

Prospectus supplement (To prospectus dated April 28, 2023)



4,939,591 shares of common stock

Pre-funded warrants to purchase up to 5,242,588 shares of common stock

We are offering 4,939,591 shares of our common stock and, in lieu of common stock to investors who so choose, pre-funded warrants to purchase up to 5,242,588 shares of our common stock. The purchase price of each pre-funded warrant equals the price per share at which shares of common stock are being sold in this offering, minus \$0.001. Each pre-funded warrant will be exercisable for one share of common stock and the exercise price of each pre-funded warrant equals \$0.001 per share. This prospectus supplement also relates to the offering of the shares of common stock issuable upon exercise of the pre-funded warrants.

Our common stock is listed on The Nasdaq Global Select Market under the symbol "SYRS." On December 18, 2023, the last reported sale price of our common stock on the Nasdaq Global Select Market was \$4.30 per share. There is no established public trading market for the pre-funded warrants, and we do not expect a market to develop. We do not intend to list the pre-funded warrants on The Nasdaq Global Select Market, any other national securities exchange or any other nationally recognized trading system.

	<i>Per share</i>	<i>Per pre-funded warrant</i>	<i>Total</i>
Offering price	\$ 4.4200	\$ 4.41900	\$ 44,999,988.59
Underwriting discounts and commissions⁽¹⁾	\$ 0.2652	\$ 0.26514	\$ 2,699,999.32
Proceeds, before expenses, to Syros Pharmaceuticals, Inc.	\$ 4.1548	\$ 4.15386	\$ 42,299,989.27

⁽¹⁾ We have agreed to reimburse the underwriters for certain FINRA-related expenses. See "Underwriting" beginning on page S-22 of this prospectus supplement.

Investing in our common stock or pre-funded warrants involves risks. See "[Risk factors](#)" beginning on page S-7 of this prospectus supplement, as well as those risk factors contained in the accompanying prospectus and the documents incorporated herein and therein.

Neither the Securities and Exchange Commission nor any other regulatory body has approved or disapproved of these securities or passed upon the accuracy or adequacy of this prospectus supplement or the accompanying prospectus. Any representation to the contrary is a criminal offense.

The underwriters expect to deliver the shares of common stock and pre-funded warrants to investors on or about December 21, 2023.

TD Cowen

Piper Sandler

December 18, 2023

Table of Contents

Prospectus supplement

Prospectus supplement summary	S-1
The offering	S-5
Risk factors	S-7
Cautionary note regarding forward-looking statements and industry data	S-10
Use of proceeds	S-12
Dilution	S-13
Description of the pre-funded warrants	S-15
Material U.S. federal income and estate tax considerations for non-U.S. holders of common stock	S-17
Underwriting	S-22
Legal matters	S-28
Experts	S-28
Where you can find more information	S-29
Incorporation of certain documents by reference	S-29

Prospectus

ABOUT THIS PROSPECTUS	1
WHERE YOU CAN FIND MORE INFORMATION	2
INCORPORATION BY REFERENCE	2
CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS AND INDUSTRY DATA	3
SYROS PHARMACEUTICALS, INC.	5
RISK FACTORS	6
USE OF PROCEEDS	7
DESCRIPTION OF DEBT SECURITIES	8
DESCRIPTION OF CAPITAL STOCK	18
DESCRIPTION OF WARRANTS	26
DESCRIPTION OF UNITS	27
FORMS OF SECURITIES	28
PLAN OF DISTRIBUTION	30
LEGAL MATTERS	33
EXPERTS	33

About this prospectus supplement

This document is in two parts. The first part is this prospectus supplement, which describes the specific terms of this common stock and pre-funded warrants offering and also adds to and updates information contained in the accompanying prospectus and the documents incorporated by reference herein. The second part, the accompanying prospectus, provides more general information. Generally, when we refer to this prospectus, we are referring to both parts of this document combined. To the extent there is a conflict between the information contained in this prospectus supplement and the information contained in the accompanying prospectus or any document incorporated by reference therein filed prior to the date of this prospectus supplement, you should rely on the information in this prospectus supplement; provided that if any statement in one of these documents is inconsistent with a statement in another document having a later date—for example, a document incorporated by reference in the accompanying prospectus—the statement in the document having the later date modifies or supersedes the earlier statement.

