such Investor acknowledges that copies of the SEC Filings are available on the EDGAR system. Based on the information such Investor has deemed appropriate, and without reliance on the Placement Agents, it has independently made its own analysis and decision to enter into the Transaction Documents. Such Investor is relying exclusively on its own investment analysis and due diligence (including professional advice it deems appropriate) with respect to the execution, delivery and performance of the Transaction Documents, the Securities and the business, condition (financial and otherwise), management, operations, properties and prospects of the Company, including but not limited to all business, legal, regulatory, accounting, credit and tax matters. Neither such inquiries nor any other due diligence investigation conducted by such Investor shall modify, limit or otherwise affect such Investor's right to rely on the Company's representations and warranties contained in this Agreement. Such Investor understands that the Placement Agents have acted solely as the agents of the Company in this placement of the Shares and such Investor has not relied on the business or legal advice of the Placement Agents or any of their agents, counsel or affiliates in making its investment decision hereunder, and confirms that none of such persons has made any representations or warranties to such Investor in connection with the transactions contemplated hereby.

5.6 **Restricted Securities**. Such Investor understands that the Securities are characterized as "restricted securities" under the U.S. federal securities laws inasmuch as they are being acquired from the Company in a transaction not involving a public offering and that under such laws and applicable regulations such securities may be resold without registration under the 1933 Act only in certain limited circumstances.

5.7 **Legends**. It is understood that, except as provided below, certificates or book-entry positions evidencing the Securities may bear the following or any similar legend:

(a) "These securities represented hereby [and the securities issuable upon exercise of these securities] have not been registered with the Securities and Exchange Commission or the securities commission of any state but have been [or will be] issued in reliance upon an exemption from registration under the Securities Act of 1933, as amended, and, accordingly, may not be transferred unless (i) such securities have been registered for sale pursuant to the Securities Act of 1933, as amended, (ii) such securities may be sold pursuant to Rule 144, (iii) the Company has received an opinion of counsel reasonably satisfactory to it that such transfer may lawfully be made without registration under the Securities Act of 1933, as amended, or (iv) the securities are transferred without consideration to an affiliate of such holder or a custodial nominee (which for the avoidance of doubt shall require neither consent nor the delivery of an opinion)."

(b) If required by the authorities of any state in connection with the issuance of sale of the Securities, the legend required by such state authority.

5.8 **Accredited Investor**. Such Investor is (a) an "accredited investor" within the meaning of Rule 501(a) of Regulation D. Such Investor has executed and delivered to the Company a questionnaire in substantially the form attached hereto as **Exhibit E** (the "**Investor Questionnaire**"), which such Investor represents and warrants is true, correct and complete. Such investor is a sophisticated institutional investor with sufficient knowledge and experience in investing in private equity transactions to properly evaluate the risks and merits of its purchase of the Securities. Such Investor has determined based on its own independent review and such professional advice as it deems appropriate that its purchase of the Securities and participation in the transactions contemplated by the Transaction Documents (i) are fully consistent with its financial needs, objectives and condition, (ii) comply and are fully consistent with all investment policies, guidelines and other restrictions applicable to such Investor,

(iii) have been duly authorized and approved by all necessary action, (iv) do not and will not violate or constitute a default under such Investor's charter, bylaws or other constituent document or under any law, rule, regulation, agreement or other obligation by which such Investor is bound and (v) are a fit, proper and suitable investment for such Investor, notwithstanding the substantial risks inherent in investing in or holding the Securities.

5.9 **No General Solicitation**. Such Investor did not learn of the investment in the Securities as a result of any general or public solicitation or general advertising, or publicly disseminated advertisements or sales literature, including (a) any advertisement, article, notice or other communication published in any newspaper, magazine, website, or similar media, or broadcast over television or radio, or (b) any seminar or meeting to which such Investor was invited by any of the foregoing means of communications.

5.10 **Brokers and Finders**. Other than the Placement Agents, no Person will have, as a result of the transactions contemplated by the Transaction Documents, any valid right, interest or claim against or upon the Company or an Investor for any commission, fee or other compensation pursuant to any agreement, arrangement or understanding entered into by or on behalf of such Investor.

5.11 **Short Sales and Confidentiality Prior to the Date Hereof** Other than consummating the transactions contemplated hereunder, such Investor has not, nor has any Person acting on behalf of or pursuant to any understanding with such Investor, directly or indirectly executed any purchases or sales, including Short Sales, of the securities of the Company during the period commencing as of the time that such Investor was first contacted by the Company, the Placement Agents or any other Person regarding the transactions contemplated hereby and ending immediately prior to the date hereof. Notwithstanding the foregoing, in the case of an Investor that is a multi-managed investment vehicle whereby separate portfolio managers manage separate portions of such Investor's assets and the portfolio managers have no direct knowledge of the investment decisions made by the portfolio managers managing other portions of such Investor's assets, the representation set forth above shall only apply with respect to the portion of assets managed by the portfolio manager that made the investment decision to purchase the Securities covered by this Agreement. Other than to other Persons party to this Agreement and other than to such Person's outside attorney, accountant, auditor or investment advisor only to the extent deemed reasonably necessary by such Investor to permit evaluation of the investment, and the performance of the necessary or required tax, accounting, financial, legal, or administrative tasks and services and other than as may be required by law, such Investor has maintained the confidentiality of all disclosures made to it in connection with this transaction (including the existence and terms of this transaction). Notwithstanding the foregoing, for avoidance of doubt, nothing contained herein shall constitute a representation or warranty, or preclude any actions, with respect to the identification of the availability of, or securing of, available shares to borrow in order to effect Short Sales or similar transactions in the future.

5.12 **No Government Recommendation or Approval**. Such Investor understands that no United States federal or state agency, or similar agency of any other country, has reviewed, approved, passed upon, or made any recommendation or endorsement of the Company or the purchase of the Securities.

5.13 **No Intent to Effect a Change of Control**. Such Investor has no present intent to effect a "change of control" of the Company as such term is understood under the rules promulgated pursuant to Section 13(d) of the 1934 Act.

5.14 **Residency**. Such Investor's office in which its investment decision with respect to the Securities was made is located at the address immediately below such Investor's name on its signature page hereto.

5.15 **No Conflicts**. The execution, delivery and performance by such Investor of the Transaction Documents and the consummation by such Investor of the transactions contemplated hereby and thereby will not (i) result in a violation of the organizational documents of such Investor, (ii) conflict with, or constitute a default (or an event which with notice or lapse of time or both would become a default) under, or give to others any rights of termination, amendment, acceleration or cancellation of, any agreement, indenture or instrument to which such

Investor is a party, or (iii) result in a violation of any law, rule, regulation, order, judgment or decree (including federal and state securities laws) applicable to such Investor, except in the case of clauses (ii) and (iii) above, for such conflicts, defaults, rights or violations which would not, individually or in the aggregate, reasonably be expected to have a material adverse effect on the ability of such Investor to perform its obligations hereunder.

5.16 **Placement Agents.** Such Investor hereby acknowledges and agrees that (a) each of the Placement Agents is acting solely as placement agent in connection with the execution, delivery and performance of the Transaction Documents and is not acting as an underwriter or in any other capacity and is not and shall not be construed as a fiduciary for such Investor, the Company or any other person or entity in connection with the execution, delivery and performance of the Transaction Documents, (b) no Placement Agent has made or will make any representation or warranty, whether express or implied, of any kind or character, or has provided any advice or recommendation in connection with the execution, delivery and performance of the Transaction Documents, (c) no Placement Agent will have any responsibility with respect to (i) any representations, warranties or agreements made by any person or entity under or in connection with the execution, delivery and performance of the Transaction Documents, or the execution, legality, validity or enforceability (with respect to any person) thereof, or (ii) the business, affairs, financial condition, operations, properties or prospects of, or any other matter concerning the Company, and (d) no Placement Agent will have any liability or obligation (including without limitation, for or with respect to any losses, claims, damages, obligations, penalties, judgments, awards, liabilities, costs, expenses or disbursements incurred by such Investor, the Company or any other person or entity), whether in contract, tort or otherwise, to such Investor, or to any person claiming through it, in respect of the execution, delivery and performance of the Transaction Documents.

6. **Conditions to Closing**.

6.1 **Conditions to the Investors' Obligations**. The obligation of each Investor to purchase the Closing Securities is subject to the fulfillment to such Investor's satisfaction, on or prior to the Closing Date, of the following conditions, any of which may be waived by such Investor (as to itself only):

(a) The representations and warranties made by the Company in Section 4 hereof, as qualified by the Disclosure Schedule and the SEC Filings filed at least one Trading Day prior to the Execution Date, shall be true and correct in all material respects, except for those representation and warranties qualified by materiality or Material Adverse Effect, which shall be true and correct in all respects, as of the date hereof and as of the Closing Date, as though made on and as of such date, except to the extent any such representation or warranty expressly speaks as of an earlier date, in which case such representation or warranty shall be true and correct in all material respects as of such earlier date. The Company shall have performed in all material respects all obligations and covenants herein required to be performed by it on or prior to the Closing Date.

(b) The Company shall have obtained any and all consents, permits, approvals, registrations and waivers necessary for the consummation of the purchase and sale of the Closing Securities and the consummation of the other transactions contemplated by the Transaction Documents (other than the Stockholder Approval), all of which shall be in full force and effect.

(c) The Company shall have executed and delivered the Registration Rights Agreement.

(d) The Company shall have filed with Nasdaq a Notification Form: Listing of Additional Shares for the listing of the Shares and the Warrant Shares, and Nasdaq shall have raised no objection to the consummation of the transactions contemplated by the Transaction Documents.

(e) All conditions precedent to the closing of the Merger set forth in the Merger Agreement, including, without limitation, the approval of the Company's stockholders and the Target's stockholders, shall have been satisfied (as determined by the parties to the Merger Agreement, and other than those conditions which, by their nature, are to be satisfied at the closing of the Merger) or waived in writing by the party entitled to the benefit thereof under the Merger Agreement, and the Merger Closing shall be scheduled to occur concurrently with the Closing.

(f) The terms of the Merger Agreement (as in effect on the date hereof) shall not have been amended, modified or waived in a manner that would reasonably be expected to materially and adversely affect the economic benefits that the Investor (in its capacity as such) would reasonably expect to receive under this Agreement unless the Investor has consented in writing to such amendment, modification or waiver.

(g) The Company shall have obtained the Stockholder Approval.

(h) No judgment, writ, order, injunction, award or decree of or by any court, or judge, justice or magistrate, including any bankruptcy court or judge, or any order of or by any governmental authority, shall have been issued, and no action or proceeding shall have been instituted by any governmental authority, enjoining or preventing the consummation of the transactions contemplated hereby or in the other Transaction Documents.

(i) The Company shall have delivered a Certificate, executed on behalf of the Company by its Chief Executive Officer or its Chief Financial Officer, dated as of the Closing Date, certifying to the fulfillment of the conditions specified in subsections (a), (b), (d), (e), (f), (g), (h), (l) and (m) of this Section 6.1.

(j) The Company shall have delivered a Certificate, executed on behalf of the Company by its Secretary, dated as of the Closing Date, certifying the resolutions adopted by the Board of Directors of the Company approving the transactions contemplated by this Agreement, the other Transaction Documents, the issuance of the Securities, certifying the current versions of the Certificate of Incorporation and Bylaws of the Company and certifying as to the signatures and authority of persons signing the Transaction Documents and related documents on behalf of the Company.

(k) The Investors shall have received an opinion from Wilmer Cutler Pickering Hale and Dorr LLP, the Company's counsel, dated as of the Closing Date, in form and substance reasonably acceptable to the Investors.

(l) There shall have been no Material Adverse Effect with respect to the Company since the date hereof.

(m) No stop order or suspension of trading shall have been imposed by Nasdaq, the SEC or any other governmental or regulatory body with respect to public trading in the Common Stock.

6.2 **Conditions to Obligations of the Company**. The Company's obligation to sell and issue Closing Securities to any Investor is subject to the fulfillment to the satisfaction of the Company on or prior to the Closing Date of the following conditions, any of which may be waived by the Company:

(a) The representations and warranties made by such Investor in Section 5 hereof shall be true and correct in all material respects as of the date hereof, and shall be true and correct in all material respects, except for those representations and warranties qualified by materiality or material adverse effect, which shall be true and correct in all respects, as of the date hereof and as of the Closing Date, as though made on and as of such date, except to the extent any such representation or warranty expressly speaks as of an earlier date, in which case such representation or warranty shall be true and correct in all material respects as of such earlier date. Such Investor shall have performed in all material respects all obligations and covenants herein required to be performed by it on or prior to the Closing Date.

(b) Such Investor shall have executed and delivered the Registration Rights Agreement and an Investor Questionnaire.

(c) Any Investor purchasing Closing Securities shall have paid in full its purchase price to the Company.

