
**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION**
Washington, D.C. 20549

SCHEDULE 14A

**Proxy Statement Pursuant to Section 14(a) of the
Securities Exchange Act of 1934
(Amendment No.)**

Filed by the Registrant Filed by a Party other than the Registrant

Check the appropriate box:

- Preliminary Proxy Statement
- Confidential, for Use of the Commission Only (as permitted by Rule 14a-6(e)(2))**
- Definitive Proxy Statement
- Definitive Additional Materials
- Soliciting Material Pursuant to §240.14a-12

SYROS PHARMACEUTICALS, INC.

(Name of Registrant as Specified in Its Charter)

(Name of Person(s) Filing Proxy Statement, if Other Than the Registrant)

Payment of Filing Fee (Check the appropriate box):

- No fee required.
- Fee computed on table below per Exchange Act Rules 14a-6(i)(1) and 0-11.

(1) Title of each class of securities to which transaction applies:

(2) Aggregate number of securities to which transaction applies:

(3) Per unit price or other underlying value of transaction computed pursuant to Exchange Act Rule 0-11 (set forth the amount on which the filing fee is calculated and state how it was determined):

(4) Proposed maximum aggregate value of transaction:

(5) Total fee paid:

Fee paid previously with preliminary materials.

Check box if any part of the fee is offset as provided by Exchange Act Rule 0-11(a)(2) and identify the filing for which the offsetting fee was paid previously. Identify the previous filing by registration statement number, or the Form or Schedule and the date of its filing.

(1) Amount Previously Paid:

(2) Form, Schedule or Registration Statement No.:

(3) Filing Party:

(4) Date Filed:



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

**NOTICE OF 2021 ANNUAL MEETING OF STOCKHOLDERS
To Be Held on June 8, 2021**

Dear Stockholders:

You are cordially invited to attend the 2021 annual meeting of stockholders of Syros Pharmaceuticals, Inc. To support the health and well-being of our stockholders, employees and directors in light of the COVID-19 pandemic, the meeting will be held virtually via the Internet at www.meetingcenter.io/225982509 on Tuesday, June 8, 2021 at 11:00 a.m., Eastern Daylight Time.

At the annual meeting, stockholders will consider and vote on the following matters:

1. The election of three Class II directors, Srinivas Akkaraju, M.D., Ph.D., Phillip A. Sharp, Ph.D., and Richard A. Young, Ph.D., nominated by our board of directors, each to serve for a three-year term expiring at the 2024 annual meeting of stockholders and until his successor has been duly elected and qualified;
2. The ratification of the appointment of Ernst & Young LLP as our independent registered public accounting firm for the fiscal year ending December 31, 2021; and
3. The transaction of any other business that may properly come before the annual meeting or any adjournment or postponement thereof.

As noted above, due to the COVID-19 pandemic, our annual meeting will be a “virtual meeting” of stockholders, which will be conducted exclusively via the Internet. There will not be a physical meeting location, and stockholders will not be able to attend the annual meeting in person. This means that you can attend the annual meeting online, vote your shares during the online meeting and submit questions for consideration prior to and during the online meeting, all by following the instructions described in the accompanying proxy statement. Stockholders of record at the close of business on April 12, 2021 will be entitled to notice of and to vote at the annual meeting or any adjournment or postponement thereof. We believe that hosting a “virtual meeting” will enable greater stockholder attendance and participation from any location around the world. We intend to resume our historical practice of holding an in-person meeting next year.

This Notice, the accompanying proxy statement and a form of proxy card are being mailed beginning on or about April 29, 2021 to all stockholders entitled to vote at the annual meeting. We have elected to provide access to our proxy materials over the Internet under the Securities and Exchange Commission’s “notice and access” rules. We believe that providing our proxy materials over the Internet expedites stockholders’ receipt of proxy materials, lowers costs and reduces the environmental impact of our annual meeting.

We encourage all stockholders to attend the annual meeting online. However, whether or not you plan to attend the annual meeting online, we encourage you to read this proxy statement and submit your proxy or voting instructions as soon as possible. Please review the instructions on each of your voting options described in the proxy statement.

Thank you for your ongoing support and continued interest in Syros.

By Order of the Board of Directors,

A handwritten signature in black ink, appearing to read "Nancy", written over a horizontal line.

Nancy A. Simonian, M.D.
President and Chief Executive Officer

Cambridge, Massachusetts
April 29, 2021

Important Notice Regarding Internet Availability of Proxy Materials: The attached proxy statement and our 2020 annual report to stockholders, which includes our Annual Report on Form 10-K for the fiscal year ended December 31, 2020, are available at www.envisionreports.com/SYRS. These documents are also available to any stockholder who wishes to receive a paper copy by calling (866) 641-4276, by emailing investorvote@computershare.com with “Proxy Materials Syros Pharmaceuticals, Inc.” in the subject line, or by submitting a request over the Internet at www.envisionreports.com/SYRS.

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

PROXY STATEMENT
2021 ANNUAL MEETING OF STOCKHOLDERS
To Be Held on June 8, 2021

INFORMATION CONCERNING SOLICITATION AND VOTING

This proxy statement and the enclosed proxy card are being furnished in connection with the solicitation of proxies by the board of directors of Syros Pharmaceuticals, Inc. for use at the annual meeting of stockholders to be held on Tuesday, June 8, 2021 at 11:00 a.m., Eastern Daylight Time, and at any adjournment thereof. To support the health and well-being of our stockholders, employees and directors in light of the COVID-19 pandemic, the meeting will be held virtually via the Internet at www.meetingcenter.io/225982509. You will be able to attend and participate in the annual meeting online, vote your shares electronically and submit your questions prior to and during the meeting, all by following the instructions described in this proxy statement in the section entitled "Important Information About the Annual Meeting and Voting." There will not be a physical meeting location, and stockholders will not be able to attend the annual meeting in person. Except where the context otherwise requires, references to "Syros Pharmaceuticals," "the Company," "we," "us," "our" and similar terms refer to Syros Pharmaceuticals, Inc.

This proxy statement summarizes information about the proposals to be considered at the meeting and other information you may find useful in determining how to vote. The proxy card is how you authorize another person to vote your shares in accordance with your instructions. We are making this proxy statement, the related proxy card and our annual report to stockholders for the fiscal year ended December 31, 2020 available to stockholders for the first time on or about April 29, 2021.

A copy of our Annual Report on Form 10-K for the fiscal year ended December 31, 2020, as filed with the Securities and Exchange Commission, or SEC, except for exhibits, will be furnished without charge to any stockholder upon written or oral request to Syros Pharmaceuticals, Inc., 35 CambridgePark Drive, 4th Floor, Cambridge, Massachusetts 02140 or by calling (866) 641-4276, by emailing investorvote@computershare.com with "Proxy Materials Syros Pharmaceuticals, Inc." in the subject line, or by submitting a request over the Internet at www.envisionreports.com/SYRS. This proxy statement and our Annual Report on Form 10-K for the fiscal year ended December 31, 2020 are also available on the SEC's website at www.sec.gov.

IMPORTANT INFORMATION ABOUT THE ANNUAL MEETING AND VOTING

Q. Why did I receive these proxy materials?

- A. Our board of directors has made these materials available to you on the Internet in connection with the solicitation of proxies for use at our 2021 annual meeting of stockholders to be held virtually at www.meetingcenter.io/225982509 on Tuesday, June 8, 2021 at 11:00 a.m., Eastern Daylight Time. As a holder of common stock, you are invited to attend the annual meeting online and are requested to vote on the items of business described in this proxy statement. This proxy statement includes information that we are required to provide to you under SEC rules and that is designed to assist you in voting your shares.

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Q. Why did I receive a notice in the mail regarding the Internet availability of proxy materials instead of a full set of proxy materials?

- A. In accordance with SEC rules, we may furnish proxy materials, including this proxy statement and our 2020 annual report, to our stockholders by providing access to such documents on the Internet instead of mailing printed copies. If you would like to receive a paper copy of our proxy materials, you should follow the instructions for requesting such materials in the notice.

Q. What is the purpose of the annual meeting?

- A. At the annual meeting, stockholders will consider and vote on the following matters:
1. The election of three Class II directors, Srinivas Akkaraju, M.D., Ph.D., Phillip A. Sharp, Ph.D., and Richard A. Young, Ph.D., nominated by our board of directors, each to serve for a three-year term expiring at the 2024 annual meeting of stockholders or until his successor has been duly elected and qualified (Proposal 1);
 2. The ratification of the appointment of Ernst & Young LLP as our independent registered public accounting firm for the fiscal year ending December 31, 2021 (Proposal 2); and
 3. The transaction of any other business that may properly come before the annual meeting or any adjournment or postponement thereof.

Q. Why is the 2021 annual meeting a virtual, online meeting?

- A. To support the health and well-being of our stockholders, employees and directors in light of the COVID-19 pandemic, our 2021 annual meeting will be a virtual meeting of stockholders where stockholders will participate by accessing a website using the Internet. There will not be a physical meeting location. We believe that hosting a virtual meeting will facilitate stockholder attendance and participation at our 2021 annual meeting by enabling stockholders to safely participate remotely from any location around the world. We have designed the virtual annual meeting to provide the same rights and opportunities to participate as stockholders have at an in-person meeting, including the right to vote and ask questions through the virtual meeting platform. We intend to return to holding an in-person annual meeting for our 2022 annual meeting of stockholders.

Q. How do I attend the annual meeting virtually?

- A. The annual meeting will be a completely virtual meeting of stockholders, which will be conducted exclusively by webcast. No physical meeting will be held. You are entitled to participate in the annual meeting only if you were a stockholder of record as of the close of business on April 12, 2021, the record date for our annual meeting, or if you hold a valid legal proxy for the annual meeting.

You will be able to attend the annual meeting online and submit your questions during the meeting by visiting www.meetingcenter.io/225982509. You also will be able to vote your shares online by attending the annual meeting by webcast.

To participate in the annual meeting, you will need to review the information included on your notice, on your proxy card or on the instructions that accompanied your proxy materials. The password for the meeting is SYRS2021.

If you hold your shares through an intermediary, such as a bank or broker, you must register in advance using the instructions below under "How do I register to attend the virtual annual meeting?".

The online meeting will begin promptly at 11:00 a.m., Eastern Daylight Time. We encourage you to access the meeting fifteen to thirty minutes prior to the start time to allow for ample time for the check in. Please follow the registration instructions as outlined in this proxy statement.

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Q. Howdo I register to attend the virtual annual meeting?

- A. If you are a “record holder” of our shares (i.e., you hold your shares through our transfer agent, Computershare Trust Company, N.A.), you do not need to register to attend the virtual annual meeting. Please follow the instructions on the notice or proxy card that you received.

If you hold your shares through an intermediary, such as a bank or broker, you must register in advance to attend the virtual annual meeting.