We further note that the representations, warranties and covenants made by us in any agreement that is filed as an exhibit to any document that is incorporated by reference herein were made solely for the benefit of the parties to such agreement, including, in some cases, for the purpose of allocating risk among the parties to such agreements, and should not be deemed to be a representation, warranty or covenant to you. Moreover, such representations, warranties or covenants were accurate only as of the date when made. Accordingly, such representations, warranties and covenants should not be relied on as accurately representing the current state of our affairs.

We and the underwriters have not authorized anyone to provide you with any information other than that contained in this prospectus supplement and the accompanying prospectus or in any free writing prospectus we may authorize to be delivered or made available to you. We and the underwriters take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. We are offering to sell, and seeking offers to buy, shares of our common stock or pre-funded warrants only in jurisdictions where offers and sales are permitted. The information contained or incorporated by reference in this prospectus supplement and the accompanying prospectus is accurate only as of the date of this prospectus supplement, regardless of the time of delivery of this prospectus supplement or any sale of shares of our common stock or pre-funded warrants. Our business, financial condition, results of operations and prospects may have changed since that date. You should also read and consider the information in the documents to which we have referred you in the sections entitled "Where you can find more information" and "Incorporation of certain documents by reference" in this prospectus supplement and in the accompanying prospectus.

For investors outside the United States: We and the underwriters have not done anything that would permit this offering or possession or distribution of this prospectus supplement and the accompanying prospectus in any jurisdiction where action for that purpose is required, other than in the United States. Persons outside the United States who come into possession of this prospectus supplement and the accompanying prospectus must inform themselves about, and observe any restrictions relating to, the offering of the shares of common stock or pre-funded warrants and the distribution of this prospectus supplement and the accompanying prospectus outside the United States.

Prospectus supplement summary

This summary does not contain all of the information that you should consider before investing in our common stock or pre-funded warrants. You should read this entire prospectus supplement and the accompanying prospectus carefully, including the consolidated financial statements and other information incorporated by reference in this prospectus supplement and the accompanying prospectus, before making an investment decision. In addition, please read the "Risk factors" section of this prospectus supplement beginning on page S-7 and the risk factors contained in our public filings including, without limitation, our Annual Report on Form 10-K for the year ended December 31, 2022 and our Quarterly Reports on Form 10-Q for the quarterly periods ended March 31, 2023, June 30, 2023 and September 30, 2023.

Overview

We are a biopharmaceutical company committed to developing new standards of care for the frontline treatment of patients with hematologic malignancies. Driven by the motivation to help patients with blood disorders that have largely eluded other targeted approaches, we are advancing tamibarotene, a selective retinoic acid receptor alpha, or RAR α , agonist for which we are conducting SELECT-MDS-1, a Phase 3 clinical trial evaluating tamibarotene in combination with azacitidine in a genomically defined subset of patients with higher-risk myelodysplastic syndrome, or HR-MDS, and for which we are conducting SELECT-AML-1, a randomized Phase 2 clinical trial evaluating tamibarotene in combination with venetoclax and azacitidine in a genomically defined subset of newly diagnosed patients with acute myeloid leukemia, or AML, who are not suitable candidates for standard intensive chemotherapy.