6.3 **Termination of Obligations to Effect Closing; Effects.**

(a) The obligations of the Company, on the one hand, and the Investors, on the other hand, to effect the Closing shall terminate as follows:

(i) Upon the mutual written consent of the Company and Investors that agreed to purchase a majority of the Shares to be issued and sold pursuant to this Agreement; or

(ii) By either the Company or any Investor (with respect to itself only) if the Closing has not occurred on or prior to the date that is six (6) months after the date hereof if the Merger Closing has not occurred on or before such date;

provided, however, that, except in the case of clause (i) above, the party seeking to terminate its obligation to effect the Closing shall not then be in breach of any of its representations, warranties, covenants or agreements contained in this Agreement or the other Transaction Documents if such breach has resulted in the circumstances giving rise to such party's seeking to terminate its obligation to effect the Closing.

(b) In the event of termination by the Company or any Investor of its obligations to effect the Closing pursuant to Section 6.3(a)(ii), written notice thereof shall be given to the other Investors by the Company and the other Investors shall have the right to terminate their obligations to effect the Closing upon written notice to the Company and the other Investors. Nothing in this Section 6.3 shall be deemed to release any party from any liability for any breach by such party of the terms and provisions of this Agreement or the other Transaction Documents or to impair the right of any party to compel specific performance by any other party of its obligations under this Agreement or the other Transaction Documents.

7. **Covenants and Agreements of the Parties**

7.1 **Nasdaq Listing**. The Company will use commercially reasonable efforts to continue the listing and trading of its Common Stock on Nasdaq and, in accordance therewith, will use commercially reasonable efforts to comply in all material respects with the Company's reporting, filing and other obligations under the bylaws or rules of such market or exchange, as applicable.

7.2 **Stockholder Approval**. Prior to the Closing Date, the Company shall hold a special meeting of stockholders providing for the approval of (i) an amendment to the Company's Certificate of Incorporation to increase the number of authorized shares of Common Stock to enable the issuance or reservation for issuance, as applicable, of all of the Securities in compliance with the rules and regulations of Nasdaq and (ii) to the extent required, the issuance of the Closing Securities in compliance with Nasdaq Listing Rule 5635(b) and/or (d) (the "**Stockholder Approval**"), with the recommendation of the Company's Board of Directors that such proposal(s) be approved, and the Company shall solicit proxies from its stockholders in connection therewith in the same manner as all other management proposals in such proxy statement and all management-appointed proxyholders shall vote their proxies in favor of such proposal(s).

7.3 **Removal of Legends**.

(a) In connection with any sale, assignment, transfer or other disposition of the Shares or Warrant Shares by an Investor pursuant to Rule 144 or pursuant to any other exemption under the 1933 Act such that the purchaser acquires freely tradable shares and upon compliance by the Investor with the requirements of this Agreement, if requested by the Investor, the Company shall request the transfer agent for the Common Stock (the "**Transfer Agent**") to timely remove any restrictive legends related to the book entry account holding such shares and make a new, unlegended entry for such book entry shares sold or disposed of without restrictive legends within two (2) Trading Days of any such request therefor from such Investor, provided that the Company has timely received from the Investor customary representations and other documentation reasonably acceptable to the Company in connection therewith.

(b) Subject to receipt from the Investor by the Company and the Transfer Agent of customary representations and other documentation reasonably acceptable to the Company and the Transfer Agent in connection therewith,

upon the earliest of such time as the Shares or Warrant Shares (i) have been registered under the 1933 Act pursuant to an effective registration statement, (ii) have been sold pursuant to Rule 144, or (iii) are eligible for resale under Rule 144(b)(1) or any successor provision, the Company shall, in accordance with the provisions of this Section 7.3(b) and within two (2) Trading Days of any request therefor from an Investor accompanied by such customary and reasonably acceptable documentation referred to above, (A) deliver to the Transfer Agent irrevocable instructions that the Transfer Agent shall make a new, unlegended entry for such book entry shares, and (B) cause its counsel to deliver to the Transfer Agent one or more opinions to the effect that the removal of such legends in such circumstances may be effected under the 1933 Act if required by the Transfer Agent to effect the removal of the legend in accordance with the provisions of this Agreement. Any shares subject to legend removal under this Section 7.3 may be transmitted by the Transfer Agent to the Investor by crediting the account of the Investor's prime broker with the DTC System as directed by such Investor. The Company shall be responsible for the fees of its Transfer Agent and all DTC fees associated with such issuance.

7.4 **Transfer Restrictions**. Each Investor agrees that it will sell, transfer or otherwise dispose of the Securities only in compliance with all applicable state and federal securities laws and that any Securities sold by such Investor pursuant to an effective registration statement will be sold in compliance with the plan of distribution set forth therein.

7.5 **Subsequent Equity Sales by the Company.** The Company shall not, and shall use its commercially reasonable efforts to ensure that no Affiliate of the Company shall, sell, offer for sale or solicit offers to buy or otherwise negotiate in respect of any security (as defined in Section 2 of the 1933 Act) that will be integrated with the offer or sale of the Securities in a manner that would require the registration under the 1933 Act of the sale of the Securities to the Investors, or that will be integrated with the offer or sale of the Securities for purposes of the rules and regulations of any trading market such that it would require stockholder approval prior to the closing of such other transaction unless stockholder approval is obtained before the closing of such subsequent transaction. The Company shall not take any action or steps that would adversely affect reliance by the Company on Section 4(a)(2) and Regulation D for the exemption from registration for the transactions contemplated hereby or require registration of the Securities under the 1933 Act.

7.6 **Fees**. The Company shall be responsible for the payment of any placement agent's fees, financial advisory fees, or broker's commissions (other than for Persons engaged by any Investor) relating to or arising out of the transactions contemplated hereby, including, without limitation, any fees or commissions payable to the Placement Agents.

7.7 **Reservation of Common Stock**. Subject to the Stockholder Approval, the Company will reserve and keep available at all times, free of preemptive rights, a sufficient number of shares of Common Stock for the purpose of enabling the Company to issue all of the Warrant Shares upon conversion of any Pre-Funded Warrant or Warrant.

7.8 **Short Sales and Confidentiality After the Date Hereof**. Each Investor covenants that it will not, nor will it cause any Affiliates acting on its behalf or pursuant to any understanding with it to, execute any Short Sales during the period from the date hereof until the earlier of such time as (i) the transactions contemplated by this Agreement are first publicly announced or (ii) this Agreement is terminated in full. Notwithstanding the foregoing, in the case of an Investor that is a multi-managed investment vehicle whereby separate portfolio managers manage separate portions of such Investor's assets and the portfolio managers have no direct knowledge of the investment decisions made by the portfolio managers managing other portions of such Investor's assets, the covenant set forth above shall only apply with respect to the portion of assets managed by the portfolio manager that made the investment decision to purchase the Securities covered by this Agreement. Each Investor covenants that until such time as the transactions contemplated by this Agreement are publicly disclosed by the Company, such Investor will maintain the confidentiality of all disclosures made to it in connection with this transaction (including the existence and terms of this transaction), other than to such Person's outside attorney, accountant, auditor or investment advisor only to the extent necessary to permit

evaluation of the investment, and the performance of the necessary or required tax, accounting, financial, legal, or administrative tasks and services and other than as may be required by law. Each Investor understands and acknowledges that the SEC currently takes the position that coverage of Short Sales of shares of the Common Stock "against the box" prior to effectiveness of a resale registration statement with securities included in such registration statement would be a violation of Section 5 of the 1933 Act, as set forth in Item 239.10 of the Securities Act Rules Compliance and Disclosure Interpretations compiled by the Office of Chief Counsel, Division of Corporation Finance.

7.9 **Tax Matters**. The parties agree that the Pre-Funded Warrants are intended to and shall be treated as stock in the Company for U.S. federal, state and local income tax purposes, and the parties shall file their tax returns and otherwise act consistently with such treatment except as otherwise required by a final determination within the meaning of Section 1313 of the Internal Revenue Code of 1986, as amended.

7.10 **Filings**. The Company shall make all filings with the SEC and its Trading Market as required by the transactions contemplated hereby. With respect to any exercise of a Pre-Funded Warrant or Warrant into Common Stock, the Company and each Investor (i) shall use their respective commercially reasonable efforts to promptly file or cause to be filed, (x) within 10 Business Days from the date that either the Company or any Investor provides any notice of exercise (for which within five Business Days the Investor determines that a filing under the Hart Scott-Rodino Antitrust Improvements Act of 1976, as amended (the "**HSR Act**"), is required, and so notifies the Company), all required filings under the HSR Act and, (y) as promptly as reasonably practicable, all required filings under other applicable antitrust laws that the Company or any Investor reasonably determines in good faith to be necessary or appropriate to effect the transactions contemplated by this Agreement including but not limited to, the exercise of any Pre-Funded Warrant or Warrant into Common Stock, (ii) shall consult and cooperate with each other in the preparation of such filings, and (iii) shall promptly inform the other parties of any material communication received by such party from any Governmental Entity regarding the transactions contemplated by this Agreement and shall enable the other party to participate in any communications and meetings with any Governmental Entity regarding the transactions contemplated by this Agreement unless prohibited by the Governmental Entity. Each of the Company and any Investor that files such notice pursuant to the HSR Act or any other applicable antitrust law in accordance with the preceding sentence acknowledges that no exercise of any Pre-Funded Warrant or Warrant into Common Stock will be consummated until any waiting period prescribed under the HSR Act or any other applicable antitrust law has elapsed.

8. **Survival and Indemnification**.

8.1 **Survival**. The representations, warranties, covenants and agreements contained in this Agreement shall survive the Closing of the transactions contemplated by this Agreement for the applicable statute of limitations.

8.2 **Indemnification**. The Company agrees to indemnify and hold harmless each Investor and its Affiliates, and their respective directors, officers, trustees, members, managers, employees, investment advisers and agents, from and against any and all losses, claims, damages, liabilities and expenses (including without limitation reasonable and documented attorney fees and disbursements and other documented out-of-pocket expenses reasonably incurred in connection with investigating, preparing or defending any action, claim or proceeding, pending or threatened and the costs of enforcement thereof) to which such Person may become subject as a result of any breach of representation, warranty, covenant or agreement made by or to be performed on the part of the Company under the Transaction Documents, and will reimburse any such Person for all such amounts as they are incurred by such Person solely to the extent such amounts have been finally judicially determined not to have resulted from such Person's fraud or willful misconduct.

8.3 **Conduct of Indemnification Proceedings.** Any person entitled to indemnification hereunder shall (i) give prompt written notice to the indemnifying party of any claim with respect to which it seeks indemnification and (ii) permit such indemnifying party to assume the defense of such claim with counsel reasonably satisfactory to the indemnified party; *provided* that any person entitled to indemnification hereunder shall have the right to

employ separate counsel and to participate in the defense of such claim, but the fees and expenses of such counsel shall be at the expense of such person unless (a) the indemnifying party has agreed in writing to pay such fees or expenses, (b) the indemnifying party shall have failed to assume the defense of such claim and employ counsel reasonably satisfactory to such person or (c) in the reasonable judgment of any such person, based upon written advice of its counsel, a conflict of interest exists between such person and the indemnifying party with respect to such claims (in which case, if the person notifies the indemnifying party in writing that such person elects to employ separate counsel at the expense of the indemnifying party, the indemnifying party shall not have the right to assume the defense of such claim on behalf of such person); and *provided, further*, that the failure of any indemnified party to give written notice as provided herein shall not relieve the indemnifying party of its obligations hereunder, except to the extent that such failure to give notice shall materially adversely affect the indemnifying party in the defense of any such claim or litigation. It is understood that the indemnifying party shall not, in connection with any proceeding in the same jurisdiction, be liable for fees or expenses of more than one separate firm of attorneys at any time for all such indemnified parties. No indemnifying party will, except with the consent of the indemnified party, which consent shall not be unreasonably withheld, conditioned or delayed, consent to entry of any judgment or enter into any settlement that does not include as an unconditional term thereof the giving by the claimant or plaintiff to such indemnified party of a release from all liability in respect of such claim or litigation. No indemnified party will, except with the consent of the indemnifying party, which consent shall not be unreasonably withheld, conditioned or delayed, consent to entry of any judgment or enter into any settlement.

9. **Miscellaneous**.

9.1 **Adjustments in Share Numbers and Prices**. In the event of any stock split, subdivision, dividend or distribution payable in shares of Common Stock (or other securities or rights convertible into, or entitling the holder thereof to receive directly or indirectly shares of Common Stock), combination or other similar recapitalization or event occurring after the date hereof and prior to the Closing, each reference in any Transaction Document to a number of shares or a price per share shall be amended to appropriately account for such event (without duplication, to the extent the relevant Transaction Document provides for such amendment therein).

9.2 **Successors and Assigns**. This Agreement may not be assigned by a party hereto without the prior written consent of the Company or each of the Investors, as applicable, provided, however, that an Investor may assign its rights and delegate its duties hereunder in whole or in part to an Affiliate or to a third party acquiring some or all of its Securities in a transaction complying with applicable securities laws without the prior written consent of the Company or the other Investors, provided such assignee agrees in writing to be bound by the provisions hereof that apply to Investors. The provisions of this Agreement shall inure to the benefit of and be binding upon the respective permitted successors and assigns of the parties. Without limiting the generality of the foregoing, in the event that the Company is a party to a merger, consolidation, share exchange or similar business combination transaction in which the Common Stock is converted into the equity securities of another Person, from and after the effective time of such transaction, such Person shall, by virtue of such transaction, be deemed to have assumed the obligations of the Company hereunder, the term "Company" shall be deemed to refer to such Person and the term "Securities" shall be deemed to refer to the securities received by the Investors in connection with such transaction. Nothing in this Agreement, express or implied, is intended to confer upon any party other than the parties hereto or their respective permitted successors and assigns any rights, remedies, obligations, or liabilities under or by reason of this Agreement, except as expressly provided in this Agreement.