To register to attend the annual meeting online by webcast you must submit proof of your proxy power (legal proxy) reflecting your holdings of shares of our common stock along with your name and email address to Computershare. A legal proxy is *not* the form of proxy included with this proxy statement. Requests for registration must be labeled as “Legal Proxy” and be received no later than 5:00 p.m., Eastern Daylight Time, on Wednesday, June 2, 2021.

You will receive a confirmation of your registration by email after we receive your registration materials.

Requests for registration should be directed to Computershare as follows:

By email: Forward the email from your broker, or attach an image of your legal proxy, to legalproxy@computershare.com.

By mail: Computershare
Syros Pharmaceuticals, Inc. Legal Proxy
P.O. Box 43001
Providence, RI 02940-3001

Q. Whatif I have trouble accessing the annual meeting virtually?

- A. The virtual meeting platform is fully supported across MS Edge, Firefox, Chrome and Safari browsers and devices (desktops, laptops, tablets and cell phones) running the most up-to-date version of applicable software and plug-ins. Please note that Internet Explorer is no longer supported. Participants should ensure that they have a strong WiFi connection wherever they intend to participate in the meeting. We encourage you to access the meeting fifteen to thirty minutes prior to the start time. A link on the meeting page will provide further assistance should you need it or you may call 1-888-724-2416 or 1-781-575-2748.

Q. Whocan vote at the annual meeting?

- A. To be entitled to vote, you must have been a stockholder of record at the close of business on April 12, 2021, the record date for our annual meeting. There were 61,849,642 shares of our common stock outstanding and entitled to vote at the annual meeting as of the record date. The list of our stockholders of record will be available, via link, during the annual meeting. In addition, we will make available a list of stockholders of record as of the record date for inspection by stockholders for any purpose germane to the annual meeting during the ten days preceding the annual meeting. To access the stockholder list during this time, please send your request, and proof of ownership, to our corporate secretary at 35 CambridgePark Drive, 4th Floor, Cambridge MA 02140, attention: Corporate Secretary.

Q. Howmany votes do I have?

- A. Eachshare of our common stock that you own as of the record date will entitle you to one vote on each matter considered at the annual meeting.

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Q. **Howdo I vote?**

- A. **If you are the “record holder” of your shares** meaning that your shares are registered in your name in the records of our transfer agent, Computershare Trust Company, N.A., you may vote your shares at the virtual meeting or by proxy as follows:
1. **Over the Internet prior to or during the annual meeting:**To vote over the Internet, please go to the following website: www.envisionreports.com/SYRS, and follow the instructions at that site for submitting your proxy electronically. If you vote over the Internet, you do not need to complete and mail your proxy card or vote your proxy by telephone. You must specify how you want your shares voted or your Internet vote cannot be completed, and you will receive an error message. You must submit your Internet proxy before the closing of the polls at the annual meeting on June 8, 2021 for your proxy to be valid and your vote to count.
 2. **By telephone prior to the annual meeting:**To vote by telephone, please call (800)652-VOTE (8683), and follow the instructions provided on the proxy card. If you vote by telephone, you do not need to complete and mail your proxy card or vote your proxy over the Internet. You must specify how you want your shares voted and confirm your vote at the end of the call or your telephone vote cannot be completed. You must submit your telephonic proxy before 11:59 p.m., Eastern Daylight Time, on June 7, 2021, the day before the annual meeting, for your proxy to be valid and your vote to count.
 3. **By mail prior to the annual meeting:**To vote by mail, you must mark, sign and date the proxy card and then mail the proxy card in accordance with the instructions on the proxy card. If you vote by mail, you do not need to vote your proxy over the Internet or by telephone. Computershare Trust Company, N.A. must receive the proxy card not later than June 7, 2021, the day before the annual meeting, for your proxy to be valid and your vote to count. If you return your proxy card but do not specify how you want your shares voted on any individual matter, your shares will be voted in accordance with the recommendations of our board of directors.
 4. **Virtually at the annual meeting:** You will also be able to vote your shares online by attending the annual meeting by webcast by visiting www.meetingcenter.io/225982509. To participate in the annual meeting, you will need to review the information included on your notice, on your proxy card or on the instructions that accompanied your proxy materials. The password for the meeting is SYRS2021.

If your shares are held in “street name,” meaning they are held for your account by an intermediary, such as a broker, then you are deemed to be the beneficial owner of your shares and the broker that actually holds the shares for you is the record holder and is required to vote the shares it holds on your behalf according to your instructions. The proxy materials, as well as voting and revocation instructions, should have been forwarded to you by the broker that holds your shares. To vote your shares, you will need to follow the instructions that your broker provides you. Many brokers solicit voting instructions over the Internet or by telephone.

If you do not give instructions to your broker, your broker will still be able to vote your shares with respect to certain “discretionary” items. The ratification of the appointment of Ernst & Young LLP as our independent registered public accounting firm (Proposal 2) is considered a discretionary item. Accordingly, your broker may vote your shares in its discretion with respect to that matter even if you do not give voting instructions on Proposal 2.

However, under applicable stock exchange rules that regulate voting by registered brokerage firms, the election of our nominees to serve as Class II directors (Proposal 1) is not considered to be a discretionary item. Accordingly, if you do not give your broker voting instructions on Proposal 1, your broker may not vote your shares with respect to this matter and your shares will be counted as “broker non-votes” with respect to the proposal. A “broker non-vote” occurs when shares held by a broker are not voted with respect to a proposal because the broker does not have or did not exercise discretionary authority to vote on the matter and has not received voting instructions from its clients.

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Regardless of whether your shares are held in street name, you are welcome to attend the meeting online. You may not vote shares held in street name during the virtual meeting, however, unless you obtain a legal proxy, executed in your favor, from the holder of record (i.e., your broker) and register for the meeting in advance as described above under “How do I register to attend the virtual annual meeting?”. A legal proxy is *not* the form of proxy included with this proxy statement.

Q. Can I change my vote?

- A. If your shares are registered directly in your name, you may revoke your proxy and change your vote at any time before the vote is taken at the annual meeting. To do so, you must do one of the following:
1. Vote over the Internet or by telephone as instructed above under “Over the Internet prior to or during the annual meeting” and “By telephone prior to the annual meeting”. Only your latest Internet or telephone vote is counted.
 2. Sign and return a new proxy card. Only your latest dated and timely received proxy card will be counted.
 3. Attend the virtual annual meeting and vote online as instructed above under “Virtually at the annual meeting”. Virtually attending the annual meeting will not alone revoke your Internet vote, telephone vote, or proxy card submitted by mail.

If your shares are held in “street name,” you may submit new voting instructions by contacting your broker or other nominee. You may also vote online during the annual meeting if you obtain a legal proxy and register in advance to attend the meeting, as described above under “How do I register to attend the virtual annual meeting?”.

Q. How many shares must be represented to have a quorum and hold the annual meeting?

- A. A majority of our shares of common stock outstanding at the record date must be present virtually or represented by proxy to hold the annual meeting. This is called a quorum. For purposes of determining whether a quorum exists, we count as present any shares that are voted over the Internet, by telephone, by completing and submitting a proxy card by mail or that are represented virtually at the meeting. Further, for purposes of establishing a quorum, we will count as present shares that a stockholder holds even if the stockholder votes to abstain or only votes on one of the proposals. In addition, we will count as present shares held in “street name” by brokers who indicate on their proxies that they do not have authority to vote those shares. If a quorum is not present, we expect to adjourn the annual meeting until we obtain a quorum.

Q. What vote is required to approve each matter and how are votes counted?

A. Proposal 1—Election of Class II Directors

A nominee will be elected as a director at the annual meeting if the nominee receives a plurality of the votes cast “for” the applicable seat on the board of directors.

Proposal 2—Ratification of the Appointment of Independent Registered Public Accounting Firm

The affirmative vote of the holders of shares of common stock representing a majority of the votes cast on the matter is required for the ratification of the appointment of Ernst & Young LLP as our independent registered public accounting firm for the year ended December 31, 2021.

Shares that abstain from voting and “broker non-votes” with respect to a matter will not be counted as votes in favor of such matter and will also not be counted as shares voting on such matter. Accordingly, abstentions and “broker non-votes” will have no effect on the voting on Proposal 1 or Proposal 2 referenced above.

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Q. Whowill count the vote?

- A. Thevotes will be counted, tabulated and certified by Computershare Trust Company, N.A.

Q. Howdoes the board of directors recommend that I vote on the proposals?

- A. Ourboard of directors recommends that you vote:

FOR the election of the three nominees to serve as Class II directors, each for a three-year term; and

FOR the ratification of the appointment of Ernst & Young LLP as our independent registered public accounting firm for the fiscal year ending December 31, 2021.

Q. Arethere other matters to be voted on at the annual meeting?

- A. Wedo not know of any matters that may come before the annual meeting other than the election of our Class II directors and the ratification of the appointment of Ernst & Young LLP as our independent registered public accounting firm. If any other matters are properly presented at the annual meeting, the persons named in the accompanying proxy intend to vote, or otherwise act, in accordance with their judgment on the matter.

Q. Howdo I submit a question at the annual meeting?

- A. You will be able to attend the annual meeting online and submit your questions during the meeting by visiting www.meetingcenter.io/225982509, as further described above under “How do I attend the virtual annual meeting?”. Questions pertinent to meeting matters will be answered during the meeting, subject to time constraints. The meeting is not to be used as a forum to present personal matters, or general economic, political or other views that are not directly related to our business and the matters properly before the meeting, and therefore questions on such matters will not be answered. All questions received from stockholders before or during the virtual annual meeting will be posted on our website at ir.syros.com as soon as practicable following the annual meeting.

Q. Wherecan I find the voting results?

- A. Weplan to announce preliminary voting results at the annual meeting and will report final voting results in a Current Report on Form8-K filed with the SEC within four business days following the date of our annual meeting.

Q. Whatare the costs of soliciting these proxies?

- A. Wewill bear the cost of soliciting proxies. In addition to solicitation by mail, our directors, officers and employees may solicit proxies by telephone, e-mail, facsimile, and in person without additional compensation. We may reimburse brokers or persons holding stock in their names, or in the names of their nominees, for their expenses in sending proxies and proxy material to beneficial owners.

Implications of Being an “Emerging Growth Company”

We are an “emerging growth company,” as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, and may remain an emerging growth company for up to five years from the date of our initial public offering, or IPO. The JOBS Act contains provisions that, among other things, reduce certain reporting requirements for an “emerging growth company.” For so long as we remain an emerging growth company, we are permitted and plan to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include reduced disclosure

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obligations regarding executive compensation. In addition, as an emerging growth company, we are not required to conduct votes seeking approval, on an advisory basis, of the compensation of our named executive officers or the frequency with which such votes must be conducted. We may take advantage of some or all these exemptions until we are no longer an emerging growth company. We would cease to be an emerging growth company if we have more than \$1.07 billion in annual revenue, we have more than \$700 million in market value of our stock held by non-affiliates or we issue more than \$1 billion of non-convertible debt over a three-year period. We have taken advantage of certain reduced reporting obligations in this proxy statement. Accordingly, the information contained herein may be different than the information you receive from other public companies in which you hold stock.