At the 62nd American Society of Hematology Annual Meeting and Exposition held in December 2020, or ASH 2020, we presented data from our fully enrolled Phase 2 clinical trial assessing the safety and efficacy of tamibarotene in combination with azacitidine in newly diagnosed AML patients who are not suitable candidates for standard intensive chemotherapy, as well as in relapsed or refractory, or R/R, AML patients who have been prospectively selected using our proprietary RARA, the gene that codes for RAR α , biomarker. As of an October 1, 2020 data cut-off, 51 newly diagnosed unfit AML patients, including patients with and without RARA gene overexpression, were eligible for a safety analysis. Among these patients, tamibarotene in combination with azacitidine was generally well-tolerated, with no evidence of increased toxicity relative to either as a single agent, including rates of myelosuppression that were comparable to single agent azacitidine. As of the data cut-off, of the 18 patients with RARA overexpression that were evaluable for clinical response, 50% of patients achieved complete response, or CR, and 11% achieved a complete response with incomplete blood count recovery, or CRi, for a total CR/CRi rate of 61%. The median time to initial CR/CRi response was 1.2 months, the median duration of CR/CRi response was 10.8 months, and the median overall survival, or OS, among patients who achieved a CR or CRi was 18.0 months. As of the data cut-off, of the 28 patients without RARA overexpression that were evaluable for clinical response, the overall response rate, or ORR, was 43%, with a CR/CRi rate of 32%, with 25% of patients achieving CR and 7% achieving CRi. The median time to initial CR/CRi response was 3.0 months, and the median duration of CR/CRi response was 10.3 months. Approximately 25,000 patients are diagnosed with unfit AML in the United States and Europe annually and we expect the overall total global market for all AML patients to grow to approximately \$7.5 billion by 2028.

Based on these data and our assessment of ongoing areas of high unmet need, we advanced tamibarotene in combination with azacitidine into a registration-enabling Phase 3 clinical trial in newly diagnosed HR-MDS patients with RARA overexpression, which we refer to as SELECT-MDS-1. HR-MDS is a hematologic malignancy that is closely related to AML, and we believe that approximately

50% of HR-MDS patients overexpress RARA. We believe that approximately 21,000 patients are diagnosed with HR-MDS in the United States and Europe annually and we expect the total global market for MDS patients of all risk groups to grow to approximately \$4.7 billion by 2028. The SELECT-MDS-1 trial is evaluating newly diagnosed HR-MDS patients with RARA overexpression in a double-blind placebo-controlled study design, randomized 2:1 to receive tamibarotene in combination with azacitidine, or placebo in combination with azacitidine, respectively. The primary efficacy endpoint is based on 190 patients to provide over 90% power to detect a difference in CR rates between the experimental and control arms with a one-sided alpha of 0.025. In recent communications, the United States Food and Drug Administration, or FDA, has continued to support the use of the CR rate as an acceptable efficacy endpoint for either full or accelerated approval for treatment of newly diagnosed HR-MDS with supporting data on durability of remission. Informed by feedback from the FDA, we amended the SELECT-MDS-1 clinical trial protocol in March 2023 to include a total of approximately 550 patients to enable us to assess OS as a key secondary endpoint, which could allow the trial to serve as a confirmatory study if needed to convert an accelerated approval to a full approval in the future. The amended clinical trial protocol is designed with 80% power to detect a difference in OS rates for the key secondary endpoint between the experimental and control arms, also with a one-sided alpha of 0.025. We are currently dosing patients in SELECT-MDS-1, and we expect to complete enrollment of the 190 patients necessary to support the CR primary endpoint analysis in the first quarter of 2024 and to report pivotal CR data from the SELECT-MDS-1 trial by the middle of the fourth quarter of 2024.

In addition, we advanced tamibarotene in combination with venetoclax and azacitidine in newly diagnosed unfit AML patients with RARA overexpression. Our ongoing Phase 2 clinical trial, known as SELECT-AML-1, is evaluating the safety and efficacy of tamibarotene in combination with venetoclax and azacitidine compared to venetoclax and azacitidine in approximately 80 patients randomized 1:1. The trial is also evaluating the triplet regimen as a salvage strategy in patients in the control arm who do not respond to venetoclax and azacitidine. The primary endpoint of the trial is the CR/CRi rate and the study is powered at 80% to detect a difference between the experimental and control arms. In December 2022, we reported data from the safety lead-in portion of SELECT-AML-1. As of the data cut-off, eight newly diagnosed, unfit patients who were positive for RARA overexpression had been enrolled in the trial, including six who were evaluable for response. In this population, tamibarotene in combination with venetoclax and azacitidine administered at approved doses showed no evidence of increased toxicity relative to the doublet combination of venetoclax and azacitidine. This includes rates of myelosuppression, which were comparable to reports with venetoclax and azacitidine in this population. Among these patients, the CR/CRi rate was 83%, consisting of two patients (33%) who achieved a CR and three patients (50%) who achieved a CRi. These data supported our decision to initiate the randomized portion of the SELECT-AML-1 trial.