9.3 **Counterparts**. This Agreement may be executed in one or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument. Counterparts may be delivered via facsimile, electronic mail (including pdf or any electronic signatures complying with the U.S. federal ESIGN Act of 2000, e.g., www.docusign.com) or other transmission method and any counterpart so delivered shall be deemed to have been duly and validly delivered and be valid and effective for all purposes.

9.4 **Titles and Subtitles**. The titles and subtitles used in this Agreement are used for convenience only and are not to be considered in construing or interpreting this Agreement.

9.5 **Notices**. Unless otherwise provided, any notice required or permitted under this Agreement shall be given in writing and shall be deemed effectively given as hereinafter described (i) if given by personal delivery, then such notice shall be deemed given upon such delivery, (ii) if given by e-mail, then such notice shall be deemed given upon receipt of confirmation of receipt of an e-mail transmission, (iii) if given by mail, then such notice shall be deemed given upon the earlier of (A) receipt of such notice by the recipient or (B) three days after such notice is deposited in first class mail, postage prepaid, and (iv) if given by an internationally recognized overnight air courier, then such notice shall be deemed given one Business Day after delivery to such carrier. All notices shall be addressed to the party to be notified at the address as follows, or at such other address as such party may designate by ten days' advance written notice to the other party:

If to the Company:

Syros Pharmaceuticals, Inc.
35 CambridgePark Drive, 4th Floor
Cambridge, MA 02140
Attention: Jason Haas
Email: jhaas@syros.com

With a copy (which shall not constitute notice) to:

Wilmer Cutler Pickering Hale and Dorr LLP
60 State Street
Boston, MA 02109
Attention: Cynthia Mazareas
Email: cynthia.mazareas@wilmerhale.com

If to the Investors:

Only to the addresses set forth on the signature pages hereto.

9.6 **Expenses**. The parties hereto shall pay their own costs and expenses in connection herewith regardless of whether the transactions contemplated hereby are consummated; it being understood that each of the Company and each Investor has relied on the advice of its own respective counsel.

9.7 **Amendments and Waivers**. Prior to Closing, no amendment or waiver of any provision of this Agreement will be effective with respect to any party unless made in writing and signed by a duly authorized representative of such party. Following the Closing, any term of this Agreement may be amended and the observance of any term of this Agreement may be waived (either generally or in a particular instance and either retroactively or prospectively), only with the written consent of the Company and the Required Investors. Notwithstanding the foregoing, this Agreement may not be amended and the observance of any term of this Agreement may not be waived with respect to any Investor without the written consent of such Investor unless such amendment or waiver applies to all Investors in the same fashion. Any amendment or waiver effected in accordance with this paragraph shall be binding upon (i) prior to Closing, each Investor that signed such amendment or waiver and (ii) following the Closing, each holder of any Securities purchased under this Agreement at the time outstanding, and in each case, each future holder of all such Securities and the Company.

9.8 **Publicity**. Except as set forth below, no public release or announcement concerning the transactions contemplated hereby shall be issued by the Investors without the prior consent of the Company, except as such release or announcement may be required by law or the applicable rules or regulations of any securities exchange or securities market, in which case the Investors shall allow the Company reasonable time to comment on such release or announcement in advance of such issuance. Notwithstanding the foregoing, each Investor may identify

the Company and the value of such Investor's security holdings in the Company in accordance with applicable investment reporting and disclosure regulations or internal policies without prior notice to or consent from the Company (including, for the avoidance of doubt, filings pursuant to Sections 13 and 16 of the 1934 Act). The Company shall not include the name of any Investor or any Affiliate or investment adviser of such Investor in any press release or public announcement (which, for the avoidance of doubt, shall not include any SEC Filing to the extent such disclosure is required by SEC rules and regulations) without the prior written consent of such Investor. No later than the Business Day immediately following the date this Agreement is executed, the Company shall issue a press release disclosing all material terms of the transactions contemplated by this Agreement and any material non-public information that the Company may have provided any Investor in connection with the transactions contemplated by this Agreement at any time prior to the issuance of such press release (the "**Press Release**"). In addition, the Company will make such other filings and notices in the manner and time required by the SEC or Nasdaq. From and after the issuance of the Press Release, no Investor shall be in possession of any material non-public information provided by the Company, its subsidiaries or any of their respective officers, directors, employees or agents (including the Placement Agents) in connection with the transactions contemplated by this Agreement.

9.9 **Third-Party Beneficiaries**. The Company acknowledges and agrees and the Investors acknowledge and agree that each Placement Agent is a third-party beneficiary of the representations and warranties contained in Section 4 and Section **Error! Reference source not found.**, respectively.

9.10 **Severability**. Any provision of this Agreement that is prohibited or unenforceable in any jurisdiction shall, as to such jurisdiction, be ineffective to the extent of such prohibition or unenforceability without invalidating the remaining provisions hereof but shall be interpreted as if it were written so as to be enforceable to the maximum extent permitted by applicable law, and any such prohibition or unenforceability in any jurisdiction shall not invalidate or render unenforceable such provision in any other jurisdiction. To the extent permitted by applicable law, the parties hereby waive any provision of law which renders any provision hereof prohibited or unenforceable in any respect.

9.11 **Entire Agreement**. This Agreement, including the signature pages, Exhibits, the other Transaction Documents and any confidentiality agreement between the Company and each Investor constitute the entire agreement among the parties hereof with respect to the subject matter hereof and thereof and supersede all prior agreements and understandings, both oral and written, between the parties with respect to the subject matter hereof and thereof.

9.12 **Further Assurances**. The parties shall execute and deliver all such further instruments and documents and take all such other actions as may reasonably be required to carry out the transactions contemplated hereby and to evidence the fulfillment of the agreements herein contained.

9.13 **Governing Law**. This Agreement shall be governed by, and construed in accordance with, the laws of the State of Delaware. Service of process in connection with any such suit, action or proceeding may be served on each party hereto anywhere in the world by the same methods as are specified for the giving of notices under this Agreement.

9.14 **Independent Nature of Investors' Obligations and Rights**. The obligations of each Investor under any Transaction Document are several and not joint with the obligations of any other Investor, and no Investor shall be responsible in any way for the performance of the obligations of any other Investor under any Transaction Document. The decision of each Investor to purchase Closing Securities pursuant to the Transaction Documents has been made by such Investor independently of any other Investor. Nothing contained herein or in any Transaction Document, and no action taken by any Investor pursuant thereto, shall be deemed to constitute the Investors as a partnership, an association, a joint venture or any other kind of entity, or create a presumption that the Investors are in any way acting in concert or as a group with respect to such obligations or the transactions contemplated by the Transaction Documents. Each Investor acknowledges that no other Investor has acted as

agent for such Investor in connection with making its investment hereunder and that no Investor will be acting as agent of such Investor in connection with monitoring its investment in the Securities or enforcing its rights under the Transaction Documents. Each Investor shall be entitled to independently protect and enforce its rights, including, without limitation, the rights arising out of this Agreement or out of the other Transaction Documents, and it shall not be necessary for any other Investor to be joined as an additional party in any proceeding for such purpose. The Company acknowledges that each of the Investors has been provided with the same Transaction Documents for the purpose of closing a transaction with multiple Investors and not because it was required or requested to do so by any Investor. It is expressly understood and agreed that each provision contained in this Agreement is between the Company and an Investor, solely, and not between the Company and the Investors collectively and not between and among the Investors.

[remainder of page intentionally left blank]

IN WITNESS WHEREOF, the parties have executed this Agreement or caused their duly authorized officers to execute this Agreement as of the date first above written.

COMPANY: **SYROS PHARMACEUTICALS, INC.**

By: /s/ Nancy Simonian
Name: Nancy Simonian
Title: Chief Executive Officer

INVESTOR: **667, L.P.**

By: BAKER BROS. ADVISORS LP, management company and investment adviser to 667, L.P., pursuant to authority granted to it by Baker Biotech Capital, L.P., general partner to 667, L.P., and not as the general partner.

By: /s/ Scott Lessing
Name: Scott Lessing
Title: President

INVESTOR: **BAKER BROTHERS LIFE SCIENCES, L.P.**

By: BAKER BROS. ADVISORS LP, management company and investment adviser to Baker Brothers Life Sciences, L.P., pursuant to authority granted to it by Baker Brothers Life Sciences Capital, L.P., general partner to Baker Brothers Life Sciences, L.P., and not as the general partner.

By: /s/ Scott Lessing
Name: Scott Lessing
Title: President

INVESTOR: **AVIDITY MASTER FUND LP**

By: Avidity Capital Partners Fund (GP) LP, its general partner
By: Avidity Capital Partners (GP) LLC, its general partner

By: /s/ Michael Gregory
Name: Michael Gregory
Title: Managing Member

INVESTOR:

AVIDITY CAPITAL FUND II LP

By: Avidity Capital Partners Fund (GP) LP, its general partner
By: Avidity Capital Partners (GP) LLC, its general partner

By: /s/ Michael Gregory
Name: Michael Gregory
Title: Managing Member

INVESTOR:

AVIDITY CAPITAL HL SUB FUND III LLC

By: Avidity Master Fund III LP, its managing member
By: Avidity Capital Partners Fund (GP) LP, its general partner
By: Avidity Capital Partners (GP) LLC, its general partner

By: /s/ Michael Gregory
Name: Michael Gregory
Title: Managing Member

INVESTOR:

AVIDITY PRIVATE MASTER FUND I LP

By: Avidity Capital Partners Fund (GP) LP, its general partner
By: Avidity Capital Partners (GP) LLC, its general partner

By: /s/ Michael Gregory
Name: Michael Gregory
Title: Managing Member

INVESTOR:

FLAGSHIP PIONEERING FUND VII, L.P.

By: Flagship Pioneering Fund VII General Partner, LLC, its General Partner

By: /s/ Charles Carelli
Name: Charles Carelli
Title: Authorized Signatory

INVESTOR:

DEEP TRACK BIOTECHNOLOGY MASTER FUND, LTD.

By: /s/ Nir Messafi
Name: Nir Messafi
Title: Authorized Person

INVESTOR:

INVUS PUBLIC EQUITIES, L.P.

By: /s/ Khalil Barrage
Name: Khalil Barrage
Title: VP of the General Partner

INVESTOR:

BCLS II EQUITY OPPORTUNITIES, LP

By: BCLS II Equity Opportunities GP, LLC, its general partner

By: Bain Capital Life Sciences Fund II, L.P., its manager

By: Bain Capital Life Sciences Investors II, LLC, its general partner

By: Bain Capital Life Sciences Investors, LLC, its manager

By: /s/ Ricky Sun
Name: Ricky Sun
Title: Managing Director

INVESTOR:

SAMSARA BIOCAPITAL, LP

By: /s/ Srinivas Akkaraju
Name: Srinivas Akkaraju, PhD
Title: Managing Director,
Samsara BioCapital GP, LLC

INVESTOR:

CHI IV PUBLIC INVESTMENTS LP

By: CHI Advisors LLC, its investment manager

By: /s/ Kevin Raidy
Name: Kevin Raidy
Title: Managing Partner

INVESTOR:

ALLY BRIDGE MEDALPHA MASTER FUND L.P.

By: Ally Bridge MedAlpha General Partner L.P., its general partner

By: Ally Bridge MedAlpha GP, LLC, its general partner

By: /s/ Fan Yu
Name: Fan Yu
Title: Manager

INVESTOR: **ADAGE CAPITAL PARTNERS LP**

By: /s/ Dan Lehan
Name: Dan Lehan
Title: COO

INVESTOR: **CVI INVESTMENTS, INC.**

By: Heights Capital Management, Inc., its authorized agent

By: /s/ Martin Kobinger
Name: Martin Kobinger
Title: President

INVESTOR: **ALTIUM GROWTH FUND, LP**

By: /s/ Mark Gottlieb
Name: Mark Gottlieb
Title: COO

INVESTOR: **DAFNA LIFESCIENCE LP**

By: /s/ Nathan Fischel
Name: Nathan Fischel
Title: CEO

INVESTOR: **DAFNA LIFESCIENCE SELECT LP**

By: /s/ Nathan Fischel
Name: Nathan Fischel
Title: CEO

INVESTOR: **JALAA EQUITIES, LP**

By: /s/ Jason Aryeh
Name: JALAA Equities, LP
Title: General Partner

EXHIBIT A

Schedule of Investors

Investor Name	Number of Shares	Number of Warrant Shares Underlying Pre-Funded Warrant	Number of Warrant Shares Underlying Warrant	Aggregate Purchase Price of Securities
667, L.P.	—	2,406,726	2,406,726	$ 2,262,081.77
Baker Brothers Life Sciences, L.P.	—	24,191,274	24,191,274	$ 22,737,378.43
Avidity Master Fund LP	3,319,700	4,500,000	7,819,700	$ 7,350,068.00
Avidity Master Fund LP	409,400	555,000	964,400	$ 906,480.50
Avidity Capital HL Sub Fund III LLC	305,600	414,200	719,800	$ 676,570.58
Avidity Private Master Fund LP	4,965,300	6,730,800	11,696,100	$ 10,993,660.92
Flagship Pioneering Fund VII, L.P.	7,000,000	14,200,000	21,200,000	$ 19,926,580.00
Deep Track Biotechnology Master Fund, Ltd.	—	15,950,000	15,950,000	$ 14,991,405.00
Invus Public Equities, L.P.	10,638,297	—	10,638,297	$ 9,999,999.18
BCLS II Equity Opportunities, LP	5,319,400	5,319,400	10,638,800	$ 9,999,940.06
Samsara BioCapital, L.P.	6,914,893	—	6,914,893	$ 6,499,999.42
CHI IV Public Investments LP	5,319,148	—	5,319,148	$ 4,999,999.12
Adage Capital Partners L.P.	5,319,148	—	5,319,148	$ 4,999,999.12
Ally Bridge MedAlpha Master Fund L.P.	5,319,148	—	5,319,148	$ 4,999,999.12
CVI Investments, Inc.	4,255,000	—	4,255,000	$ 3,999,700.00
Altium Growth Fund, LP	3,191,000	—	3,191,000	$ 2,999,540.00
Dafna Lifescience LP	1,010,000	—	1,010,000	$ 949,400.00
Dafna Lifescience Select LP	319,787	—	319,787	$ 300,599.78
JALAA Equities, LP	265,957	—	265,957	$ 249,999.58

SYROS PHARMACEUTICALS, INC.