BOARD OF DIRECTORS AND CORPORATE GOVERNANCE

Election of Directors

Our board of directors is divided into three classes, with members of each class holding office for staggered three-year terms. There are currently three Class II directors (Srinivas Akkaraju, M.D., Ph.D., Phillip A. Sharp, Ph.D., and Richard A. Young, Ph.D.) whose terms expire at this annual meeting of stockholders, three Class III directors (S. Gail Eckhardt, M.D., Marsha H. Fanucci and Nancy A. Simonian, M.D.) whose terms expire at the 2022 annual meeting of stockholders, and three Class I directors (Mark J. Alles, Amir Nashat, Ph.D., and Peter Wirth) whose terms expire at the 2023 annual meeting of stockholders (in all cases subject to the election and qualification of their successors or to their earlier death, resignation or removal). We believe that our classified board structure:

- enhances the effectiveness of our board by helping ensure that, at any given time, a majority of directors have experience and familiarity with our business; and
- promotes continuity and stability on our board, which allows it to focus on long-term planning intended to enhance stockholder value.

Set forth below are the names of and certain information for each member of our board, including the nominees for election as Class II directors, as of March 31, 2021. The information presented includes each director's and nominee's principal occupation and business experience for the past five years, and the names of other public companies of which he or she has served as a director during the past five years. The information presented below regarding the specific experience, qualifications, attributes and skills of each director and nominee led our nominating and corporate governance committee and our board of directors to conclude that he or she should serve as a director. In addition, we believe that all of our directors and nominees possess the attributes or characteristics described in "Corporate Governance Matters—Director Nomination Process" that the nominating and corporate governance committee expects of each director. There are no family relationships among any of our directors, nominees for director, or executive officers.

Name	Age	Position(s)
<i>Class II Director Nominees</i>		
Srinivas Akkaraju, M.D., Ph.D. (1)(2)	53	Director
Phillip A. Sharp, Ph.D. (2)(3)	76	Director
Richard A. Young, Ph.D. (2)	67	Director
<i>Class III Directors</i>		
S. Gail Eckhardt, M.D.(2)	63	Director
Marsha H. Fanucci (4)	67	Director
Nancy A. Simonian, M.D.	60	President and Chief Executive Officer, Director
<i>Class I Directors</i>		
Mark J. Alles (4)	61	Director
Amir Nashat, Ph.D. (1)(4)	48	Director
Peter Wirth (3)	70	Chair of the Board of Directors

- (1) Member of the nominating and corporate governance committee.
- (2) Member of the research and development committee.
- (3) Member of the compensation committee.
- (4) Member of the audit committee.

Class II Director Nominees

Srinivas Akkaraju, M.D., Ph.D. has served on our 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. 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. We believe that Dr. Akkaraju is qualified to serve on our board of directors because of his strong scientific background and extensive experience in private equity and venture capital investing.

Phillip A. Sharp, Ph.D. has served on our 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. We believe Dr. Sharp is qualified to serve on our board of directors due to his scientific expertise and his experience as a director of a publicly traded company.

Richard A. Young, Ph.D. has served on our board of directors since our inception in November 2011. He is also one of our scientific co-founders and a member of our 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 received his Ph.D. in molecular biophysics and biochemistry from Yale University. We believe Dr. Young is qualified to serve on our board of directors because of his scientific expertise and his role as one of our scientific co-founders.

Class III Directors

S. Gail Eckhardt, M.D. has been a member of our 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 until 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 has served on the Board of Directors of NuGenerex Immuno-Oncology, Inc., a public biotechnology company, since March 2020, and has served on numerous committees and study sections, including the ASCO Molecular Oncology Task Force, the ASCO Board of Directors, the FDA

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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. We believe that Dr. Eckhardt is qualified for service on our 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 our board of directors since October 2015. Since 2009, Ms. Fanucci has been an independent consultant. From 2004 through 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., Cycleron 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. We believe Ms. Fanucci is qualified to serve on our board of directors due to her expertise with public and financial accounting matters and her experience leading financial organizations in biotechnology companies.

Nancy A. Simonian, M.D. has been our 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 boards of directors of Seattle Genetics, Inc. and Evelo Biosciences, Inc., each a publicly traded biopharmaceutical company, the Damon Runyon Cancer Research Foundation and the Biotechnology Industry Organization. Dr. Simonian has delivered her resignation as a member of the board of directors of Evelo Biosciences, Inc., effective June 10, 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. We believe Dr. Simonian is qualified to serve on our board because of her role as our chief executive officer, her experience in the biopharmaceutical industry and her other executive leadership and board of directors experience.

Class I Directors

Mark J. Alles has served on our board of directors since December 2019. Mr. Alles served as chairman and chief executive officer of Celgene Corporation, a global biopharmaceutical company, or Celgene, from March 2016 until its acquisition by Bristol-Myers Squibb Company in November 2019. Prior to this role, 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 joined Celgene in April 2004. Before joining Celgene, he served in senior commercial management roles at Aventis Pharmaceuticals Inc. (Rhône-Poulenc Rorer) from 1993 to 2004. Mr. Alles received B.S. degree from Lock Haven University of Pennsylvania and served as a Captain in the United States Marine Corps. We believe that Mr. Alles is qualified for service on our board of directors due to his extensive executive experience and his track record of building successful global oncology organizations and commercializing innovative therapies.

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Amir Nashat, Ph.D. has served on our 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. We believe Dr. Nashat is qualified to serve on our 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.

Peter Wirth has served as Chair of our 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., 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. We believe Mr. Wirth is qualified to serve on our board of directors due to his expertise in corporate governance and his experience in corporate strategy, product development and law in the biotechnology industry.

Corporate Governance Matters

Our board of directors believes that good corporate governance is important to ensure that our company is managed for the long-term benefit of stockholders. This section describes key corporate governance guidelines and practices that our board of directors has adopted. Complete copies of our corporate governance guidelines, committee charters and code of conduct are available on the "Investors & Media—Governance" section of our website, which is located at www.syros.com. Alternatively, you can request a copy of any of these documents by writing us at Syros Pharmaceuticals, Inc., 35 CambridgePark Drive, 4th Floor, Cambridge, Massachusetts 02140, Attention: Chief Financial Officer.

Corporate Governance Guidelines

Our board of directors has adopted corporate governance guidelines to assist in the exercise of its duties and responsibilities and to serve the best interests of our company and our stockholders. These guidelines, which provide a framework for the conduct of our board of directors' business, provide that:

- the principal responsibility of our board of directors is to oversee our management;
- a majority of the members of the board of directors must be independent directors, unless otherwise permitted by Nasdaq rules;
- the independent directors meet at least twice a year in executive session;
- directors have full and free access to management and, as necessary and appropriate, independent advisors; and
- new directors participate in an orientation program and all directors are expected to participate in continuing director education on an ongoing basis.

Board Leadership Structure

Our corporate governance guidelines provide that the nominating and corporate governance committee shall periodically assess the board of directors' leadership structure, including whether the offices of chief executive

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officer and chair of the board of directors should be separate. Our guidelines provide the board of directors with flexibility to determine whether the two roles should be combined or separated based upon our needs and the board of directors' assessment of its leadership from time to time. We currently separate the roles of chief executive officer and chair of the board of directors. Dr. Simonian, as our president and chief executive officer, is responsible for setting the strategic direction for our company and for providing day-to-day leadership of our company, while Mr. Wirth, as chair of our board of directors, presides over meetings of the board of directors, including executive sessions of the board of directors, and performs oversight responsibilities. We do not currently have a lead independent director because the chair of our board of directors is independent within the meaning of the Nasdaq Listing Rules. Our board of directors has standing audit, compensation and nominating and corporate governance committees that currently consist of, and are chaired by, independent directors. Our board of directors delegates substantial responsibilities to the committees, which then report their activities and actions back to the full board of directors. We believe that the independent committees of our board of directors and their chairpersons promote effective independent governance. We believe this structure currently represents an appropriate allocation of roles and responsibilities for our company because it strikes an effective balance between management and independent leadership participation in our board of directors proceedings.

Board Determination of Independence

Rule 5605 of the Nasdaq Listing Rules requires a majority of a listed company's board of directors to be comprised of independent directors within one year of listing. In addition, the Nasdaq Listing Rules require that, subject to specified exceptions, each member of a listed company's audit, compensation and nominating and corporate governance committees be independent under the Securities Exchange Act of 1934, as amended, or the Exchange Act. Audit committee members must also satisfy the independence criteria set forth in Rule 10A-3 under the Exchange Act, and compensation committee members must also satisfy the independence criteria set forth in Rule 10C-1 under the Exchange Act. Under Rule 5605(a)(2) of the Nasdaq Listing Rules, a director will only qualify as an "independent director" if, in the opinion of our board of directors, that person does not have a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director. In order to be considered independent for purposes of Rule 10A-3, a member of an audit committee of a listed company may not, other than in his or her capacity as a member of the audit committee, the board of directors, or any other board committee, accept, directly or indirectly, any consulting, advisory, or other compensatory fee from the listed company or any of its subsidiaries or otherwise be an affiliated person of the listed company or any of its subsidiaries. In order to be considered independent for purposes of Rule 10C-1, the board must consider, for each member of a compensation committee of a listed company, all factors specifically relevant to determining whether a director has a relationship to such company which is material to that director's ability to be independent from management in connection with the duties of a compensation committee member, including, but not limited to: (1) the source of compensation of the director, including any consulting advisory or other compensatory fee paid by such company to the director; and (2) whether the director is affiliated with the company or any of its subsidiaries or affiliates.

Our board of directors undertook a review of the composition of our board of directors and its committees and the independence of each director. Based upon information requested from and provided by each director concerning his or her background, employment and affiliations, including family relationships, our board of directors has determined that each of our directors other than Drs. Simonian and Young is an "independent director" as defined under Rule 5605(a)(2) of the Nasdaq Listing Rules. Dr. Simonian is not an independent director under Rule 5605(a)(2) because she is our president and chief executive officer, and Dr. Young is not an independent director because of consideration paid to him for consulting services. Our board of directors also determined that Mark J. Alles, Marsha H. Fanucci, and Amir Nashat, Ph.D., who currently comprise our audit committee, Phillip A. Sharp, Ph.D., and Peter Wirth, who currently comprise our compensation committee, and Srinivas Akkaraju, M.D., Ph.D., and Amir Nashat, Ph.D., who currently comprise our nominating and corporate governance committee, satisfy the independence standards for such committees established by the SEC and the Nasdaq Listing Rules, as applicable, including in the case of all members of the audit committee, the independence requirements contemplated by Rule 10A-3 under the Exchange Act and, in the case of all members

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of the compensation committee, the independence requirements contemplated by Rule 10C-1 under the Exchange Act. In addition, our board of directors determined that Michael W. Bonney, who served on the compensation committee for part of 2020, at the time of such service, satisfied the applicable independence standards for such committees. In making such determinations, our board of directors considered the relationships that each such non-employee director has with our company and all other facts and circumstances our board of directors deemed relevant in determining independence, including the beneficial ownership of our capital stock by each non-employee director.