Recent Developments

On December 6, 2023, we announced initial data from the randomized portion of SELECT-AML-1. As of November 13, 2023, 23 newly diagnosed unfit AML patients positive for RARA overexpression had enrolled in the randomized portion of the trial, including 19 who were evaluable for response. The CR/CRi rate was 100% among response evaluable patients (nine of nine) treated with the combination of tamibarotene, venetoclax and azacitidine, as compared to 70% of patients (seven of ten) treated with the control arm of venetoclax and azacitidine. Seven of the nine response evaluable patients (78%) treated with the combination of tamibarotene, venetoclax and azacitidine achieved a CR and two patients (22%) achieved a CRi. Three of the ten response evaluable patients (30%) treated with the control achieved a CR and four patients (40%) achieved a CRi. The median time to CR/CRi response was 21 days (ranging from 14-28) among patients treated with the combination of tamibarotene, venetoclax and azacitidine, as compared to 25 days (ranging from 17-56) among patients treated with

the control, with the CR/CRi being reached by 100% of patients in the triplet arm by the end of cycle one, compared with 60% of patients in the doublet control arm. Consistent with prior clinical experience from the safety lead-in portion of this study, tamibarotene administered in combination with approved doses of venetoclax and azacitidine was generally well tolerated, and the overall safety profile demonstrated no additive toxicities or new safety signals, or evidence of increased myelosuppression compared to treatment with the doublet combination of venetoclax and azacitidine. The majority of non-hematologic adverse events were low-grade and reversible, and rates of serious adverse events were comparable between the study arms. As of the data cut-off, there was comparable exposure across the treatment arms, consisting of 66 days (ranging from 8-188) among patients treated with the combination of tamibarotene, venetoclax and azacitidine, and 75 days (ranging from 7-227) for patients treated with the control. Patients will be followed for duration of response, minimal residual disease-negative response, and survival. We continue to enroll patients in SELECT-AML-1 and anticipate reporting additional data from the trial in 2024.

Risks associated with our business

Our business is subject to a number of risks of which you should be aware before making an investment decision. These risks are discussed more fully in the risk factors contained in our public filings including, without limitation, our Annual Report on Form 10-K for the year ended December 31, 2022, our Quarterly Reports on Form 10-Q for the quarterly periods ended March 31, 2023, June 30, 2023 and September 30, 2023. These risks include the following:

- We have incurred significant losses since inception, expect to incur significant and increasing losses for at least the next several years, and may never achieve or maintain profitability.
- We will need substantial additional funding to execute our operating plan, and if we are unable to raise capital, we could be forced to delay, reduce or eliminate our product development programs or commercialization efforts.
- Unstable market and economic conditions may have serious adverse consequences on our business, financial condition and stock price.
- In the near term, we are dependent on the success of tamibarotene. If we are unable to complete the clinical development of, obtain marketing approval for, or successfully commercialize tamibarotene, either alone or with a collaborator, or if we experience significant delays in doing so, our business will be substantially harmed.
- If clinical trials of any product candidates that we, or any collaborators, may develop fail to satisfactorily demonstrate safety and efficacy to the U.S. Food and Drug Administration, or the FDA, and other regulators, we, or any collaborators, may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of these product candidates.
- Adverse events or undesirable side effects caused by, or other unexpected properties of, product candidates that we develop may be identified during development and could delay or prevent their marketing approval or limit their use.
- We rely on third parties to conduct our clinical trials and certain aspects of our research and testing, and those third parties may not perform satisfactorily, including by failing to meet deadlines for the completion of such trials, research or testing.
- The regulatory approval process is expensive, time consuming and uncertain and may prevent us or any collaborators from obtaining approvals for the commercialization of any product candidates.
- If we fail to comply with our obligations under our existing and any future intellectual property licenses with third parties, we could lose license rights that are important to our business.

- If we are unable to obtain and maintain sufficient patent protection for any product candidates, or if the scope of the patent protection is not sufficiently broad, our competitors could develop and commercialize products similar or identical to ours, and our ability to successfully commercialize tamibarotene or any future product candidates may be adversely affected.