[FORM OF] LOCK-UP AGREEMENT

[•], 2022

Syros Pharmaceuticals, Inc.
35 CambridgePark Drive
Cambridge, Massachusetts 02140

Ladies and Gentlemen:

The undersigned signatory of this lock-up agreement (this "Lock-Up Agreement") understands that Syros Pharmaceuticals, Inc., a Delaware corporation ("Syros"), has entered into an Agreement and Plan of Merger, dated as of July 3, 2022 (as the same may be amended from time to time, the "Merger Agreement") with Tack Acquisition Corp., a Delaware corporation and a wholly owned subsidiary of Syros, and Tyme Technologies, Inc., a Delaware corporation ("Tyme"). Capitalized terms used but not otherwise defined herein shall have the respective meanings ascribed to such terms in the Merger Agreement.

As a condition and inducement to Syros and Tyme to enter into the Merger Agreement and to consummate the transactions contemplated thereby, and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the undersigned hereby irrevocably agrees that, subject to the exceptions set forth herein, without the prior written consent of Syros, the undersigned will not, during the period commencing upon the Closing and ending on the date that is 90 days after the Closing Date (the "Restricted Period"):

(1) offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, or otherwise transfer or dispose of, directly or indirectly, any shares of Syros Common Stock or any securities convertible into or exercisable or exchangeable for Syros Common Stock (including without limitation, Syros Common Stock or such other securities which may be deemed to be beneficially owned by the undersigned in accordance with the rules and regulations of the SEC and securities of Syros which may be issued upon exercise of an option to purchase Syros Common Stock or a warrant to purchase Syros Common Stock) that are currently or hereafter owned by the undersigned (collectively, the "Undersigned's Shares"), or publicly disclose the intention to make any such offer, sale, pledge, grant, transfer or disposition;

(2) enter into any swap, short sale, hedge or other agreement that transfers, in whole or in part, any of the economic consequences of ownership of the Undersigned's Shares regardless of whether any such transaction described in clause (1) above or this clause (2) is to be settled by delivery of Syros Common Stock or other securities, in cash or otherwise; or

(3) make any demand for, or exercise any right with respect to, the registration of any shares of Syros Common Stock or any security convertible into or exercisable or exchangeable for Syros Common Stock (other than such rights set forth in the Merger Agreement).

The restrictions and obligations contemplated by this Lock-Up Agreement shall not apply to:

(a) transfers of the Undersigned's Shares:

(1) if the undersigned is a natural person, (A) to any person related to the undersigned by blood or adoption who is an immediate family member of the undersigned, or by marriage or domestic partnership (a "Family Member"), or to a trust formed for the benefit of the undersigned or any of the undersigned's Family Members, (B) to the undersigned's estate, following the death of the undersigned, by will, intestacy or other

operation of Law, (C) as a bona fide gift or a charitable contribution, (D) by operation of Law pursuant to a qualified domestic order or in connection with a divorce settlement or (E) to any partnership, corporation or limited liability company which is controlled by the undersigned and/or by any such Family Member(s);

(2) if the undersigned is a corporation, partnership or other entity, (A) to another corporation, partnership, or other entity that is an affiliate (as defined under Rule 12b-2 of the Exchange Act) of the undersigned, including investment funds or other entities under common control or management with the undersigned, (B) as a distribution or dividend to equity holders, current or former general or limited partners, members or managers (or to the estates of any of the foregoing), as applicable, of the undersigned (including upon the liquidation and dissolution of the undersigned pursuant to a plan of liquidation approved by the undersigned's equity holders), (C) as a bona fide gift or a charitable contribution or (D) transfers or dispositions not involving a change in beneficial ownership; or

(3) if the undersigned is a trust, to any grantors or beneficiaries of the trust;

provided that, in the case of any transfer or distribution pursuant to this clause (a), such transfer is not for value and each donee, heir, beneficiary or other transferee or distributee shall sign and deliver to Syros a lock-up agreement in the form of this Lock-Up Agreement with respect to the shares of Syros Common Stock or such other securities that have been so transferred or distributed;

(b) the exercise of an option or warrant to purchase Syros Common Stock (including a net or cashless exercise of an option to purchase Syros Common Stock), and any related transfer of shares of Syros Common Stock to Syros for the purpose of paying the exercise price of such options or for paying taxes (including estimated taxes) due as a result of the exercise of such options; provided that, for the avoidance of doubt, the underlying shares of Syros Common Stock shall continue to be subject to the restrictions on transfer set forth in this Lock-Up Agreement;

(c) transfers to Syros in connection with the net settlement of any other equity award that represents the right to receive in the future shares of Syros Common Stock, settled in Syros Common Stock, to pay any tax withholding obligations; provided that, for the avoidance of doubt, the underlying shares of Syros Common Stock shall continue to be subject to the restrictions on transfer set forth in this Lock-Up Agreement;

(d) the establishment of a trading plan pursuant to Rule 10b5-1 under the Exchange Act for the transfer of Syros Common Stock; provided that such plan does not provide for any transfers of Syros Common Stock during the Restricted Period;

(e) transfers by the undersigned of shares of Syros Common Stock purchased by the undersigned on the open market or in a public offering by Syros, in each case following the Closing Date;

(f) pursuant to a bona-fide third party tender offer, merger, consolidation or other similar transaction made to all holders of Syros's capital stock involving a change of control of Syros, provided that in the event that such tender offer, merger, consolidation or other such transaction is not completed, the Undersigned's Shares shall remain subject to the restrictions contained in this Lock-Up Agreement; or

(g) pursuant to an order of a court or regulatory agency;

and provided, further, that, with respect to each of (a), (b), (c), and (d) above, no filing by any party (including any donor, donee, transferor, transferee, distributor or distributee) under Section 16 of the Exchange Act or other public announcement shall be required or shall be made voluntarily in connection with such transfer or disposition during the Restricted Period (other than (x) any exit filings or public announcements that may be required under applicable federal and state securities Laws or (y) in respect of a required filing under the Exchange Act in connection with the exercise of an option to purchase Syros Common Stock or in connection

with the net settlement of any other equity award that represents the right to receive in the future shares of Syros Common Stock, settled in Syros Common Stock, that would otherwise expire during the Restricted Period, provided that reasonable notice shall be provided to Syros prior to any such filing).

Any attempted transfer in violation of this Lock-Up Agreement will be of no effect and null and void, regardless of whether the purported transferee has any actual or constructive knowledge of the transfer restrictions set forth in this Lock-Up Agreement, and will not be recorded on the share register of Syros. In furtherance of the foregoing, the undersigned agrees that Syros and any duly appointed transfer agent for the registration or transfer of the securities described herein are hereby authorized to decline to make any transfer of securities if such transfer would constitute a violation or breach of this Lock-Up Agreement. Syros may cause the legend set forth below, or a legend substantially equivalent thereto, to be placed upon any certificate(s) or other documents, ledgers or instruments evidencing the undersigned's ownership of Syros Common Stock:

> THE SHARES REPRESENTED BY THIS CERTIFICATE ARE SUBJECT TO AND MAY ONLY BE TRANSFERRED IN COMPLIANCE WITH A LOCK-UP AGREEMENT, A COPY OF WHICH IS ON FILE AT THE PRINCIPAL OFFICE OF THE COMPANY.

The undersigned hereby represents and warrants that the undersigned has full power and authority to enter into this Lock-Up Agreement. All authority herein conferred or agreed to be conferred and any obligations of the undersigned shall be binding upon the successors, assigns, heirs or personal representatives of the undersigned.

The undersigned understands that if the Merger Agreement is terminated for any reason, the undersigned shall automatically and be immediately be released from all obligations under this Lock-Up Agreement. The undersigned understands that each of Syros and Tyme is proceeding with the transactions contemplated by the Merger Agreement in reliance upon this Lock-Up Agreement.

Any and all remedies herein expressly conferred upon Syros will be deemed cumulative with and not exclusive of any other remedy conferred hereby, or by Law or equity, and the exercise by Syros of any one remedy will not preclude the exercise of any other remedy. The undersigned agrees that irreparable damage would occur to Syros in the event that any provision of this Lock-Up Agreement was not performed in accordance with its specific terms or were otherwise breached. It is accordingly agreed that Syros shall be entitled to an injunction or injunctions to prevent breaches of this Lock-Up Agreement and to enforce specifically the terms and provisions hereof in any court of the United States or any state having jurisdiction, this being in addition to any other remedy to which Syros is entitled at Law or in equity, and the undersigned waives any bond, surety or other security that might be required of Syros with respect thereto.

In the event that any holder of Syros's securities that are subject to a substantially similar agreement entered into by such holder, other than the undersigned, is permitted by Syros to sell or otherwise transfer or dispose of shares of Syros Common Stock for value other than as permitted by this or a substantially similar agreement entered into by such holder, the same percentage of shares of Syros Common Stock held by the undersigned shall be immediately and fully released on the same terms from any remaining restrictions set forth herein (the "Pro-Rata Release"); provided, however, that such Pro-Rata Release shall not be applied unless and until permission has been granted by Syros to an equity holder or equity holders to sell or otherwise transfer or dispose of all or a portion of such equity holders shares of Syros Common Stock in an aggregate amount in excess of 1% of the number of shares of Syros Common Stock originally subject to a substantially similar agreement.

Upon the release of any of the Undersigned's Shares from this Lock-Up Agreement, Syros will cooperate with the undersigned to facilitate the timely preparation and delivery of certificates representing the Undersigned Shares without the restrictive legend above or the withdrawal of any stop transfer instructions by virtue of this Lock-Up Agreement.

This Lock-Up Agreement and any claim, controversy or dispute arising under or related to this Lock-Up Agreement shall be governed by and construed in accordance with the Laws of the state of Delaware, without regard to the conflict of Laws principles thereof.

This Lock-Up Agreement may be executed in several counterparts, each of which shall be deemed an original and all of which shall constitute one and the same instrument. The exchange of a fully executed Lock-Up Agreement (in counterparts or otherwise) by Syros and the undersigned by facsimile or electronic transmission in .pdf format shall be sufficient to bind such parties to the terms and conditions of this Lock-Up Agreement.

[SIGNATURE PAGE FOLLOWS]

Very truly yours,

Print Name of Stockholder:

_____

Signature (for individuals):

_____

Signature (for entities):

_____

By:
Name:
Title:

SIGNATURE PAGE TO LOCK UP AGREEMENT

Accepted and Agreed
by Syros Pharmaceuticals, Inc.:

By: _____
Name:
Title:

SIGNATURE PAGE TO LOCK UP AGREEMENT

CERTIFICATE OF AMENDMENT
OF
RESTATED CERTIFICATE OF INCORPORATION
OF
SYROS PHARMACEUTICALS, INC.

Syros Pharmaceuticals, Inc. (the "Corporation"), a corporation organized and existing under and by virtue of the provisions of the General Corporation Law of the State of Delaware (the "General Corporation Law"), does hereby certify as follows:

1. The name of the Corporation is Syros Pharmaceuticals, Inc.

2. Article FOURTH of the Restated Certificate of Incorporation of the Corporation, as amended, is hereby amended by replacing the first paragraph thereof with the following:

   "FOURTH: The total number of shares of all classes of stock which the Corporation shall have authority to issue is 710,000,000 shares, consisting of (i) 700,000,000 shares of Common Stock, $0.001 par value per share ("Common Stock") and (ii) 10,000,000 shares of Preferred Stock, $0.001 par value per share ("Preferred Stock")."

3. This Certificate of Amendment has been duly adopted by the Board of Directors and stockholders of the Corporation in accordance with Section 242 of the General Corporation Law.

IN WITNESS WHEREOF, the Corporation has caused its duly authorized officer to execute this Certificate of Amendment on this day of , 2022.