Board of Director Meetings and Attendance

Our board of directors held seven meetings, and acted by written consent twice, during the year ended December 31, 2020, or fiscal 2020. During fiscal 2020, each of the directors then in office attended at least 75% of the aggregate number of board of director meetings and the number of meetings held by all committees of the board of directors on which such director then served. Our corporate governance guidelines provide that directors are expected to attend the annual meeting of stockholders. Six of the eight directors who were then serving on our board of directors attended our 2020 annual meeting of stockholders.

Communicating with the Independent Directors

Our 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 we receive repetitive or duplicative communications.

Stockholders who wish to send communications on any topic to our board of directors should address such communications to Syros Pharmaceuticals, Inc., Attention: Board of Directors, 35 CambridgePark Drive, 4th Floor, Cambridge, Massachusetts 02140.

Committees of the Board of Directors

We have established an audit committee, a compensation committee, a nominating and corporate governance committee, and a research and development committee. Each of these committees operates under a charter that has been approved by our board of directors. A copy of each committee's charter can be found under the "Investors & Media—Governance" section of our website, which is located at www.syros.com.

Audit Committee

Our audit committee's responsibilities include:

- appointing, approving the compensation of, and assessing the independence of our registered public accounting firm;
- overseeing the work of our independent registered public accounting firm, including through the receipt and consideration of reports from such firm;
- reviewing and discussing with management and our independent registered public accounting firm our annual and quarterly financial statements and related disclosures;

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- monitoring our internal control over financial reporting, disclosure controls and procedures and code of business conduct and ethics;
- overseeing our internal audit function, if any;
- overseeing our risk assessment and risk management policies;
- establishing procedures for the receipt and retention of accounting related complaints and concerns;
- meeting independently with our internal auditing staff, if any, our 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 current members of our audit committee are Mark J. Alles, Marsha H. Fanucci and Amir Nashat, Ph.D. Ms. Fanucci chairs the audit committee. Our board of directors has determined that Ms. Fanucci qualifies as an “audit committee financial expert” within the meaning of applicable SEC rules. The audit committee held five meetings during fiscal 2020.

Compensation Committee

Our compensation committee’s responsibilities include:

- reviewing and approving, or making recommendations to our board with respect to, the compensation of our chief executive officer and other executive officers;
- overseeing the evaluation of our senior executives;
- overseeing and administering our cash and equity incentive plans;
- reviewing and making recommendations to our board of directors with respect to director compensation and management succession planning;
- reviewing and discussing annually with management our “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.

To the extent permitted by and consistent with applicable law and the provisions of a given equity-based plan, the compensation committee may delegate to one or more of our executive officers the power to grant options or other stock awards pursuant to an equity-based plan to our employees who are not directors or executive officers.

The current members of our compensation committee are Phillip A. Sharp, Ph.D., and Peter Wirth. Mr. Wirth chairs the compensation committee. Michael W. Bonney served on this committee until March 2020. The compensation committee held four meetings during fiscal 2020.

Nominating and Corporate Governance Committee

Our nominating and corporate governance committee’s responsibilities include:

- identifying individuals qualified to become members of our board of directors;
- recommending to our board the persons to be nominated for election as directors and to each of our board’s committees;
- reviewing and making recommendations to our board of directors with respect to our board leadership structure and board committee structure;

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- making recommendations to our board of directors with respect to accepting director resignations;
- developing and recommending to our board corporate governance principles; and
- overseeing an annual evaluation of our board.

The current members of our nominating and corporate governance committee are Srinivas Akkaraju, M.D., Ph.D., and Amir Nashat, Ph.D. Dr. Nashat chairs the nominating and corporate governance committee. The nominating and corporate governance committee held two meetings, and acted by written consent once, during fiscal 2020.

Research and Development Committee

Our research and development committee's responsibilities include:

- reviewing our current and planned research and development, or R&D, programs and initiatives from a scientific perspective, providing feedback to our R&D management on those programs and initiatives, and from time to time providing observations and strategic recommendations to our board of directors;
- serving as a sounding board for our R&D organization on R&D matters;
- as requested, assisting management in identifying world-class experts to provide strategic scientific and clinical advice regarding our programs; and
- identifying and discussing with the board significant emerging scientific and clinical issues and trends, as well as benchmarking our programs and R&D activities against our competitors.

The current members of our research and development committee are Srinivas Akkaraju, M.D., Ph.D., S. Gail Eckhardt, M.D., Phillip A. Sharp, Ph.D., and Richard A. Young, Ph.D. Dr. Young chairs the research and development committee. The research and development committee held four meetings during fiscal 2020.

Director Nomination Process

The process followed by our nominating and corporate governance committee to identify and evaluate director candidates includes requests to board members and others for recommendations, meetings from time to time to evaluate biographical information and background material relating to potential candidates and interviews of selected candidates by members of the nominating and corporate governance committee and our board of directors.

Criteria and Diversity

In considering whether to recommend to our board of directors any specific candidate for inclusion in our board of directors' slate of recommended director nominees, including candidates recommended by stockholders, the nominating and corporate governance committee of our board of directors applies the criteria set forth in our corporate governance guidelines. These criteria include the candidate's integrity, business acumen, knowledge of our business and industry, the ability to act in the interests of all stockholders, and lack of conflicts of interest.

The director biographies on pages 8 to 10 indicate each nominee's experience, qualifications, attributes and skills that led our nominating and corporate governance committee and our board of directors to conclude he or she should continue to serve as a director. Our nominating and corporate governance committee and our board of directors believe that each of the nominees has the individual attributes and characteristics required of each of our directors, and the nominees as a group possess the skill sets and specific experience desired of our board of directors as a whole.

Our nominating and corporate governance committee does not have a policy (formal or informal) with respect to diversity, but believes that our board, taken as a whole, should embody a diverse set of skills, experiences and

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backgrounds. In this regard, the nominating and corporate governance committee also takes into consideration the diversity (for example, with respect to gender, race and national origin) of our board members. The nominating and corporate governance committee does not make any particular weighting of diversity or any other characteristic in evaluating nominees and directors.

Stockholder Nominations

Stockholders may recommend individuals to our nominating and corporate governance committee for consideration as potential director candidates by submitting their names, together with appropriate biographical information and background materials, a statement as to the number of shares of our common stock beneficially owned by the stockholder making the recommendation, and certain other information as set forth in our by-laws, to Syros Pharmaceuticals, Inc., Attention: Nominating and Corporate Governance Committee, 35 CambridgePark Drive, 4th Floor, Cambridge, Massachusetts 02140. If appropriate biographical and background material has been provided on or before the dates set forth in this proxy statement under the heading “Other Matters – Stockholder Proposals for our 2022 Annual Meeting,” the committee will evaluate stockholder-recommended candidates by following substantially the same process, and applying substantially the same criteria, as it follows for candidates submitted by others. If the board determines to nominate a stockholder-recommended candidate and recommends his or her election, then his or her name will be included in our proxy card for the next annual meeting.

Stockholders also have the right under our by-laws to directly nominate director candidates, without any action or recommendation on the part of the nominating and corporate governance committee or our board of directors, by following the procedures set forth under “Other Matters – Stockholder Proposals for our 2022 Annual Meeting.”

Oversight of Risk

Our board of directors oversees our risk management processes directly and through its committees. Our management is responsible for risk management on a day-day basis. The role of our board of directors and its committees is to oversee the risk management activities of management. Our board of directors fulfills this duty by discussing with management the policies and practices utilized by management in assessing and managing risks and providing input on those policies and practices. In general, our board of directors oversees risk management activities relating to business strategy, acquisitions, capital allocation, organizational structure and certain operational risks; our audit committee oversees risk management activities related to financial controls, legal and compliance risks, and cybersecurity risks; our compensation committee oversees risk management activities relating to our compensation policies and practices and management succession planning; and our nominating and corporate governance committee oversees risk management activities relating to the composition of our board of directors and corporate governance. Each committee reports to the full board of directors on a regular basis, including reports with respect to the committee’s risk oversight activities as appropriate. In addition, since risk issues often overlap, committees from time to time request that the full board of directors discuss particular risks.

Compensation Committee Interlocks and Insider Participation

None of our executive officers serves, or in the past has served, as a member of the board of directors or compensation committee, or other committee serving an equivalent function, of any entity that has one or more executive officers who serve as members of our board of directors or our compensation committee. None of the members of our compensation committee is, or ever has been, an officer or employee of our company.

Code of Business Conduct and Ethics

We have adopted a written code of business conduct and ethics that applies to our directors, officers and employees, including our principal executive officer and principal financial officer. A copy of the code is

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available on the “Investors & Media—Governance” section of our website, which is located at www.syros.com. Our board of directors is responsible for overseeing the code of business conduct and ethics and must approve any waivers of the code for directors, officers and employees. If we make any substantive amendments to, or grant any waivers from, the code of business conduct and ethics for any officer or director, we will disclose the nature of such amendment or waiver on our website or in a current report on Form 8-K.

Policies and Procedures for Related Person Transactions

Our board of directors has adopted a written related person transaction policy to set forth policies and procedures for the review of any transaction, arrangement or relationship in which our company is a participant, the amount involved exceeds the lesser of \$120,000 or 1% of the average of our total assets at year-end for the last two completed fiscal years, and one of our executive officers, directors, director nominees or 5% stockholders, or their immediate family members, each of whom we refer to as a “related person,” has a direct or indirect material interest.

If a related person proposes to enter into such a transaction, arrangement or relationship, which we refer to as a “related party transaction,” the related person must report the proposed related person transaction to our principal financial officer. The policy calls for the proposed related person transaction to be reviewed and approved by our audit committee. Whenever practicable, the reporting, review and approval will occur prior to entry into the transaction. If advance review and approval is not practicable, the committee will review and, in its discretion, may ratify the related person transaction. The policy also permits the chair of the audit committee to review and, if deemed appropriate, approve proposed related person transactions that arise between committee meetings, subject to ratification by the committee at its next meeting. Any related person transactions that are ongoing in nature will be reviewed annually.

A related person transaction reviewed under this policy will be considered approved or ratified if it is authorized by the audit committee in accordance with the standards set forth in the policy after full disclosure of the related person’s interests in the transaction. As appropriate for the circumstances, the policy provides that the audit committee will review and consider:

- the related person’s interest in the related person transaction;
- the approximate dollar value of the amount involved in the related person transaction;
- the approximate dollar value of the amount of the related person’s interest in the transaction without regard to the amount of any profit or loss;
- whether the transaction was undertaken in the ordinary course of our business;
- whether the terms of the transaction are no less favorable to us than the terms that could have been reached with an unrelated third party;
- the purpose of, and the potential benefits to us of, the transaction; and
- any other information regarding the related person transaction or the related person in the context of the proposed transaction that would be material to investors in light of the circumstances of the particular transaction.