Our corporate information

We were incorporated under the laws of the State of Delaware on November 9, 2011 under the name LS22, Inc. Our executive offices are located at 35 CambridgePark Drive, 4th Floor, Cambridge, Massachusetts 02140, and our telephone number is (617) 744-1340. Our website address is www.syros.com. The information contained on, or that can be accessed through, our website is not a part of this prospectus supplement. We have included our website address in this prospectus supplement solely as an inactive textual reference.

Except as otherwise indicated herein or as the context otherwise requires, references in this prospectus supplement to “Syros,” “the company,” “we,” “us” and “our” refer to Syros Pharmaceuticals, Inc. and its consolidated subsidiaries.

The Syros logo, “Syros” and “Syros Pharmaceuticals” are our trademarks. Solely for convenience, the trademarks and trade names in this prospectus supplement are referred to without the ® and ™ symbols, but such references should not be construed as any indicator that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto. The trademarks, trade names and service marks appearing in this prospectus supplement are the property of their respective owners.

The offering	
Common stock offered	4,939,591 of shares.
Pre-funded warrants offered	We are also offering, in lieu of shares of common stock to investors who so choose, pre-funded warrants to purchase up to 5,242,588 shares of common stock. The purchase price of each pre-funded warrant equals the price per share at which the shares of common stock are being sold in this offering, minus \$0.001, and the exercise price of each pre-funded warrant will be \$0.001 per share. Each pre-funded warrant will be exercisable for one share of common stock. Each pre-funded warrant will be exercisable at any time after the date of issuance of such pre-funded warrant, subject to a beneficial ownership limitation described herein. This prospectus supplement also relates to the offering of the shares of common stock issuable upon exercise of such pre-funded warrants. See “Description of Pre-Funded Warrants” on page S-15 of this prospectus supplement.
Common stock to be outstanding after this offering	25,660,038 shares.
Use of proceeds	We intend to use the net proceeds from this offering to fund the ongoing clinical development of tamibarotene and related regulatory and commercial preparation activities, as well as for working capital and other general corporate purposes. See “Use of proceeds” for more information.
Risk factors	You should read the “Risk factors” beginning on page S-7 and the risk factors contained in our Annual Report on Form 10-K for the year ended December 31, 2022, our Quarterly Reports on Form 10-Q for the quarterly periods ended March 31, 2023, June 30, 2023 and September 30, 2023, as well as the other information included in, or incorporated by reference into, this prospectus supplement and the accompanying prospectus, for a discussion of factors to consider carefully before deciding to invest in shares of our common stock or pre-funded warrants.
Nasdaq Global Select Market symbol	“SYRS”

There is no established trading market for the pre-funded warrants, and we do not expect a market to develop. We do not intend to list the pre-funded warrants on The Nasdaq Global Select Market, any other national securities exchange or any other nationally recognized trading system.

The number of shares of our common stock to be outstanding after this offering is based on 20,720,447 shares of our common stock outstanding as of September 30, 2023 and excludes:

- 1,746,177 shares of common stock issuable upon exercise of stock options outstanding as of September 30, 2023 at a weighted-average exercise price of \$36.43 per share;
- 2,393,891 shares of common stock issuable upon the vesting of restricted stock units outstanding as of September 30, 2023;
- 14,142,298 shares of common stock issuable upon exercise of warrants outstanding as of September 30, 2023 at a weighted-average exercise price of \$12.06 per share;
- 7,279,819 shares of common stock issuable upon exercise of pre-funded warrants outstanding as of September 30, 2023;
- 731,107 shares of common stock reserved as of September 30, 2023 for future issuance under our 2022 Equity Incentive Plan, as amended;
- 661,622 shares of common stock reserved as of September 30, 2023 for future issuance under our 2022 Inducement Stock Incentive Plan, as amended;
- 385,718 shares of common stock reserved as of September 30, 2023 for future issuance under our 2016 Employee Stock Purchase Plan;
- 350,000 shares of our common stock issued and sold pursuant to our "at the market offering" sales agreement, or the Sales Agreement, with Cowen and Company, LLC subsequent to September 30, 2023; and
- 5,242,588 shares of common stock issuable upon exercise of the pre-funded warrants being offered hereby.