SYROS PHARMACEUTICALS, INC.

By: _____
Name:
Title:

CERTIFICATE OF AMENDMENT
OF
RESTATED CERTIFICATE OF INCORPORATION
OF
SYROS PHARMACEUTICALS, INC.

Syros Pharmaceuticals, Inc. (the "Corporation"), a corporation organized and existing under and by virtue of the provisions of the General Corporation Law of the State of Delaware (the "General Corporation Law"), does hereby certify as follows:

1. The name of the Corporation is Syros Pharmaceuticals, Inc.

2. Article FOURTH of the Restated Certificate of the Corporation, as amended, is hereby amended by replacing the first paragraph thereof with the following:

   "FOURTH: Effective upon the filing of this Certificate of Amendment of the Restated Certificate of Incorporation with the Secretary of State of the State of Delaware (the "Effective Time"), each [ ][14] shares of the Corporation's common stock, par value $0.001 per share (the "Common Stock"), issued and outstanding or held by the Corporation in treasury immediately prior to the Effective Time shall be reclassified and combined into one validly issued, fully paid and nonassessable share of outstanding Common Stock or treasury share, as applicable, automatically and without any action by the holder thereof upon the Effective Time and shall represent one share of Common Stock from and after the Effective Time (such reclassification and combination of shares, the "Reverse Stock Split"). The par value of the Common Stock following the Reverse Stock Split shall remain at $0.001 par value per share. No fractional shares of Common Stock shall be issued as a result of the Reverse Stock Split and, in lieu thereof, upon surrender after the Effective Time of a certificate or a book-entry position which formerly represented shares of Common Stock that were issued and outstanding immediately prior to the Effective Time, any person who would otherwise be entitled to a fractional share of Common Stock as a result of the Reverse Stock Split, following the Effective Time, shall be entitled to receive a cash payment (without interest) equal to the fraction of a share of Common Stock to which such holder would otherwise be entitled multiplied by the average (after taking into account the exact ratio of the Reverse Stock Split determined by the Board of Directors of the Corporation) of the high and low trading prices of the Common Stock on The Nasdaq Global Select Market during regular trading hours for the five trading days immediately preceding the Effective Time.

   Each stock certificate or book entry position that, immediately prior to the Effective Time, represented shares of Common Stock that were issued and outstanding immediately prior to the Effective Time shall, from and after the Effective Time, automatically and without the necessity of presenting the same for exchange, represent that number of whole shares of Common Stock after the Effective Time into which the shares formerly represented by such certificate or book entry position have been reclassified (as well as the right to receive cash in lieu of fractional shares of Common Stock after the Effective Time); provided, however, that each person of record holding a certificate or book entry position that represented shares of Common Stock that were issued and outstanding immediately prior to the Effective Time shall receive, upon surrender of such certificate or book entry position, a new certificate or book entry position

[14] Shall be a number greater than or equal to five (5) and equal to or lesser than fifteen (15) (it being understood that any number within such range shall, together with the remaining provisions this Certificate of Amendment not appearing in brackets, constitute a separate amendment being approved and adopted by the Syros board of directors and stockholders in accordance with Section 242 of the General Corporation Law of the State of Delaware, with all amendments other than the amendment filed with the Secretary of State of the State of Delaware to be abandoned upon the filing of such amendment).

evidencing and representing the number of whole shares of Common Stock after the Effective Time into which the shares of Common Stock formerly represented by such certificate or book entry position shall have been reclassified.

The total number of shares of all classes of stock which the Corporation shall have authority to issue is [ ][15] shares, consisting of

(i) [ ][16] shares of Common Stock, $0.001 par value per share ("Common Stock") and

(ii) 10,000,000 shares of Preferred Stock, $0.001 par value per share ("Preferred Stock")."

3. This Certificate of Amendment has been duly adopted by the Board of Directors and stockholders of the Corporation in accordance with the provisions of Section 242 of the General Corporation Law.

IN WITNESS WHEREOF, the Corporation has caused its duly authorized officer to execute this Certificate of Amendment on this day of , 20 .

SYROS PHARMACEUTICALS, INC.

By: _____
Name:
Title:

(15) This number will be equal to the sum of (x) 10,000,000 shares of Preferred Stock plus (y) a number of shares of Common Stock ascertained by dividing (i) the total number of authorized shares of Common Stock set forth in the Restated Certificate as in effect immediately prior to the Effective Time by (ii) the number (between five (5) and fifteen (15)) that equals the number of shares of Common Stock to be reclassified into one share of Common Stock, as determined by the Board of Directors of the Corporation and publicly announced by the Corporation prior to the Effective Time in accordance with the first paragraph of Article FOURTH (it being understood that any number of authorized shares ascertainable pursuant to the foregoing formula shall, together with the remaining provisions this Certificate of Amendment not appearing in brackets, constitute a separate amendment being approved and adopted by the Board of Directors and stockholders in accordance with Section 242 of the General Corporation Law, with all amendments other than the amendment filed with the Secretary of State of the State of Delaware to be abandoned upon the filing of such amendment).

(16) This number will be equal to a number of shares of Common Stock ascertained by dividing (i) the total number of authorized shares of Common Stock set forth in the Restated Certificate as in effect immediately prior to the Effective Time by (ii) the number (between five (5) and fifteen (15)) that equals the number of shares of Common Stock to be reclassified into one share of Common Stock, as determined by the Board of Directors of the Corporation and publicly announced by the Corporation prior to the Effective Time in accordance with the first paragraph of Article FOURTH (it being understood that any number of authorized shares ascertainable pursuant to the foregoing formula shall, together with the remaining provisions this Certificate of Amendment not appearing in brackets, constitute a separate amendment being approved and adopted by the Board of Directors and stockholders in accordance with Section 242 of the General Corporation Law, with all amendments other than the amendment filed with the Secretary of State of the State of Delaware to be abandoned upon the filing of such amendment).

SYROS PHARMACEUTICALS, INC.

2022 EQUITY INCENTIVE PLAN

1. Purpose

The purpose of this 2022 Equity Incentive Plan (the "***Plan***") of Syros Pharmaceuticals, Inc. a Delaware corporation (the "***Company***"), is to advance the interests of the Company's stockholders by enhancing the Company's ability to attract, retain and motivate persons who are expected to make important contributions to the Company and by providing such persons with equity ownership opportunities and performance-based incentives that are intended to better align the interests of such persons with those of the Company's stockholders. Except where the context otherwise requires, the term "***Company***" shall include any of the Company's present or future parent or subsidiary corporations as defined in Sections 424(e) or (f) of the Internal Revenue Code of 1986, as amended, and any regulations thereunder (the "***Code***") and any other business venture (including, without limitation, joint venture or limited liability company) in which the Company has a controlling interest, as determined by the Board of Directors of the Company (the "***Board***").

2. Eligibility

All of the Company's employees, officers and directors, as well as consultants and advisors to the Company (as the terms consultants and advisors are defined and interpreted for purposes of Form S-8 under the Securities Act of 1933, as amended (the "***Securities Act***"), or any successor form) are eligible to be granted Awards (as defined below) under the Plan. Each person who is granted an Award under the Plan is deemed a "***Participant***." The Plan provides for the following types of awards, each of which is referred to as an "***Award***": Options (as defined in Section 5), SARs (as defined in Section 6), Restricted Stock (as defined in Section 7), RSUs (as defined in Section 7), Other Stock-Based Awards (as defined in Section 8) and Cash-Based Awards (as defined in Section 8). Any type of Award may be granted as a Performance Award under Section 9. Except as otherwise provided by the Plan, each Award may be made alone or in addition or in relation to any other Award. The terms of each Award need not be identical, and the Board need not treat Participants uniformly.

3. Administration and Delegation

(a) Administration by Board of Directors. The Plan will be administered by the Board. The Board shall have authority to grant Awards and to adopt, amend and repeal such administrative rules, guidelines and practices relating to the Plan as it shall deem advisable. The Board may construe and interpret the terms of the Plan and any Award agreements entered into under the Plan. The Board may correct any defect, supply any omission or reconcile any inconsistency in the Plan or any Award. All actions and decisions by the Board with respect to the Plan and any Awards shall be made in the Board's discretion and shall be final and binding on all persons having or claiming any interest in the Plan or in any Award.

(b) Appointment of Committees. To the extent permitted by applicable law, the Board may delegate any or all of its powers under the Plan to one or more committees or subcommittees of the Board (a "***Committee***"). All references in the Plan to the "***Board***" shall mean the Board or a Committee of the Board or the officers referred to in Section 3(c) to the extent that the Board's powers or authority under the Plan have been delegated to such Committee or officers.

(c) Delegation to Officers. Subject to any requirements of applicable law (including as applicable Sections 152 and 157(c) of the General Corporation Law of the State of Delaware), the Board may delegate to one or more officers of the Company the power to grant Awards (subject to any limitations under the Plan) to employees or officers of the Company and to exercise such other powers under the Plan as the Board may determine, provided

that the Board shall fix the terms of Awards to be granted by such officers, the maximum number of shares subject to Awards that the officers may grant, and the time period in which such Awards may be granted; and provided further, that no officer shall be authorized to grant Awards to any "executive officer" of the Company (as defined by Rule 3b-7 under the Securities Exchange Act of 1934, as amended (the "Exchange Act")) or to any "officer" of the Company (as defined by Rule 16a-1(f) under the Exchange Act).

(d) Awards to Non-Employee Directors. Awards to non-employee directors will be granted and administered by a Committee, all of the members of which are independent directors as defined by Section 5605(a)(2) of the Nasdaq Marketplace Rules.

4. Stock Available for Awards

(a) Number of Shares; Share Counting.

(1) Authorized Number of Shares. Subject to adjustment under Section 10, Awards may be made under the Plan (any or all of which Awards may be in the form of Incentive Stock Options, as defined in Section 5(b)) for up to a number of shares of common stock, $0.001 par value per share, of the Company (the "***Common Stock***"), as is equal to the sum of:

(A) 30,000,000 shares of Common Stock; and

(B) such additional number of shares of Common Stock (up to 17,375,343) as is equal to the sum of (x) the number of shares of Common Stock reserved for issuance under the Company's 2016 Stock Incentive Plan (the "***Existing Plan***") that remain available for grant under the Existing Plan immediately prior to the date that the Plan is approved by the Company's stockholders (the "***Effective Date***") and (y) the number of shares of Common Stock subject to (I) awards granted under the Existing Plan and the Company's 2012 Equity Incentive Plan, as amended, in each case that are outstanding as of the Effective Date and (II) stock options assumed by the Company pursuant to the Agreement and Plan of Merger, dated as of July 3, 2022, between the Company, TYME Technologies, Inc. and Tack Acquisition Corp., as it may be amended from time to time (the "***Merger Agreement***"), as of the closing of the merger contemplated by the Merger Agreement (the awards described in the foregoing clauses (I) and (II), together, the "***Outstanding Awards***"), in each case which Outstanding Awards expire, terminate or are otherwise surrendered, cancelled, forfeited or repurchased by the Company at their original issuance price pursuant to a contractual repurchase right (subject, however, in the case of Incentive Stock Options to any limitations under the Code).

Shares of Common Stock issued under the Plan may consist in whole or in part of authorized but unissued shares or treasury shares.

(2) Share Counting. For purposes of counting the number of shares available for the grant of Awards under the Plan under this Section 4(a):

(A) all shares of Common Stock covered by SARs shall be counted against the number of shares available for the grant of Awards under the Plan; *provided, however*, that (i) SARs that may be settled only in cash shall not be so counted and (ii) if the Company grants an SAR in tandem with an Option for the same number of shares of Common Stock and provides that only one such Award may be exercised (a "***Tandem SAR***"), only the shares covered by the Option, and not the shares covered by the Tandem SAR, shall be so counted, and the expiration of one in connection with the other's exercise will not restore shares to the Plan;

(B) to the extent that an RSU may be settled only in cash, no shares shall be counted against the shares available for the grant of Awards under the Plan;

(C) if any Award (i) expires or is terminated, surrendered or cancelled without having been fully exercised or is forfeited in whole or in part (including as the result of shares of Common Stock subject to such Award being repurchased by the Company at the original issuance price pursuant to a contractual repurchase right) or (ii) results in any Common Stock not being issued (including as a result of an SAR or an RSU that was settleable either in cash or in stock actually being settled in cash), the unused Common Stock covered by such Award shall again be available for the grant of Awards; *provided, however*, that (1) in the case of Incentive Stock Options, the foregoing shall be subject to any limitations under the Code, (2) in the case of the exercise of an SAR, the number of shares counted against the shares available under the Plan shall be the full number of shares subject to the SAR multiplied by the percentage of the SAR actually exercised, regardless of the number of shares actually used to settle such SAR upon exercise and (3) the shares covered by a Tandem SAR shall not again become available for grant upon the expiration or termination of such Tandem SAR;

(D) shares of Common Stock delivered (either by actual delivery, attestation or net exercise) to the Company by a Participant to (i) purchase shares of Common Stock upon the exercise of an Award or (ii) satisfy tax withholding obligations with respect to Awards (including shares retained from the Award creating the tax obligation) shall not be added back to the number of shares available for the future grant of Awards; and

(E) shares of Common Stock repurchased by the Company on the open market using the proceeds from the exercise of an Award shall not increase the number of shares available for future grant of Awards.