The audit committee may approve or ratify the related person transaction only if the audit committee determines that, under all of the circumstances, the transaction is in our best interests. The audit committee may impose any conditions on the related person transaction as it deems appropriate.

The policy also provides that transactions involving compensation of executive officers will be reviewed and approved by our compensation committee in the manner specified in its charter.

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Related Person Transactions

In addition to the compensation arrangements with directors and executive officers described elsewhere in this proxy statement, since January 1, 2019, we have engaged in the following transactions in which the amount involved exceeded the lesser of \$120,000 or 1% of the average of our total assets at year-end for the last two completed fiscal years, and any of our executive officers, directors, director nominees or 5% stockholders, or their immediate family members, or any person who was in any of those categories at the time of such transaction, had a direct or indirect material interest. We believe that all of these transactions were on terms comparable to terms that could have been obtained from unrelated third parties.

Financing Transactions

In December 2020, we completed a private placement of 10,312,500 shares of our common stock and, in lieu 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). Samsara BioCapital, L.P., a venture capital firm, purchased 625,000 shares of our common stock and accompanying warrants to purchase 156,250 shares of our 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. is one of the managers of Samsara BioCapital GP, LLC, which is the general partner of Samsara BioCapital, L.P.

In April 2019, we completed a public offering of 8,667,333 shares of our common stock and accompanying Class A warrants to purchase 1,951,844 shares of our common stock, at a combined price to the public of \$7.50 per common share and accompanying warrant. Samsara BioCapital, L.P. purchased 533,332 shares of our common stock and warrants to purchase 133,333 shares of our common stock in this public offering at an aggregate purchase price of \$4.0 million.

Consulting Agreement with Dr. Young

Richard A. Young, Ph.D., earned \$115,000 and \$120,000 during fiscal 2020 and fiscal 2019, respectively, pursuant to the terms of a consulting agreement he entered with our company that is unrelated to his service as a member of our board of directors.

Investors' Rights Agreement

We are a party to an amended and restated investors' rights agreement, dated as of October 9, 2014, with the purchasers of preferred stock prior to our IPO, 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 is a managing partner), Nancy A. Simonian, M.D., and Phillip A. Sharp, Ph.D. The investors' rights agreement provides these holders the right to demand that we file a registration statement or request that their shares be covered by a registration statement that we are otherwise filing.

Restrictions on the Hedging or Pledging of Our Securities

Our insider trading policy prohibits our employees and directors from purchasing financial instruments or otherwise engaging in transactions that hedge or offset, or are designed to hedge or offset, any decrease in the market value of any of our securities, including:

- short sales and short sales "against the box";
- purchases or sales of puts, calls or other derivative securities; and
- purchases of financial instruments (including prepaid variable forward contracts, equity swaps, collars and exchange funds).

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These prohibitions also apply to family members living in the same household as our employees and directors, as well as entities influenced or controlled by our employees or directors.

Core Values and Corporate Sustainability

Our Core Values speak to how we work together, every day, to achieve our mission of transforming patients' lives and deliver our vision of becoming a fully integrated biopharmaceutical company that creates unparalleled value for patients and other stakeholders.

AS ONE TEAM, STRENGTHENED BY OUR DIVERSITY, WE:



We understand that delivering on our mission over the long term requires a focus on corporate sustainability, including environmental, social, and governance considerations. Specifically, we focus on the following:

- **Valuing Patients' Lives:** We work with urgency because each day of a patient's life matters, and we are committed to doing everything we can now to speed the discovery and development of medicines that provide a profound benefit for patients.
- **Diversity, Equity and Inclusion:** We are committed to fostering an environment where all employees, regardless of race, sex, sexual orientation, gender identity, religion, ethnicity, national origin, physical disability or age, are empowered to achieve their full potential. The unique talents, backgrounds and perspectives of each employee strengthens our coordinated expression, making our company stronger and helping us to achieve our mission of developing medicines to transform patients' lives. Our Diversity, Equity & Inclusion (DEI) committee is an employee-led organization that implements a variety of grassroots initiatives including, among other things, a DEI speaker series, a book club, and a company-wide allyship program. We are proud of the fact that women comprise roughly half of our functional leaders and one-third of the members of our board of directors, and we are committed to continuing to expand the representation of historically underrepresented individuals throughout our company through activities such as targeted recruiting through industry affinity groups and historically Black colleges and universities. In addition, Dr. Simonian was an early signatory of the MassBio DEI pledge, making commitments to enhance equity, diversity and inclusion at our company and in our industry.
- **Environment:** We sponsor various programs in an effort to reduce our environmental impact. For example, we are partnered with the Green Streets Initiative, a Cambridge-based organization dedicated to celebrating and promoting the use of sustainable and active transportation. We also provide incentives for our employees to use public transportation.
- **Health and Wellness:** We offer our employees a competitive health benefits program and many other resources to support their physical, mental and emotional health. For example, we believe our parenting leave and paid-time-off programs are among the most progressive in our industry.
- **Community Engagement:** As a company, we are committed to supporting our local community and participate in a host of volunteer and charitable activities. We are actively engaged with Life Science

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Cares in supporting a number of healthcare, education and sustainability programs in the greater Boston area. For example, through our partnership Life Sciences Cares, we have been providing meals to area shelters during the COVID-19 pandemic.

In response to the COVID-19 pandemic, we have taken steps to provide for the safety and wellbeing of our employees. We have restricted access to our facility to those individuals whose job responsibilities require or are significantly enhanced by on site presence, limited the number of people that can be present at our facility at any one time, and implemented a number of additional health and safety protocols. We have also formed a COVID-19 Task Force, consisting of a cross-section of individuals with functional expertise and distinct perspectives, to proactively address issues relating to the pandemic such as adapting our guidelines for working on-site, optimizing work-from-home conditions, developing appropriate contingency plans, developing a plan for when and how best to transition back to the office, and implementing additional initiatives for keeping our employees safe, healthy and connected. In addition, we have conducted several additional surveys to assess employee well-being and productivity in light of the pandemic.

EXECUTIVE AND DIRECTOR COMPENSATION

Executive Officers

Certain information regarding our executive officers as of March 31, 2021 is set forth below.

<u>Name</u>	<u>Age</u>	<u>Position(s)</u>
Nancy A. Simonian, M.D. ⁽¹⁾	60	President & Chief Executive Officer
Joseph J. Ferra, Jr.	45	Chief Financial Officer
Eric R. Olson, Ph.D.	63	Chief Scientific Officer
Gerald E. Quirk, Esq.	53	Chief Legal & Administrative Officer
David A. Roth, M.D.	58	Chief Medical Officer

(1) Please refer to page 9 for Dr. Simonian's biography.

Joseph J. Ferra, Jr. has served as our chief financial officer since March 2018. Mr. Ferra joined us from JMP Securities LLC, where he served as managing director from March 2014 to March 2018 and co-head of healthcare investment banking from March 2017 to March 2018. Previously, he was employed by UBS Investment Bank from September 2009 to March 2014 serving, most recently, as executive director of global healthcare investment banking. Mr. Ferra received a B.S. in chemistry with distinction from Purdue University and an M.B.A. from The Stephen M. Ross School of Business at the University of Michigan.

Eric R. Olson, Ph.D. has been our 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.

Gerald E. Quirk, Esq. has served as our chief legal officer from September 2016 to June 2017 and as our chief legal and administrative officer since June 2017. He previously served as executive vice president, business operations and general counsel of Tokai Pharmaceuticals, Inc., a biopharmaceutical company, from May 2015 to August 2016. Prior to that, Mr. Quirk was a partner and co-chair of the life sciences practice at Choate, Hall & Stewart LLP, a Boston law firm, from August 2012 until May 2015. Mr. Quirk previously served as vice president, corporate affairs and general counsel at Infinity Pharmaceuticals, Inc., a pharmaceutical company, or

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Infinity, from August 2006 until August 2012, and prior to that held legal and business development positions of increasing responsibility at Genzyme. Mr. Quirk holds a B.A. in political science from Swarthmore College, an Ed.M. in educational administration from Harvard University, and a J.D. from Northeastern University.

David A. Roth, M.D. has been our 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.

Executive Compensation

This section discusses the material elements of our executive compensation policies for our "named executive officers" and the most important factors relevant to an analysis of these policies. For 2020, our named executive officers are Nancy A. Simonian, M.D., our President and Chief Executive Officer, Eric R. Olson, Ph.D., our Chief Scientific Officer, and David A. Roth, M.D., our Chief Medical Officer. In addition, this section provides qualitative information regarding the manner and context in which compensation is awarded to and earned by our named executive officers and is intended to place in perspective the data presented in the following tables and the corresponding narrative.

Summary Compensation Table

The following table sets forth information regarding compensation earned by our named executive officers during the years indicated.

Name and Position of Current Named Executive Officers	Year	Salary (\$)	Stock Awards (\$)(1)	Option Awards (\$)(1)	Non-Equity Incentive Plan Compensation (\$)(2)	All Other Compensation (\$)(3)	Total (\$)
Nancy A. Simonian, M.D. (4)	2020	597,692	—	1,503,457	429,000	360	2,530,509
President & Chief Executive Officer	2019	577,692	1,261,480	1,455,487	319,000	360	3,614,019
David A. Roth, M.D.	2020	468,269	—	480,697	244,400	360	1,193,726
Chief Medical Officer	2019	452,115	583,770	383,023	189,000	360	1,608,268
Eric R. Olson, Ph.D.	2020	457,385	—	480,697	238,680	360	1,177,122
Chief Scientific Officer	2019	443,269	583,770	383,023	195,000	360	1,605,422

- (1) The amounts reported in the "Stock Awards" and "Option Awards" columns reflect 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 our financial statements included in our Annual Report on Form 10-K regarding assumptions underlying the valuation of equity awards.
- (2) The amounts reported in the "Non-Equity Incentive Plan Compensation" column reflect awards to our named executive officers under our 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 us of life insurance premiums paid for the named executive officer.

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(4) Dr. Simonian also serves as a member of our board of directors but does not receive any additional compensation for her service as a director.

Narrative Disclosure to Summary Compensation Table

We review compensation for our executive officers annually. The material terms of the elements of our executive compensation program for 2020 are described below.

Our compensation committee sets base salaries and bonuses and grants equity incentive awards to our executive officers. In setting base salaries and bonuses and granting equity incentive awards, our compensation committee considers compensation for comparable positions in the market, the historical compensation levels of our executives, individual and corporate performance as compared to our expectations and objectives, our desire to motivate our employees to achieve short- and long-term results that are in the best interests of our stockholders, and a long-term commitment to our company. As part of this process, Dr. Simonian, as our 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 board of directors as to the achievement of corporate objectives that drive contingent compensation awards.

During its annual compensation review, our compensation committee also consults with external advisors. In fiscal 2020, the compensation committee engaged Compensia Inc. as its independent compensation consultant to provide comparative data on executive compensation practices in our industry and assess our executives' compensation relative to comparable companies.

Base Salary

We use base salaries to recognize the experience, skills, knowledge and responsibilities required of all our employees, including our named executive officers. None of our 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 2019, the compensation committee of our board of directors set Dr. Simonian's annualized base salary at \$580,000 effective February 11, 2019. In February 2020, the compensation committee increased 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 2019, the compensation committee of our board of directors set Dr. Roth's annualized base salary at \$455,000 effective February 11, 2019. In February 2020, the compensation committee increased 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 2019, the compensation committee of our board of directors set Dr. Olson's annualized base salary at \$445,000 effective February 11, 2019. In February 2020, the compensation committee increased Dr. Olson's annualized base salary to \$459,000 effective February 10, 2020. In February 2021, the compensation committee increased Dr. Olson's annualized base salary to \$473,000 effective February 22, 2021.

Cash Incentives

We have established a framework under which the compensation committee would, in its discretion, award annual performance-based cash bonuses to our executive officers for up to a specific percentage of his or her

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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, 2019, or fiscal 2019, and fiscal 2020. Our 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 our other named executive officers was 40% of the applicable officer's annual base salary for both fiscal 2019 and fiscal 2020.

In February 2020, we made cash bonus awards of \$319,000 to Dr. Simonian, \$189,000 to Dr. Roth and \$195,000 to Dr. Olson based on the compensation committee's assessment of achievement of corporate and individual goals during fiscal 2019, and in February 2021 we made cash bonus awards of \$429,000 to Dr. Simonian, \$244,400 to Dr. Roth and \$238,680 to Dr. Olson based on the compensation committee's assessment of achievement of corporate and individual goals during fiscal 2020.

Equity Incentives

Although we do not have a formal policy with respect to the grant of equity incentive awards to our executive officers, or any formal equity ownership guidelines applicable to them, we believe that equity grants provide our executives with a strong link to our long-term performance, create an ownership culture and help to align the interests of our executives and our stockholders. In addition, we believe that equity grants with a time-based vesting feature promote executive retention because this feature incents our executive officers to remain in our employment during the vesting period, and equity grants with a performance-based feature incents our executive officers to focus on what we see as key business goals. Accordingly, the compensation committee periodically reviews the equity incentive compensation of our named executive officers and from time to time may grant equity incentive awards to them in the form of stock options.

In February 2019, Dr. Simonian and was granted an option to purchase 285,000 shares of our common stock and Drs. Roth and Olson were each granted an option to purchase 75,000 shares of our common stock. These options vested as to 25% of the shares on February 29, 2020, with the remaining shares vesting in equal monthly installments thereafter through February 28, 2023, subject to the applicable officer's continued service through the applicable vesting date. In addition, Dr. Simonian was granted a restricted stock unit award with respect to 188,000 shares of our common stock and Drs. Roth and Olson were each granted a restricted stock unit award with respect to 87,000 shares of our common stock. These restricted stock units will vest in full on March 31, 2022, subject to the applicable officer's continued service through the vesting date.

In February 2020, Dr. Simonian was granted an option to purchase 294,000 shares of our common stock and Drs. Roth and Olson were each granted an option to purchase 94,000 shares of our 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.

Outstanding Equity Awards at Fiscal Year End 2020

The following table sets forth information regarding outstanding equity awards held by our named executive officers as of December 31, 2020.

Current Named Executive Officers	Option Awards				Stock Awards	
	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(7)	2,039,800
	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		
	167,708(3)	7,292(3)	10.90	2/9/2027		
	196,884(4)	83,128(4)	10.09	2/15/2028		
	130,623(5)	154,377(5)	6.71	2/11/2029		
	—(6)	294,000(6)	7.54	2/12/2030		
David R. Roth, M.D.	223,661(2)	—	9.08	12/22/2015	87,000(7)	943,950
	60,854(3)	2,646(3)	10.90	2/9/2027		
	53,123(4)	21,877(4)	10.09	2/15/2028		
	34,374(5)	40,626(5)	6.71	2/11/2029		
	—(6)	94,000(6)	7.54	2/12/2030		
Eric R. Olson, Ph.D.	119,350(2)	—	1.01	5/21/2023	87,000(7)	943,950
	4,533(2)	—	1.39	9/3/2024		
	34,776(2)	—	3.04	2/4/2025		
	25,848(2)	—	3.04	6/8/2025		
	60,854(3)	2,646(3)	10.90	2/9/2027		
	53,123(4)	21,877(4)	10.09	2/15/2028		
	34,374(5)	40,626(5)	6.71	2/11/2029		
	—(6)	94,000(6)	7.54	2/12/2030		

(1) Calculated based on the closing price per share of our common stock on December 31, 2020, which was \$10.85.

(2) This option is fully vested.

(3) This option was granted on February 10, 2017 and vested as to 25% of the shares on February 10, 2018 with the remaining shares vesting in equal monthly installments thereafter through February 28, 2021, subject to continued service.

(4) 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.

(5) 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.

(6) 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 28, 2024, subject to continued service.

(7) This restricted stock unit award vests in full on March 31, 2022.

Employment Agreements; Potential Payments upon Termination or Change in Control

We have entered into written offer letters with each of our 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 our employees. In connection with the commencement of their employment with us, our named executive officers executed our 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 us 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 us, subject to certain conditions, including the execution of a release of all claims against the Company. In addition, in the event of a change in control of our company, 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 us 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 our other named executive officers provides that if his employment is terminated by us 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 the Company. Our other named executive officers are also eligible for the CIC Equity Vesting.

Other Agreements

We have also entered into employee confidentiality, inventions, non-solicitation, and non-competition agreements with each of our 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 us 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 our 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 our confidential and proprietary information and (4) to assign to us related intellectual property developed during the course of his or her employment.

401(k) Retirement Plan

We maintain 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 our 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. We make 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.

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Indemnification

For a summary of certain indemnification agreements with our named executive officers, see “Limitation of Liability and Indemnification” below.

Tax Deductibility

Section 162(m) of the Internal Revenue Code of 1986, as amended, or the Code, generally disallows a tax deduction to public companies for compensation in excess of \$1 million paid in any taxable year to each of certain of the company’s current and former executive officers. Historically, compensation that qualified under Section 162(m) as performance-based compensation was exempt from the deduction limitation. However, subject to certain transition rules, the tax reform legislation signed into law on December 22, 2017 eliminated the qualified performance-based compensation exception. As a result, for taxable years beginning after December 31, 2017, all compensation in excess of \$1 million paid in any taxable year to each of the specified officers that is not covered by the transition rules will not be deductible by us. The Compensation Committee has and will continue to review on a periodic basis the potential effect of Section 162(m) and may use its judgment to authorize compensation payments that may be in excess of the limit when it believes such payments are appropriate and in the best interests of our company and our stockholders.

Director Compensation

We pay our non-employee directors a cash retainer for service on the 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 our board of directors effective upon completion of our 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, our board of directors amended the director compensation program to increase the cash retainer for our 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 our 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, we will grant to new non-employee directors upon their initial election to the board, an initial option to purchase 35,000 shares of our common stock, with an exercise price equivalent to fair market value of a share of 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 our company. The option will have a term of ten years. Prior to December 2019, the initial option granted to non-employee directors upon their initial election to the board was for 22,000 shares of our common stock.

Immediately following each annual meeting of our stockholders, we will grant to each non-employee director who has served on our board of directors for at least six months an option to purchase 17,500 shares of our

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common stock, with an exercise price equivalent to fair market value of a share of 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 our company. The option will have a term of ten years. Prior to December 2019, the annual option granted to each non-employee director with at least six months of service on the board was for 11,000 shares of our common stock.

We also reimburse our non-employee directors for reasonable travel and out-of-pocket expenses incurred in connection with attending our board of directors and committee meetings.

We do not pay any compensation to our president and chief executive officer in connection with her service on our board of directors. The compensation that we pay to our president and chief executive officer is discussed earlier in this “Executive Compensation” section.

The following table sets forth information regarding compensation earned by our non-employee directors during fiscal 2020.

<u>Name</u>	<u>Fees Earned or Paid in Cash (\$)</u>	<u>Option Awards (\$)(1)</u>	<u>All Other Compensation (\$)</u>	<u>Total (\$)</u>
Srinivas Akkaraju, M.D., Ph.D.	49,000	103,661	—	152,661
Mark J. Alles	47,500	103,661	—	151,161
Michael W. Bonney (2)	7,650	—	—	7,650
S. Gail Eckhardt, M.D.(3)	14,002	209,181	—	223,183
Marsha H. Fanucci	55,000	103,661	—	158,661
Amir Nashat, Ph.D.	55,500	103,661	—	159,161
Phillip A. Sharp, Ph.D.	50,000	103,661	—	153,661
Peter Wirth	80,000	103,661	—	183,661
Richard A. Young, Ph.D.	50,000	103,661	115,000(4)	268,661

- (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 our financial statements included in our Annual Report on Form 10-K regarding assumptions underlying the valuation of equity awards.

As of December 31, 2020, our non-employee directors held the following stock options, all of which were granted under our 2012 Equity Incentive Plan, as amended, or 2012 Plan, and our 2016 Stock Incentive Plan, or 2016 Plan:

<u>Name</u>	<u>Option Awards</u>
Srinivas Akkaraju, M.D., Ph.D.	61,500
Mark J. Alles	52,500
S. Gail Eckhardt, M.D.	35,000
Marsha H. Fanucci	87,166
Amir Nashat, Ph.D.	72,500
Phillip A. Sharp, Ph.D.	115,357
Peter Wirth	61,500
Richard A. Young, Ph.D.	147,500

- (2) Mr. Bonney resigned from our board of directors in March 2020.
(3) Dr. Eckhardt was appointed to our board of directors in September 2020.

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- (4) Represents consideration paid during fiscal 2020 pursuant to the terms of a consulting agreement Dr. Young entered with our company that is unrelated to his service on our board of directors.

Limitation of Liability and Indemnification

As permitted by Delaware law, we have adopted provisions in our certificate of incorporation that limit or eliminate the personal liability of our directors. Our certificate of incorporation limits the liability of directors to the maximum extent permitted by Delaware law. Delaware law provides that directors of a corporation will not be personally liable for monetary damages for breaches of their fiduciary duties as directors, except liability for:

- any breach of the director's duty of loyalty to us or our stockholders;
- any act or omission not in good faith or that involves intentional misconduct or a knowing violation of law;
- any unlawful payments related to dividends or unlawful stock repurchases, redemptions or other distributions; or
- any transaction from which the director derived an improper personal benefit.

These limitations do not apply to liabilities arising under federal securities laws and do not affect the availability of equitable remedies, including injunctive relief or rescission. If Delaware law is amended to authorize the further elimination or limiting of a director, then the liability of our directors will be eliminated or limited to the fullest extent permitted by Delaware law as so amended.

As permitted by Delaware law, our certificate of incorporation also provides that:

- we will indemnify our directors and officers to the fullest extent permitted by law;
- we may indemnify our other employees and other agents to the same extent that we indemnify our officers and directors, unless otherwise determined by our board of directors; and
- we will advance expenses to our directors and officers in connection with legal proceedings to the fullest extent permitted by law.