(b) Limit on Awards to Non-Employee Directors. The maximum aggregate amount of cash and value of Awards (calculated based on grant date fair value for financial reporting purposes) granted in any calendar year to any individual non-employee director shall not exceed $750,000 in the case of an incumbent director; provided, however, that such maximum aggregate amount shall not exceed $1,000,000 in any calendar year for any individual non-employee director in such non-employee director's initial year of election or appointment; and provided, further, however, that fees paid by the Company on behalf of any non-employee director in connection with regulatory compliance and any amounts paid to anon-employee director as reimbursement of an expense shall not count against the foregoing limit. The Board may make exceptions to this limit for individual non-employee directors in extraordinary circumstances, as the Board may determine in its discretion, provided that the non-employee director receiving such additional compensation may not participate in the decision to award such compensation. For the avoidance of doubt, this limitation shall not apply to cash or Awards granted to a non-employee director in his or her capacity as an advisor or consultant to the Company.

(c) Substitute Awards. In connection with a merger or consolidation of an entity with the Company or the acquisition by the Company of property or stock of an entity, the Board may grant Awards in substitution for any options or other stock or stock-based awards granted by such entity or an affiliate thereof. Substitute Awards may be granted on such terms as the Board deems appropriate in the circumstances, notwithstanding any limitations on Awards contained in the Plan. Substitute Awards shall not count against the overall share limit set forth in Section 4(a)(1), except as may be required by reason of Section 422 and related provisions of the Code.

5. Stock Options

(a) General. The Board may grant options to purchase Common Stock (each, an "***Option***") and determine the number of shares of Common Stock to be covered by each Option, the exercise price of each Option and the conditions and limitations applicable to the exercise of each Option, including conditions relating to applicable federal or state securities laws, as the Board considers necessary or advisable.

(b) Incentive Stock Options. An Option that the Board intends to be an "incentive stock option" as defined in Section 422 of the Code (an "***Incentive Stock Option***") shall only be granted to employees of Syros Pharmaceuticals, Inc., any of Syros Pharmaceuticals, Inc.'s present or future parent or subsidiary corporations as

defined in Sections 424(e) or (f) of the Code, and any other entities the employees of which are eligible to receive Incentive Stock Options under the Code, and shall be subject to and shall be construed consistently with the requirements of Section 422 of the Code. An Option that is not intended to be an Incentive Stock Option shall be designated a "***Nonstatutory Stock Option***." The Company shall have no liability to a Participant, or any other person, if an Option (or any part thereof) that is intended to be an Incentive Stock Option is not an Incentive Stock Option or if the Company converts an Incentive Stock Option to a Nonstatutory Stock Option.

(c) Exercise Price. The Board shall establish the exercise price of each Option or the formula by which such exercise price will be determined. The exercise price shall be specified in the applicable Option agreement. The exercise price shall be not less than 100% of the Grant Date Fair Market Value (as defined below) of the Common Stock on the date the Option is granted; *provided* that if the Board approves the grant of an Option with an exercise price to be determined on a future date, the exercise price shall be not less than 100% of the Grant Date Fair Market Value on such future date. "***Grant Date Fair Market Value***" of a share of Common Stock for purposes of the Plan will be determined as follows:

(1) if the Common Stock trades on a national securities exchange, the closing sale price (for the primary trading session) on the date of grant; or

(2) if the Common Stock does not trade on any such exchange, the average of the closing bid and asked prices on the date of grant as reported by an over-the-counter marketplace designated by the Board; or

(3) if the Common Stock is not publicly traded, the Board will determine the Grant Date Fair Market Value for purposes of the Plan using any measure of value it determines to be appropriate (including, as it considers appropriate, relying on appraisals) in a manner consistent with the valuation principles under Code Section 409A of the Code or any successor provision thereto, and the regulations thereunder ("***Section 409A***"), except as the Board may expressly determine otherwise.

For any date that is not a trading day, the Grant Date Fair Market Value of a share of Common Stock for such date will be determined by using the closing sale price or average of the bid and asked prices, as appropriate, for the immediately preceding trading day and with the timing in the formulas above adjusted accordingly. The Board can substitute a particular time of day or other measure of "closing sale price" or "bid and asked prices" if appropriate because of exchange or market procedures or can, use weighted averages either on a daily basis or such longer period, in each case to the extent permitted by Section 409A.

The Board shall determine the Grant Date Fair Market Value for purposes of the Plan, and all Awards are conditioned on the Participant's agreement that the Board's determination is conclusive and binding even though others might make a different determination.

(d) Duration of Options. Each Option shall be exercisable at such times and subject to such terms and conditions as the Board may specify in the applicable Option agreement; *provided, however*, that no Option will be granted with a term in excess of 10 years.

(e) Exercise of Options. Options may be exercised by delivery to the Company of a notice of exercise in a form (which may be electronic) approved by the Company, together with payment in full (in the manner specified in Section 5(f)) of the exercise price for the number of shares for which the Option is exercised. Shares of Common Stock subject to the Option will be delivered by the Company as soon as practicable following exercise.

(f) Payment Upon Exercise. Common Stock purchased upon the exercise of an Option granted under the Plan shall be paid for as follows:

(1) in cash or by check, payable to the order of the Company;

(2) except as may otherwise be provided in the applicable Option agreement or approved by the Board, by (i) delivery of an irrevocable and unconditional undertaking by a creditworthy broker to deliver promptly to the Company sufficient funds to pay the exercise price and any required tax withholding or (ii) delivery by the Participant to the Company of a copy of irrevocable and unconditional instructions to a creditworthy broker to deliver promptly to the Company funds sufficient to pay the exercise price and any required tax withholding;

(3) to the extent provided for in the applicable Option agreement or approved by the Board, by delivery (either by actual delivery or attestation) of shares of Common Stock owned by the Participant valued at their fair market value (valued in the manner determined or approved by the Board), provided (i) such method of payment is then permitted under applicable law, (ii) such Common Stock, if acquired directly from the Company, was owned by the Participant for such minimum period of time, if any, as may be established by the Board and (iii) such Common Stock is not subject to any repurchase, forfeiture, unfulfilled vesting or other similar requirements;

(4) to the extent provided for in the applicable Nonstatutory Stock Option agreement or approved by the Board, by delivery of a notice of "net exercise" to the Company, as a result of which the Participant would receive (i) the number of shares underlying the portion of the Option being exercised, less (ii) such number of shares as is equal to (A) the aggregate exercise price for the portion of the Option being exercised divided by (B) the fair market value of the Common Stock (valued in the manner determined or approved by the Board) on the date of exercise;

(5) to the extent permitted by applicable law and provided for in the applicable Option agreement or approved by the Board, by payment of such other lawful consideration as the Board may determine; or

(6) by any combination of the above permitted forms of payment.

(g) Limitation on Repricing. Unless such action is approved by the Company's stockholders, the Company may not (except as provided for under Section 10): (1) amend any outstanding Option granted under the Plan to provide an exercise price per share that is lower than the then-current exercise price per share of such outstanding Option; (2) cancel any outstanding option (whether or not granted under the Plan) and grant in substitution therefor new Awards under the Plan (other than Awards granted pursuant to Section 4(c)) covering the same or a different number of shares of Common Stock and having an exercise or measurement price per share lower than the then-current exercise price per share of the cancelled option; (3) cancel in exchange for a cash payment any outstanding Option with an exercise price per share above the then-current fair market value of the Common Stock (valued in the manner determined or approved by the Board); or (4) take any other action under the Plan that constitutes a "repricing" within the meaning of the rules of the Nasdaq Stock Market or any other exchange or marketplace on which the Company's stock is listed or traded (the "***Exchange***").

(h) No Reload Options. No Option granted under the Plan shall contain any provision entitling the Participant to the automatic grant of additional Options in connection with any exercise of the original Option.

(i) No Dividend Equivalents. No Option shall provide for the payment or accrual of dividend equivalents.

6. Stock Appreciation Rights

(a) General. The Board may grant Awards consisting of stock appreciation rights ("***SARs***") entitling the holder, upon exercise, to receive an amount of Common Stock or cash or a combination thereof (such form to be determined by the Board) determined by reference to appreciation, from and after the date of grant, in the fair market value of a share of Common Stock (valued in the manner determined or approved by the Board) over the measurement price established pursuant to Section 6(b). The date as of which such appreciation is determined shall be the exercise date.

(b) Measurement Price. The Board shall establish the measurement price of each SAR and specify it in the applicable SAR agreement. The measurement price shall not be less than 100% of the Grant Date Fair Market Value of the Common Stock on the date the SAR is granted; *provided* that if the Board approves the grant of an SAR effective as of a future date, the measurement price shall be not less than 100% of the Grant Date Fair Market Value on such future date.

(c) Duration of SARs. Each SAR shall be exercisable at such times and subject to such terms and conditions as the Board may specify in the applicable SAR agreement; *provided, however*, that no SAR will be granted with a term in excess of 10 years.

(d) Exercise of SARs. SARs may be exercised by delivery to the Company of a notice of exercise in a form (which may be electronic) approved by the Company, together with any other documents required by the Board.

(e) Limitation on Repricing. Unless such action is approved by the Company's stockholders, the Company may not (except as provided for under Section 10): (1) amend any outstanding SAR granted under the Plan to provide a measurement price per share that is lower than the then-current measurement price per share of such outstanding SAR; (2) cancel any outstanding SAR (whether or not granted under the Plan) and grant in substitution therefor new Awards under the Plan (other than Awards granted pursuant to Section 4(c)) covering the same or a different number of shares of Common Stock and having an exercise or measurement price per share lower than the then-current measurement price per share of the cancelled SAR; (3) cancel in exchange for a cash payment any outstanding SAR with a measurement price per share above the then-current fair market value of the Common Stock (valued in the manner determined or approved by the Board); or (4) take any other action under the Plan that constitutes a "repricing" within the meaning of the rules of the Exchange.

(f) No Reload SARs. No SAR granted under the Plan shall contain any provision entitling the Participant to the automatic grant of additional SARs in connection with any exercise of the original SAR.

(g) No Dividend Equivalents. No SAR shall provide for the payment or accrual of dividend equivalents.

7. Restricted Stock; RSUs

(a) General. The Board may grant Awards entitling recipients to acquire shares of Common Stock ("***Restricted Stock***"), subject to the right of the Company to repurchase all or part of such shares at their issue price or other stated or formula price (or to require forfeiture of such shares if issued at no cost) from the recipient in the event that conditions specified by the Board in the applicable Award are not satisfied prior to the end of the applicable restriction period or periods established by the Board for such Award. The Board may also grant Awards entitling the recipient to receive shares of Common Stock or cash to be delivered at the time such Award vests or on a deferred basis ("***RSUs***").

(b) Terms and Conditions for Restricted Stock and RSUs. The Board shall determine the terms and conditions of Restricted Stock and RSUs, including the conditions for vesting and repurchase (or forfeiture) and the issue price, if any.

(c) Additional Provisions Relating to Restricted Stock.

(1) Dividends. Any dividends (whether paid in cash, stock or property) declared and paid by the Company with respect to shares of Restricted Stock ("***Unvested Dividends***") shall be paid to the Participant only if and when such shares become free from the restrictions on transferability and forfeitability that apply to such shares. Each payment of Unvested Dividends will be made no later than the end of the calendar year in which the dividends are paid to stockholders of that class of stock or, if later, the 15th day of the third month following the lapsing of the restrictions on transferability and the forfeitability provisions applicable to the underlying shares of Restricted Stock. No interest will be paid on Unvested Dividends.

(2) Stock Certificates/Issuance. The Company may require that any stock certificates issued in respect of shares of Restricted Stock, as well as dividends or distributions paid on such Restricted Stock, shall be deposited in escrow by the Participant, together with a stock power endorsed in blank, with the Company (or its designee) or, alternatively, that such shares be issued in book entry only, in the name of the Participant with appropriate transfer and forfeiture restrictions. At the expiration of the applicable restriction periods, the Company (or such designee) shall deliver the certificates no longer subject to such restrictions (or, to the extent the Restricted Stock was issued in book entry, remove the restrictions) to the Participant or if the Participant has died, to his or her Designated Beneficiary (as defined below).

(d) Additional Provisions Relating to RSUs.

(1) Settlement. Upon the vesting of and/or lapsing of any other restrictions with respect to each RSU, the Participant shall be entitled to receive from the Company (i.e., settlement) the number of shares of Common Stock specified in the Award agreement or (if so provided in the applicable Award agreement or otherwise determined by the Board) an amount of cash equal to the fair market value (valued in the manner determined or approved by the Board) of such number of shares or a combination thereof. The Board may provide that settlement of RSUs shall be deferred, on a mandatory basis or at the election of the Participant, in a manner that complies with Section 409A.

(2) Voting Rights. A Participant shall have no voting rights with respect to any RSUs.

(3) Dividend Equivalents. The Award agreement for RSUs may provide Participants with the right to receive an amount equal to any dividends or other distributions declared and paid on an equal number of outstanding shares of Common Stock ("***Dividend Equivalents***"). Dividend Equivalents may be credited to an account for the Participant and may be settled in cash and/or shares of Common Stock, in each case to the extent provided in the applicable Award agreement. Dividend Equivalents with respect to RSUs will be subject to the same restrictions on transfer and forfeitability as the RSUs with respect to which paid. No interest will be paid on Dividend Equivalents.

8. Other Stock-Based and Cash-Based Awards

(a) General. The Board may grant other Awards of shares of Common Stock, and other Awards that are valued in whole or in part by reference to, or are otherwise based on, shares of Common Stock or other property ("***Other Stock-Based Awards***"). Such Other Stock-Based Awards shall also be available as a form of payment in the settlement of other Awards granted under the Plan or as payment in lieu of compensation to which a Participant is otherwise entitled. Other Stock-Based Awards may be paid in shares of Common Stock or cash, as the Board shall determine. The Company may also grant Awards denominated in cash rather than shares of Common Stock ("***Cash-Based Awards***").

(b) Terms and Conditions. Subject to the provisions of the Plan, the Board shall determine the terms and conditions of each Other Stock-Based Award or Cash-Based Award, including any purchase price applicable thereto.

(c) Dividend Equivalents. The Award agreement for an Other Stock-Based Award may provide Participants with the right to receive Dividend Equivalents. Dividend Equivalents may be credited to an account for the Participant and may be settled in cash and/or shares of Common Stock, in each case to the extent provided in the applicable Award agreement. Dividend Equivalents with respect to Other-Stock Based Awards will be subject to the same restrictions on transfer and forfeitability as the Other Stock-Based Award with respect to which paid. No interest will be paid on Dividend Equivalents.

9. Performance Awards.

(a) Grants. Awards under the Plan may be made subject to the achievement of performance goals pursuant to this Section 9 ("***Performance Awards***").

(b) Performance Measures. The Board may specify that the degree of granting, vesting and/or payout of any Performance Award shall be subject to the achievement of one or more performance measures established by the Board, which may be based on the relative or absolute attainment of specified levels of one or any combination of the following, and which may be determined pursuant to generally accepted accounting principles ("***GAAP***") or on a non-GAAP basis, as determined by the Board: (i) the entry into an arrangement or agreement with a third party for the development, commercialization, marketing or distribution of products, services or technologies, or for conducting a research program to discover and develop a product, service or technology, and/or the achievement of milestones under such arrangement or agreement, including events that trigger an obligation or payment right; (ii) achievement of domestic and international regulatory milestones, including the submission of filings required to advance products, services and technologies in clinical development and the achievement of approvals by regulatory authorities relating to the commercialization of products, services and technologies; (iii) the achievement of discovery, preclinical and clinical stage scientific objectives, discoveries or inventions for products, services and technologies under research and development; (iv) the entry into or completion of a phase of clinical development for any product, service or technology, such as the entry into or completion of phase 1, 2 and/or 3 clinical trials; (v) the consummation of debt or equity financing transactions, or acquisitions of business, technologies and assets; (vi) new product or service releases; (vii) the achievement of qualitative or quantitative performance measures set forth in operating plans approved by the Board from time to time; (viii) specified levels of product sales, net income, earnings before or after discontinued operations, interest, taxes, depreciation and/or amortization, operating profit before or after discontinued operations and/or taxes, sales, sales growth, earnings growth, cash flow or cash position, gross margins, stock price, market share, return on sales, assets, equity or investment; (ix) improvement of financial ratings; (x) achievement of balance sheet or income statement objectives; (xi) total stockholder return or stock price; (xii) other comparable measures of financial and operational performance; and/ or (xiii) any other measure selected by the Board. Such goals may reflect absolute entity or business unit performance or a relative comparison to the performance of a peer group of entities or other external measure of the selected performance criteria and may be absolute in their terms or measured against or in relationship to other companies comparably, similarly or otherwise situated. The Board may specify that such performance measures shall be adjusted to exclude any one or more of: (I) extraordinary items; (II) gains or losses on the dispositions of discontinued operations; (III) the cumulative effects of changes in accounting principles; (IV) the writedown of any asset; (V) fluctuation in foreign currency exchange rates; (VI) charges for restructuring and rationalization programs; (VII) non-cash, mark-to-market adjustments on derivative instruments; (VIII) amortization of purchased intangibles; (IX) the net impact of tax rate changes; (X) non-cash asset impairment charges; (XI) gains on extinguishment of the tax receivable agreement; and (XII) any other factors as the Board may determine. Such performance measures: (A) may vary by Participant and may be different for different Awards; (B) may be particular to a Participant or the department, branch, line of business, subsidiary or other unit in which the Participant works; and (C) may cover such period as may be specified by the Board. The Board shall have the authority to make equitable adjustments to the performance goals in recognition of unusual or non-recurring events affecting the Company or the financial statements of the Company, in response to changes in applicable laws or regulations or to account for items of gain, loss or expense determined to be extraordinary or unusual in nature or infrequent in occurrence or related to the disposal of a segment of a business or related to a change in accounting principles.

(c) Adjustments. The Board may adjust the cash or number of shares payable pursuant to such Performance Award, and the Board may, at any time, waive the achievement of the applicable performance measures.

(d) Dividends; Dividend Equivalents. Notwithstanding its designation as a Performance Award, no Option or SAR shall provide for the payment or accrual of dividend equivalents in accordance with Sections 5(i) and 6(g), as applicable, any dividends declared and paid by the Company with respect to shares of Restricted Stock shall be subject to Section 7(c)(i), and any right to receive Dividend Equivalents on an award of RSUs and Other Stock-Based Awards shall be subject to Sections 7(d)(1) and 8(c), as applicable.

10. Adjustments for Changes in Common Stock and Certain Other Events

(a) Changes in Capitalization. In the event of any stock split, reverse stock split, stock dividend, recapitalization, combination of shares, reclassification of shares, spin-off or other similar change in capitalization or event, or any dividend or distribution to holders of Common Stock other than an ordinary cash dividend, (i) the number and class of securities available under the Plan, (ii) the share counting rules set forth in Section 4(a), (iii) the number and class of securities and exercise price per share of each outstanding Option, (iv) the share and per-share provisions and the measurement price of each outstanding SAR, (v) the number of shares subject to and the repurchase price per share subject to each outstanding award of Restricted Stock and (vi) the share and per-share-related provisions and the purchase price, if any, of each outstanding RSU and each Other Stock-Based Award, shall be equitably adjusted by the Company (or substituted Awards may be made, if applicable) in the manner determined by the Board. Without limiting the generality of the foregoing, in the event the Company effects a split of the Common Stock by means of a stock dividend and the exercise price of and the number of shares subject to an outstanding Option are adjusted as of the date of the distribution of the dividend (rather than as of the record date for such dividend), then an optionee who exercises an Option between the record date and the distribution date for such stock dividend shall be entitled to receive, on the distribution date, the stock dividend with respect to the shares of Common Stock acquired upon such Option exercise, notwithstanding the fact that such shares were not outstanding as of the close of business on the record date for such stock dividend.

(b) Reorganization Events.

(1) Definition. A "***Reorganization Event***" shall mean: (a) any merger or consolidation of the Company with or into another entity as a result of which all of the Common Stock of the Company is converted into or exchanged for the right to receive cash, securities or other property or is canceled, (b) any transfer or disposition of all of the Common Stock of the Company for cash, securities or other property pursuant to a share exchange or other transaction or (c) any liquidation or dissolution of the Company.

(2) Consequences of a Reorganization Event on Awards Other than Restricted Stock

(A) In connection with a Reorganization Event, the Board may take any one or more of the following actions as to all or any (or any portion of) outstanding Awards other than Restricted Stock on such terms as the Board determines (except to the extent specifically provided otherwise in an applicable Award agreement or another agreement between the Company and the Participant):

(i) provide that such Awards shall be assumed, or substantially equivalent Awards shall be substituted, by the acquiring or succeeding corporation (or an affiliate thereof);

(ii) upon written notice to a Participant, provide that all of the Participant's unvested Awards will be forfeited immediately prior to the consummation of such Reorganization Event and/ or that all of the Participant's unexercised Awards will terminate immediately prior to the consummation of such Reorganization Event unless exercised by the Participant (to the extent then exercisable) within a specified period following the date of such notice;

(iii) provide that outstanding Awards shall become exercisable, realizable or deliverable, or restrictions applicable to an Award shall lapse, in whole or in part prior to or upon such Reorganization Event;

(iv) in the event of a Reorganization Event under the terms of which holders of Common Stock will receive upon consummation thereof a cash payment for each share surrendered in the Reorganization Event (the "***Acquisition Price***"), make or provide for a cash payment to Participants with respect to each Award held by a Participant equal to (A) the number of shares of Common Stock subject to the vested portion of the Award (after giving effect to any acceleration of vesting that occurs upon or immediately prior to such Reorganization Event) multiplied by (B) the excess, if any, of (I) the Acquisition Price over (II) the exercise, measurement or purchase

price of such Award and any applicable tax withholdings, in exchange for the termination of such Award, *provided,* that if the Acquisition Price per share (as determined by the Board) does not exceed the exercise price of such Award, then the Award shall be canceled without any payment of consideration therefor;

(v) provide that, in connection with a liquidation or dissolution of the Company, Awards shall convert into the right to receive liquidation proceeds (if applicable, net of the exercise, measurement or purchase price thereof and any applicable tax withholdings); and

(vi) any combination of the foregoing.

In taking any of the actions permitted under this Section 10(b)(2)(A), the Board shall not be obligated by the Plan to treat all Awards, all Awards held by a Participant, or all Awards of the same type, identically.

(B) Notwithstanding the terms of Section 10(b)(2)(A)(i), in the case of outstanding RSUs that are subject to Section 409A: (i) if the applicable RSU agreement provides that the RSUs shall be settled upon a "change in control event" within the meaning of Treasury Regulation Section 1.409A-3(i)(5)(i), and the Reorganization Event constitutes such a "change in control event", then no assumption or substitution shall be permitted pursuant to Section 10(b)(2)(A)(i) and the RSUs shall instead be settled in accordance with the terms of the applicable RSU agreement; and (ii) the Board may only undertake the actions set forth in clauses (iii), (iv) or (v) of Section 10(b)(2)(A) if the Reorganization Event constitutes a "change in control event" as defined under Treasury Regulation Section 1.409A-3(i)(5)(i) and such action is permitted or required by Section 409A; if the Reorganization Event is not a "change in control event" as so defined or such action is not permitted or required by Section 409A, and the acquiring or succeeding corporation does not assume or substitute the RSUs pursuant to clause (i) of Section 10(b)(2)(A), then the unvested RSUs shall terminate immediately prior to the consummation of the Reorganization Event without any payment in exchange therefor.

(C) For purposes of Section 10(b)(2)(A)(i), an Award (other than Restricted Stock) shall be considered assumed if, following consummation of the Reorganization Event, such Award confers the right to purchase or receive pursuant to the terms of such Award, for each share of Common Stock subject to the Award immediately prior to the consummation of the Reorganization Event, the consideration (whether cash, securities or other property) received as a result of the Reorganization Event by holders of Common Stock for each share of Common Stock held immediately prior to the consummation of the Reorganization Event (and if holders were offered a choice of consideration, the type of consideration chosen by the holders of a majority of the outstanding shares of Common Stock); *provided, however*, that if the consideration received as a result of the Reorganization Event is not solely common stock of the acquiring or succeeding corporation (or an affiliate thereof), the Company may, with the consent of the acquiring or succeeding corporation, provide for the consideration to be received upon the exercise or settlement of the Award to consist solely of such number of shares of common stock of the acquiring or succeeding corporation (or an affiliate thereof) that the Board determined to be equivalent in value (as of the date of such determination or another date specified by the Board) to the per share consideration received by holders of outstanding shares of Common Stock as a result of the Reorganization Event.

(D) The Board may impose a limitation on the ability of Participants holding Options and/or SARs to exercise their Awards for the minimum number of days prior to the closing of the Reorganization Event as is reasonably necessary to facilitate the orderly closing of the Reorganization Event. The Company shall provide reasonable notice to Participants of any such limitation on exercise.

(3) Consequences of a Reorganization Event on Restricted Stock. Upon the occurrence of a Reorganization Event other than a liquidation or dissolution of the Company, the repurchase and other rights of the Company with respect to outstanding Restricted Stock shall inure to the benefit of the Company's successor and shall, unless the Board determines otherwise, apply to the cash, securities or other property which the Common Stock was converted into or exchanged for pursuant to such Reorganization Event in the same manner

and to the same extent as they applied to such Restricted Stock; *provided, however*, that the Board may either provide for termination or deemed satisfaction of such repurchase or other rights under the instrument evidencing any Restricted Stock or any other agreement between a Participant and the Company, either initially or by amendment, or provide for forfeiture of such Restricted Stock if issued at no cost. Upon the occurrence of a Reorganization Event involving the liquidation or dissolution of the Company, except to the extent specifically provided to the contrary in the instrument evidencing any Restricted Stock or any other agreement between a Participant and the Company, all restrictions and conditions on all Restricted Stock then outstanding shall automatically be deemed terminated or satisfied.