The indemnification provisions contained in our certificate of incorporation are not exclusive. In addition, we have entered into indemnification agreements with each of our directors and executive officers. Each of these indemnification agreements provides, among other things, that we 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, our 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 we do not assume the defense of a claim against a director or executive officer, as applicable, we are 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 us.

We believe 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 of 1933, as amended, or the Securities Act, may be permitted to directors, officers or persons controlling our company pursuant to the foregoing provisions, we understand 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, we maintain standard policies of insurance under which coverage is provided to our directors and officers against losses arising from claims made by reason of breach of duty or other wrongful act, and to us with respect to payments which may be made by us to such directors and officers pursuant to the above indemnification provisions or otherwise as a matter of law.

SECURITIES AUTHORIZED FOR ISSUANCE UNDER EQUITY COMPENSATION PLANS

The following table contains information about our equity compensation plans as of December 31, 2020. As of December 31, 2020, we had three equity compensation plans, each of which was approved by our stockholders: our 2012 Plan, our 2016 Plan and our 2016 Employee Stock Purchase Plan, or 2016 ESPP.

Equity Compensation Plan Information

<u>Plan Category</u>	<u>Number of securities to be issued upon exercise of outstanding options, warrants and rights</u> (a)	<u>Weighted average exercise price of outstanding options, warrants and rights</u> (b)	<u>Number of securities remaining available for future issuance under equity compensation plans (excluding securities reflected in column (a))</u> (c)
Equity compensation plans approved by security holders	7,165,288 ⁽¹⁾	\$ 7.17	3,746,100 ⁽²⁾
Equity compensation plans not approved by security holders	37,700 ⁽³⁾	\$ 0.04	—
Total	7,202,988	\$ 7.13	3,746,100⁽⁴⁾

- (1) Consists of (i) 720,662 shares to be issued upon exercise of outstanding options under our 2012 Plan as of December 31, 2020 (ii) 4,710,243 shares to be issued upon exercise of outstanding options under our 2016 Plan, and (iii) 1,734,383 shares to be issued upon vesting of outstanding restricted stock units under our 2016 Plan as of December 31, 2020.
- (2) Consists of (i) 1,976,944 shares that remained available for future issuance under our 2016 Plan as of December 31, 2020, and (ii) 1,769,156 shares that remained available for future issuance under our 2016 ESPP as of December 31, 2020. No shares remained available for future issuance under the 2012 Plan as of December 31, 2020.
- (3) Consists entirely of a non-statutory stock option granted by our board of directors to the Branta Group, LLC on December 5, 2012 in consideration for consulting services. This option, which is fully vested, was granted outside of any of our equity incentive plans.
- (4) Our 2016 Plan has an evergreen provision that allows for an annual increase in the number of shares available for issuance under the 2016 Plan to be added on the first day of each fiscal year through the 2025 fiscal year, equal to the least of 1,600,000 shares of our common stock, 4% of the number of shares of our common stock outstanding on the first day of the applicable fiscal year and an amount determined by our board of directors. On January 1, 2021, 1,600,000 additional shares were reserved for issuance under the 2016 Plan pursuant to this provision. Our 2016 ESPP has an evergreen provision that allows for an annual increase in the number of shares available for issuance under the 2016 ESPP to be added on the first day of each fiscal year through the 2025 fiscal year, in an amount equal to the least of 1,173,333 shares of our common stock, 1% of the total number of shares of our common stock outstanding on the first day of the applicable fiscal year and an amount determined by our board of directors. On January 1, 2021, 562,227 additional shares were reserved for issuance under the 2016 ESPP pursuant to this provision.

REPORT OF THE AUDIT COMMITTEE OF THE BOARD OF DIRECTORS

Our audit committee has reviewed our audited consolidated financial statements for the fiscal year ended December 31, 2020 and discussed them with our management and our independent registered public accounting firm, Ernst & Young LLP.

Our audit committee has also received from, and discussed with, Ernst & Young LLP various communications that Ernst & Young LLP is required to provide to our audit committee, including the matters required to be discussed by the applicable requirements of the Public Company Accounting Oversight Board and the Securities Exchange Commission.

In addition, Ernst & Young LLP provided our audit committee with the written disclosures and the letter required by applicable requirements of the Public Company Accounting Oversight Board regarding the independent registered public accounting firm's communications with the audit committee concerning independence and has discussed with the Company's independent registered public accounting firm their independence.

Based on the review and discussions referred to above, our audit committee recommended to our board of directors that the audited consolidated financial statements be included in our Annual Report on Form 10-K for the year ended December 31, 2020.

By the audit committee of the board of directors of Syros Pharmaceuticals, Inc.

Marsha H. Fanucci, Chair
Mark J. Alles
Amir Nashat, Ph.D.

MATTERS TO BE VOTED ON

Proposal 1: Election of Directors

Our certificate of incorporation provides for a classified board of directors. This means our board of directors is divided into three classes, with each class having as nearly as possible an equal number of directors. The term of service of each class of directors is staggered so that the term of one class expires at each annual meeting of the stockholders.

Our board of directors currently consists of nine members, divided into three classes as follows:

- Class I is comprised of Mark J. Alles, Amir Nashat, Ph.D., and Peter Wirth, each with a term ending at the 2023 annual meeting of stockholders;
- Class II is comprised of Srinivas Akkaraju, M.D., Ph.D., Phillip A. Sharp, Ph.D., and Richard A. Young, Ph.D., each with a term ending at the 2021 annual meeting of stockholders; and
- Class III is comprised of S. Gail Eckhardt, M.D., Marsha H. Fanucci and Nancy A. Simonian, M.D., each with a term ending at the 2022 annual meeting of stockholders.

At each annual meeting of stockholders, directors are elected for a full term of three years to succeed those directors whose terms are expiring. Our board of directors, on the recommendation of our nominating and corporate governance committee, has set the number of directors at nine and nominated Srinivas Akkaraju, M.D., Ph.D., Phillip A. Sharp, Ph.D., and Richard A. Young, Ph.D., for re-election as Class II directors, each with a term ending at the 2024 annual meeting of stockholders.

Unless otherwise instructed in the proxy or unless authority to vote is withheld, all executed proxies will be voted "FOR" the election of each of the Class II director nominees identified above to a three-year term ending at the 2024 annual meeting of stockholders, each such nominee to hold office until his successor has been duly elected and qualified. Each of the nominees has indicated a willingness to continue to serve as director, if elected. If any nominee should be unable to serve, discretionary authority is reserved for the named proxy holders to vote for a substitute, or to reduce the number of directors to be elected, or both. We do not expect that any of the nominees will be unable to serve if elected.

A plurality of the combined voting power of the shares of common stock present virtually or represented by proxy at the annual meeting and entitled to vote is required to elect each nominee as a director.

OUR BOARD OF DIRECTORS RECOMMENDS THAT STOCKHOLDERS VOTE "FOR" THE ELECTION OF SRINIVAS AKKARAJU, M.D., PH.D., PHILLIP A. SHARP, PH.D., AND RICHARD A. YOUNG, PH.D., TO SERVE AS CLASS II DIRECTORS.

Proposal 2: Ratification of the Appointment of Independent Registered Public Accounting Firm

Our audit committee has appointed the firm of Ernst & Young LLP, or E&Y, an independent registered public accounting firm, as independent auditors for the fiscal year ending December 31, 2021. Although stockholder approval of our audit committee's appointment of E&Y is not required by law, our board of directors believes that it is advisable to give stockholders an opportunity to ratify this appointment. If this proposal is not approved at the annual meeting, our audit committee will reconsider its appointment of E&Y. E&Y has no direct or indirect material financial interest in our company or our subsidiaries. Representatives of E&Y are expected to attend the virtual annual meeting and will have the opportunity to make a statement, if they desire to do so, and will be available to respond to appropriate questions from our stockholders.

Audit Fees and Services

E&Y was our independent registered public accounting firm for the years ended December 31, 2020 and December 31, 2019. The following table summarizes the fees of E&Y billed to us for each of the last two fiscal

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years. All such services and fees were pre-approved by our audit committee in accordance with the “Pre-Approval Policies and Procedures” described below.

<u>Fee Category</u>	<u>2020</u>	<u>2019</u>
Audit Fees (1)	\$ 599,910	\$ 672,509
Tax Fees (2)	50,040	31,688
All Other Fees (3)	1,790	1,790
Total Fees	<u>\$ 651,740</u>	<u>\$ 705,987</u>

- (1) “Audit Fees” consist of fees for the audit of our annual financial statements, the review of the interim financial statements included in our quarterly reports on Form 10-Q, our follow-on public offerings completed in April 2019, and other professional services provided in connection with regulatory filings or engagements.
- (2) “Tax Fees” consist of fees for professional services, including tax consulting and compliance performed by E&Y.
- (3) “All Other Fees” consist of database subscription fees paid to E&Y.

Pre-Approval Policies and Procedures

Our audit committee has adopted procedures requiring the pre-approval of all non-audit services performed by our independent registered public accounting firm in order to assure that these services do not impair the auditor’s independence. These procedures generally approve the performance of specific services subject to a cost limit for all such services. This general approval is to be reviewed, and if necessary modified, at least annually. Management must obtain the specific prior approval of the audit committee for each engagement of the independent registered public accounting firm to perform other audit-related or other non-audit services. The audit committee does not delegate its responsibility to approve services performed by the independent registered public accounting firm to any member of management. Our audit committee has delegated authority to the committee chair to pre-approve any audit or non-audit service to be provided to us by our independent registered public accounting firm provided that the fees for such services do not exceed \$100,000. Any approval of services by the committee chair pursuant to this delegated authority must be reported to the audit committee at the next meeting of the committee.

The standard applied by the audit committee, or the chair of the audit committee, in determining whether to grant approval of any type of non-audit service, or of any specific engagement to perform a non-audit service, is whether the services to be performed, the compensation to be paid therefore and other related factors are consistent with the independent registered public accounting firm’s independence under guidelines of the SEC and applicable professional standards. Relevant considerations include whether the work product is likely to be subject to, or implicated in, audit procedures during the audit of our financial statements, whether the independent registered public accounting firm would be functioning in the role of management or in an advocacy role, whether the independent registered public accounting firm’s performance of the service would enhance our ability to manage or control risk or improve audit quality, whether such performance would increase efficiency because of the independent registered public accounting firm’s familiarity with our business, personnel, culture, systems, risk profile and other factors, and whether the amount of fees involved, or the non-audit services portion of the total fees payable to the independent registered public accounting firm in the period would tend to reduce the independent registered public accounting firm’s ability to exercise independent judgment in performing the audit.

OUR BOARD OF DIRECTORS RECOMMENDS THAT STOCKHOLDERS VOTE “FOR” THE RATIFICATION OF THE APPOINTMENT OF ERNST & YOUNG LLP AS OUR INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM FOR THE FISCAL YEAR ENDING DECEMBER 31, 2021.

STOCK OWNERSHIP AND REPORTING

Security Ownership of Certain Beneficial Owners and Management

Unless otherwise provided below, the following table sets forth information regarding beneficial ownership of our common stock as of March 31, 2021 by:

- each person, or group of affiliated persons, known to us to be the beneficial owner of 5% or more of the outstanding shares of our common stock;
- each of our current directors;
- our named executive officers; and
- all of our current executive officers and directors as a group.

Beneficial ownership is determined in accordance with the rules and regulations of the SEC and includes voting or investment power with respect to our common stock. Percentage of beneficial ownership is based on 61,849,642 shares of our common stock outstanding as of March 31, 2021. In addition, shares of common stock subject to options or other rights currently exercisable, or exercisable within 60 days of March 31, 2021, are deemed outstanding and beneficially owned for the purpose of computing the percentage beneficially owned by (i) the individual holding such options, warrants or other rights (but not any other individual) and (ii) the directors and executive officers as a group. Except as otherwise noted, the persons and entities in this table have sole voting and investing power with respect to all of the shares of our common stock beneficially owned by them, subject to community property laws, where applicable. Except as otherwise set forth below, the address of the beneficial owner 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	Percentage of Shares Beneficially Owned
5% Stockholders						
ARK Investment Management LLC	8,589,598		—		8,589,598(1)	13.9%
Entities affiliated with FMR LLC	6,912,335		—		6,912,335(2)	11.2%
Entities affiliated with Bain Capital Life Sciences, L.P.	4,000,000(3)		1,000,000(4)		5,000,000	8.0%
Entities affiliated with Nikko Asset Management Americas, Inc.	4,381,992		—		4,381,992(5)	7.1%
BlackRock, Inc.	3,325,560		—		3,325,560(6)	5.4%
Named Executive Officers and Directors						
Nancy Simonian, M.D.	723,606(7)		890,074		1,613,680	2.6%
David A. Roth, Ph.D.	—		416,532		416,532	*
Eric R. Olson, Ph.D.	—		373,750		373,750	*
Srinivas Akkaraju, M.D., Ph.D.	1,899,616(8)		193,374(9)		2,092,990	3.4%
Mark J. Alles	10,000		32,567		42,567	*
S. Gail Eckhardt, M.D.	—		7,775		7,775	*
Marsha H. Fanucci	—		85,707		85,707	*
Amir Nashat, Ph.D.	1,586,653(10)		71,041		1,657,694	2.7%
Phillip A. Sharp, Ph.D.	266,666(11)		113,898		380,564	*
Peter Wirth	—		60,041		60,041	*
Richard A. Young, Ph.D.	321,711		71,041		392,752	*
All Current Executive Officers and Directors as a Group (13 persons)	4,808,252		2,863,917		7,672,169	11.9%

* Represents beneficial ownership of less than 1% of our outstanding stock.

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- (1) ARK Investment Management LLC (“ARK”) reports holding sole voting power over 7,848,713 shares, shared voting power over 186,593 shares, and sole dispositive power over 8,589,598 shares. ARK has an address at 3 East 28th Street, 7th Floor, New York, NY 10016. For information regarding ARK, we have relied, without independent investigation, on the Schedule 13G/A filed by ARK with the SEC on March 10, 2021.
- (2) FMR LLC (“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 6,912,335 of the shares listed herein. FMR reports sole voting power over 2,251,175 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 (the “1940 Act”) to form a controlling group with respect to FMR. Neither FMR nor Ms. Johnson has the sole power to vote or direct the voting of the shares owned directly by the various investment companies registered under the 1940 Act advised by Fidelity Management & Research Company LLC, a wholly owned subsidiary of FMR (“FMR Co. LLC”), which power resides with the funds’ boards of trustees. FMR Co. LLC carries out the voting of the shares under written guidelines established by the funds’ boards of trustees. FMR has an address at 245 Summer Street, Boston, Massachusetts 02210. For information regarding FMR, we have relied, without independent investigation, on the Schedule 13G/A filed by FMR with the SEC on February 8, 2021.
- (3) Bain Capital Life Sciences Fund II, L.P. (“BCLS II”) reports holding shared voting and dispositive power over 3,565,714 shares, and BCIP Life Sciences Associates, LP (“BCIPLS” and, together with BCLS II, the “Bain Capital Life Science Entities”) reports holding shared voting and dispositive power over 434,286 shares. Bain Capital Life Sciences Investors, LLC (“BCLSI”), whose managers are Jeffrey Schwartz and Adam Koppel, 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, each of BCLSI, Mr. Schwartz and Dr. Koppel 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, we have relied, without independent investigation, on the Schedule 13G filed by the Bain Capital Life Science Entities with the SEC on December 14, 2020.
- (4) Includes pre-funded warrants to purchase 891,429 shares of common stock that are owned by BCLS II and pre-funded warrants to purchase 108,571 shares of common stock that are owned by BCIPLS, all of which are currently exercisable. In addition, BCLS II holds warrants to purchase 1,114,286 shares of common stock (or pre-funded warrants in lieu thereof), and BCIPLS holds warrants to purchase 135,714 shares of common stock (or pre-funded warrants in lieu thereof) that are not included in the beneficial ownership table because they are not exercisable until June 8, 2021. 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, we have relied, without independent investigation, on the Schedule 13G filed by the Bain Capital Life Science Entities with the SEC on December 14, 2020.
- (5) Nikko Asset Management Americas, Inc. (“NAMA”) reports holding shared voting power over 3,385,301 shares and shared dispositive power over 4,381,992 shares. The parent holding companies of NAMA, Sumitomo Mitsui Trust Holdings, Inc. (“SMTH”) and Nikko Asset Management Co., Ltd. (“NAM”) each report holding shared voting and dispositive power over 4,381,992 shares. NAMA has an address at 605 Third Avenue, 38th Floor, New York, NY 10158. SMTH has an address at 1-4-1 Marunouchi, Chiyoda-ku, Tokyo, 100-8233, Japan. NAM has an address at Midtown Tower, 9-7-1 Akasaka, Minato-ku, Tokyo, 107-6242, Japan. For information regarding NAMA, SMTH and NAM, we have relied, without independent

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investigation, on the Schedule 13G/A filed by NAMA with the SEC on February 11, 2021 and the Schedule 13G/A filed jointly by SMTH and NAM with the SEC on February 5, 2021.

- (6) BlackRock, Inc. (“BlackRock”) reports holding sole voting power as to 3,305,388 of the shares and sole dispositive power over all of the shares listed herein. BlackRock has an address at 55 East 52nd Street, New York, NY 10055. For information regarding BlackRock, we have relied, without independent investigation, on the Schedule 13G/A filed by BlackRock with the SEC on February 1, 2021.
- (7) Consists of (i) 563,606 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. (“Samsara LP”). The general partner of Samsara LP is Samsara BioCapital GP, LLC (“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 133,333 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. (“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, Massachusetts 02210. For information regarding Polaris Partners VII, L.P. we have 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.

OTHER MATTERS

As of the date of this proxy statement, we know of no matter not specifically referred to above as to which any action is expected to be taken at the annual meeting. The persons named as proxies will vote the proxies, insofar as they are not otherwise instructed, regarding such other matters and the transaction of such other business as may be properly brought before the meeting, as seems to them to be in the best interest of our company and our stockholders.

Stockholder Proposals for our 2022 Annual Meeting

Stockholder Proposals Included in Proxy Statement

In order to be considered for inclusion in our proxy statement and proxy card relating to our 2022 annual meeting of stockholders, stockholder proposals must be received by us no later than December 30, 2021, which is 120 days prior to the first anniversary of the mailing date of this proxy, unless the date of the 2022 annual meeting of stockholders is changed by more than 30 days from the anniversary of our 2021 annual meeting, in which case, the deadline for such proposals will be a reasonable time before we begin to print and send our proxy materials. Upon receipt of any such proposal, we 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, our by-laws establish an advance notice procedure for nominations for election to our board of directors and other matters that stockholders wish to present for action at an annual meeting other than those to be included in our proxy statement. In general, we must receive other proposals of stockholders (including director nominations) intended to be presented at the 2022 annual meeting of stockholders but not included in the proxy statement by March 10, 2022, but not before February 8, 2022, 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 2022 annual meeting of stockholders may exercise discretionary voting power regarding any such proposal. Stockholders are advised to review our 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.

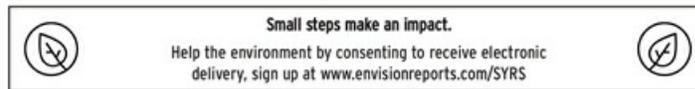
Householding of Annual Meeting Materials

Some brokers and other nominee record holders may be "householding" our proxy materials. This means a single notice and, if applicable, the proxy materials, will be delivered to multiple stockholders sharing an address unless contrary instructions have been received. We will promptly deliver a separate copy of the notice and, if applicable, the proxy materials and our 2020 annual report to stockholders, which consists of our Annual Report on Form 10-K for the fiscal year ended December 31, 2020, to you if you write or call us at Syros Pharmaceuticals, Inc., 35 CambridgePark Drive, 4th Floor, Cambridge, Massachusetts 02140, Attention: Chief Financial Officer, telephone: (617) 744-1340. If you would like to receive separate copies of our proxy materials and annual reports in the future, or if you are receiving multiple copies and would like to receive only one copy for your household, you should contact your bank, broker, or other nominee record holder, or you may contact us at the above address and telephone number.

The 2021 Annual Meeting of Stockholders of Syros Pharmaceuticals, Inc. will be held on Tuesday, June 8, 2021, 11:00 a.m. local time, virtually via the internet at www.meetingcenter.io/225982509.

To access the virtual meeting, you must have the information that is printed in the shaded bar located on the reverse side of this form.

The password for this meeting is – SYRS2021.



▼ IF VOTING BY MAIL, SIGN, DETACH AND RETURN THE BOTTOM PORTION IN THE ENCLOSED ENVELOPE. ▼

Proxy – Syros Pharmaceuticals, Inc.



Notice of 2021 Annual Meeting of Stockholders

Proxy Solicited by Board of Directors for Annual Meeting – June 8, 2021

Nancy A. Simonian, Gerald E. Quirk, or either of them (the "Proxies"), each with the power of substitution, are hereby authorized to represent and vote the shares of the undersigned, with all the powers which the undersigned would possess if personally present, at the Annual Meeting of Stockholders of Syros Pharmaceuticals, Inc. to be held virtually via the internet on June 8, 2021 or at any postponement or adjournment thereof.

Shares represented by this proxy will be voted by the stockholder. If no such directions are indicated, the Proxies will have authority to vote FOR each of the nominees listed in Proposal 1 and FOR Proposal 2.

In their discretion, the Proxies are authorized to vote upon such other business as may properly come before the meeting or at any postponement or adjournment thereof.

(Items to be voted appear on reverse side)

C Non-Voting Items

Change of Address – Please print new address below.

Comments – Please print your comments below.