11. General Provisions Applicable to Awards

(a) Transferability of Awards. Awards shall not be sold, assigned, transferred, pledged or otherwise encumbered by a Participant, either voluntarily or by operation of law, except by will or the laws of descent and distribution or, other than in the case of an Incentive Stock Option, pursuant to a qualified domestic relations order, and, during the life of the Participant, shall be exercisable only by the Participant; *provided, however*, that, except with respect to Awards subject to Section 409A and Incentive Stock Options, the Board may permit or provide in an Award for the gratuitous transfer of the Award by the Participant to or for the benefit of any immediate family member, family trust or other entity established for the benefit of the Participant and/or an immediate family member thereof if the Company would be eligible to use a Form S-8 under the Securities Act for the registration of the sale of the Common Stock subject to such Award to such proposed transferee; *provided further*, that the Company shall not be required to recognize any such permitted transfer until such time as such permitted transferee shall, as a condition to such transfer, deliver to the Company a written instrument in form and substance satisfactory to the Company confirming that such transferee shall be bound by all of the terms and conditions of the Award. References to a Participant, to the extent relevant in the context, shall include references to authorized transferees. For the avoidance of doubt, nothing contained in this Section 11(a) shall be deemed to restrict a transfer to the Company.

(b) Documentation. Each Award shall be evidenced in such form (written, electronic or otherwise) as the Board shall determine. Each Award may contain terms and conditions in addition to those set forth in the Plan.

(c) Termination of Status. The Board shall determine the effect on an Award of the disability, death, termination or other cessation of employment or service, authorized leave of absence or other change in the employment or other service status of a Participant and the extent to which, and the period during which, the Participant, or the Participant's legal representative, conservator, guardian or Designated Beneficiary, may exercise rights, or receive any benefits, under an Award. "***Designated Beneficiary***" means (i) the beneficiary designated, in a manner determined by the Board, by a Participant to receive amounts due or exercise rights of the Participant in the event of the Participant's death or (ii) in the absence of an effective designation by a Participant, the Participant's estate.

(d) Withholding. The Participant must satisfy all applicable federal, state, and local or other income and employment tax withholding obligations before the Company will deliver stock certificates or otherwise recognize ownership of Common Stock under an Award. The Company may elect to satisfy the withholding obligations through additional withholding on salary or wages. If the Company elects not to or cannot withhold from other compensation, the Participant must pay the Company the full amount, if any, required for withholding or have a broker tender to the Company cash equal to the withholding obligations. Payment of withholding obligations is due before the Company will issue any shares on exercise, vesting or release from forfeiture of an Award or at the same time as payment of the exercise or purchase price, unless the Company determines otherwise. If provided for in an Award or approved by the Board, a Participant may satisfy the tax obligations in whole or in part by delivery (either by actual delivery or attestation) of shares of Common Stock, including shares retained from the Award creating the tax obligation, valued at their fair market value (valued in the manner determined or approved by the Company); *provided, however*, except as otherwise provided by the Board, that the total tax withholding where stock is being used to satisfy such tax obligations cannot exceed the

Company's minimum statutory withholding obligations (based on minimum statutory withholding rates for federal and state tax purposes, including payroll taxes, that are applicable to such supplemental taxable income), except that, to the extent that the Company is able to retain shares of Common Stock having a fair market value (determined or approved by the Company) that exceeds the statutory minimum applicable withholding tax without financial accounting implications or the Company is withholding in a jurisdiction that does not have a statutory minimum withholding tax, the Company may retain such number of shares of Common Stock (up to the number of shares having a fair market value equal to the maximum individual statutory rate of tax (determined or approved by, the Company)) as the Company shall determine to be necessary to satisfy the tax liability associated with any Award. Shares used to satisfy tax withholding requirements cannot be subject to any repurchase, forfeiture, unfulfilled vesting or other similar requirements.

(e) Amendment of Award. Except as otherwise provided in Sections 5(g) and 6(e) with respect to repricings, and Section 12(d) with respect to amendments to the Plan, the Board may amend, modify or terminate any outstanding Award, including but not limited to, substituting therefor another Award of the same or a different type, changing the date of exercise or realization, and converting an Incentive Stock Option to a Nonstatutory Stock Option. The Participant's consent to such action shall be required unless (i) the Board determines that the action, taking into account any related action, does not materially and adversely affect the Participant's rights under the Plan or (ii) the change is permitted under Section 10.

(f) Conditions on Delivery of Stock. The Company will not be obligated to deliver any shares of Common Stock pursuant to the Plan or to remove restrictions from shares previously issued or delivered under the Plan until (i) all conditions of the Award have been met or removed to the satisfaction of the Company, (ii) in the opinion of the Company's counsel, all other legal matters in connection with the issuance and delivery of such shares have been satisfied, including any applicable securities laws and regulations and any applicable stock exchange or stock market rules and regulations, and (iii) the Participant has executed and delivered to the Company such representations or agreements as the Company may consider appropriate to satisfy the requirements of any applicable laws, rules or regulations.

(g) Limitations on Vesting. Subject to Section 11(h), no Award shall vest earlier than the first anniversary of its date of grant, unless such Award is granted in lieu of salary, bonus or other compensation otherwise earned by or payable to the Participant. The foregoing sentence shall not apply to Awards granted, in the aggregate, for up to 5% of the maximum number of authorized shares set forth in Section 4(a).

(h) Acceleration. The Board may at any time provide that any Award shall become immediately exercisable in whole or in part, free from some or all restrictions or conditions or otherwise realizable in whole or in part, as the case may be.

12. Miscellaneous

(a) No Right To Employment or Other Status. No person shall have any claim or right to be granted an Award by virtue of the adoption of the Plan, and the grant of an Award shall not be construed as giving a Participant the right to continued employment or any other relationship with the Company. The Company expressly reserves the right at any time to dismiss or otherwise terminate its relationship with a Participant free from any liability or claim under the Plan, except as expressly provided in the applicable Award.

(b) No Rights As Stockholder; Clawback. Subject to the provisions of the applicable Award, no Participant or Designated Beneficiary shall have any rights as a stockholder with respect to any shares of Common Stock to be issued with respect to an Award until becoming the record holder of such shares. In accepting an Award under the Plan, the Participant agrees to be bound by any clawback policy that the Company has in effect or may adopt in the future.

(c) Effective Date and Term of Plan. The Plan shall become effective on the Effective Date. No Awards shall be granted under the Plan after the expiration of 10 years from the Effective Date, but Awards previously granted may extend beyond that date.

(d) Amendment of Plan. The Board may amend, suspend or terminate the Plan or any portion thereof at any time provided that (i) neither Section 5(g) nor Section 6(e) requiring stockholder approval of any Option or SAR repricing may be amended without stockholder approval; (ii) no amendment that would require stockholder approval under the rules of the national securities exchange on which the Company then maintains its primary listing will be effective unless and until the Company's stockholders approve such amendment; and (iii) if the national securities exchange on which the Company then maintains its primary listing does not have rules regarding when stockholder approval of amendments to equity compensation plans is required (or if the Company's Common Stock is not then listed on any national securities exchange), then no amendment to the Plan (A) materially increasing the number of shares authorized under the Plan (other than pursuant to Section 4(c) or 10), (B) expanding the types of Awards that may be granted under the Plan, or (C) materially expanding the class of participants eligible to participate in the Plan shall be effective unless and until the Company's stockholders approve such amendment. In addition, if at any time the approval of the Company's stockholders is required as to any other modification or amendment under Section 422 of the Code or any successor provision with respect to Incentive Stock Options, the Board may not effect such modification or amendment without such approval. Unless otherwise specified in the amendment, any amendment to the Plan adopted in accordance with this Section 12(d) shall apply to, and be binding on the holders of, all Awards outstanding under the Plan at the time the amendment is adopted, provided the Board determines that such amendment, taking into account any related action, does not materially and adversely affect the rights of Participants under the Plan. No Award shall be made that is conditioned upon stockholder approval of any amendment to the Plan unless the Award provides that (i) it will terminate or be forfeited if stockholder approval of such amendment is not obtained within no more than 12 months from the date of grant and (2) it may not be exercised or settled (or otherwise result in the issuance of Common Stock) prior to such stockholder approval.

(e) Authorization of Sub-Plans (including for Grants to non-U.S. Employees). The Board may from time to time establish one or more sub-plans under the Plan for purposes of satisfying applicable securities, tax or other laws of various jurisdictions. The Board shall establish such sub-plans by adopting supplements to the Plan containing (i) such limitations on the Board's discretion under the Plan as the Board deems necessary or desirable or (ii) such additional terms and conditions not otherwise inconsistent with the Plan as the Board shall deem necessary or desirable. All supplements adopted by the Board shall be deemed to be part of the Plan, but each supplement shall apply only to Participants within the affected jurisdiction and the Company shall not be required to provide copies of any supplement to Participants in any jurisdiction which is not the subject of such supplement.

(f) Compliance with Section 409A. If and to the extent (i) any portion of any payment, compensation or other benefit provided to a Participant in connection with his or her employment termination constitutes "nonqualified deferred compensation" within the meaning of Section 409A and (ii) the Participant is a specified employee as defined in Section 409A(a)(2)(B)(i) of the Code, in each case as determined by the Company in accordance with its procedures, by which determinations the Participant (through accepting the Award) agrees that to be bound, such portion of the payment, compensation or other benefit shall not be paid before the day that is six months plus one day after the date of "separation from service" (as determined under Section 409A) (the "***New Payment Date***"), except as Section 409A may then permit. The aggregate of any payments that otherwise would have been paid to the Participant during the period between the date of separation from service and the New Payment Date shall be paid to the Participant in a lump sum on such New Payment Date, and any remaining payments will be paid on their original schedule.

The Company makes no representations or warranty and shall have no liability to the Participant or any other person if any provisions of or payments, compensation or other benefits under the Plan are determined to constitute nonqualified deferred compensation subject to Section 409A but do not to satisfy the conditions of that section.

(g) Limitations on Liability. Notwithstanding any other provisions of the Plan, no individual acting as a director, officer, employee or agent of the Company will be liable to any Participant, former Participant, spouse, beneficiary, or any other person for any claim, loss, liability, or expense incurred in connection with the Plan, nor will such individual be personally liable with respect to the Plan because of any contract or other instrument such individual executes in his or her capacity as a director, officer, employee or agent of the Company. The Company will indemnify and hold harmless each director, officer, employee or agent of the Company to whom any duty or power relating to the administration or interpretation of the Plan has been or will be delegated, against any cost or expense (including attorneys' fees) or liability (including any sum paid in settlement of a claim with the Board's approval) arising out of any act or omission to act concerning the Plan unless arising out of such person's own fraud or bad faith.

(h) Governing Law. The provisions of the Plan and all Awards made hereunder shall be governed by and interpreted in accordance with the laws of the State of Delaware, excluding choice-of-law principles of the law of such state that would require the application of the laws of a jurisdiction other than the State of Delaware.

Second Certificate of Amendment

Of

Amended And Restated Certificate of Incorporation, As Amended

of

Tyme Technologies, Inc.

Tyme Technologies, Inc. (the "Corporation"), a corporation organized and existing under the General Corporation Law of the State of Delaware (the "DGCL"), hereby adopts this Second Certificate of Amendment (this "Certificate of Amendment"), which amends its Amended and Restated Certificate of Incorporation, as amended (the "Certificate of Incorporation"), as described below, and does hereby further certify that:

1. The Board of Directors of the Corporation duly adopted a resolution proposing and declaring advisable the amendment to the Certificate of Incorporation described herein, and the Corporation's stockholders duly adopted such amendment, all in accordance with the provisions of Section 242 of the DGCL.

2. Article 4 of the Certificate of Incorporation is hereby amended by inserting the following as a new Article 4.5:

"4.5 Reverse Stock Split. Without any other action on the part of the Corporation or any other person, effective immediately on [●] (the "Effective Time"), each [●][17] shares of the Corporation's Common Stock issued and outstanding immediately prior to the Effective Time ("Old Common Stock") shall automatically, without further action on the part of the Corporation or any holder of Old Common Stock, convert into one fully paid and nonassessable share of new Common Stock. The conversion described in the foregoing sentence shall be collectively referred to herein as the "Common Stock Reverse Stock Split." The par value of the Common Stock following the Common Stock Reverse Stock Split shall remain at $0.0001. No shares of fractional Common Stock shall be issued upon the Common Stock Reverse Stock Split and instead of issuing fractional of Common Stock, the Corporation transfer agent shall aggregate all such fractional shares of Common Stock and sell them as soon as practicable after the effective time of this Certificate of Amendment at the then prevailing prices on the open market, on behalf of those stockholders who would otherwise be entitled to receive a fractional share of Common Stock (the "Fractional Share Sale"). After the Corporation's transfer agent's completion of the Fractional Share Sale, each stockholder who would otherwise be entitled to receive a fractional share shall receive a cash payment from the Corporation's transfer agent in an amount equal to such stockholder's respective pro rata share of the total net proceeds of the Fractional Share Sale."

[17] To be a number not less than 15 and not more than 75.

IN WITNESS WHEREOF, Tyme Technologies, Inc. has caused this Certificate of Amendment to be executed and delivered on its behalf by its Chief Executive Officer on this [●] day of [●], 2022.

TYME TECHNOLOGIES, INC.

By: _____
Richard Cunningham
Chief Executive Officer