Unless otherwise indicated, all information in this prospectus supplement:

- assumes no exercise of the outstanding stock options and warrants described above;
- assumes no exercise of the pre-funded warrants being offered hereby; and
- does not reflect the potential issuance of up to \$48.6 million of shares of our common stock that remains available for sale as of the date of this prospectus supplement under our Sales Agreement with Cowen and Company, LLC.

Risk factors

An investment in our common stock or pre-funded warrants involves risks. You should carefully consider the following risk factors, as well as the risk factors included in our Annual Report on Form 10-K for the year ended December 31, 2022, our Quarterly Reports on Form 10-Q for the quarterly periods ended March 31, 2023, June 30, 2023 and September 30, 2023, together with all of the other information included in, or incorporated by reference into, this prospectus supplement and the accompanying prospectus in evaluating an investment in our common stock or pre-funded warrants. If any of the following risks were to occur, our business, financial condition or results of operations could be materially adversely affected. In that case, the trading price of our common stock could decline and you could lose all or part of your investment.

Risks related to our common stock and this offering

If you purchase shares of common stock or pre-funded warrants in this offering, you will suffer immediate dilution of your investment.

The public offering price of our common stock is substantially higher than the as adjusted net tangible book value per share of our common stock after this offering. Therefore, if you purchase shares of our common stock or pre-funded warrants in this offering, you will pay a price per share that substantially exceeds our as adjusted net tangible book value per share after giving effect to this offering. If you purchase common stock or pre-funded warrants in this offering, you will incur an immediate and substantial dilution in net tangible book value of \$1.37 per share of common stock, after giving effect to the issuance and sale by us of the shares of common stock and pre-funded warrants being offered in this offering. To the extent that any options or warrants are exercised, new equity awards are granted under our equity incentive plans, additional shares of common stock are issued pursuant to our Sales Agreement, with Cowen and Company, LLC or we otherwise issue additional shares of common stock in the future, there may be further dilution to investors. Furthermore, if the pre-funded warrants are exercised, you will incur further dilution.

We have broad discretion in the use of the net proceeds from this offering and may not use them effectively.

Our management will have broad discretion in the application of the net proceeds from this offering and could spend the proceeds in ways that do not improve our results of operations or enhance the value of our common stock. The failure by our management to apply these funds effectively could result in financial losses, and these financial losses could have a material adverse effect on our business, cause the price of our common stock to decline and delay the development of tamibarotene or any future product candidates. Pending their use, we may invest the net proceeds from this offering, in a manner that does not produce income or that loses value. See "Use of proceeds" for more information.

Future sales and issuances of our common stock or rights to purchase common stock could result in additional dilution of the percentage ownership of our stockholders and could cause our stock price to fall.

We expect that significant additional capital will be needed in the future to continue our planned operations. To raise capital, we may sell common stock, convertible securities or other equity securities in one or more transactions at prices and in a manner we determine from time to time. If we sell common stock, convertible securities or other equity securities in more than one transaction, investors may be materially diluted by subsequent sales. Such sales may also result in material dilution to our existing stockholders, and new investors could gain rights, preferences and privileges senior to those of holders of our common stock.

Table of Contents

In addition, we entered into the Sales Agreement with Cowen and Company, LLC, as agent, in April 2023, under which we may issue and sell from time to time through Cowen and Company, LLC shares of our common stock, in an aggregate amount not to exceed \$50.0 million, of which \$48.6 remains available as of the date of this prospectus supplement, after the expiration or waiver of the 60-day lock-up period applicable to us and described under the section of this prospectus supplement entitled "Underwriting". To the extent that we sell additional shares of our common stock pursuant to our Sales Agreement with Cowen and Company, LLC, investors purchasing shares of common stock in this offering could experience further dilution. See "Dilution" for more information.

We do not anticipate paying any cash dividends on our capital stock in the foreseeable future. Accordingly, you must rely on capital appreciation, if any, for any return on your investment.

We have never declared nor paid cash dividends on our capital stock. We currently plan to retain all of our future earnings, if any, to finance the operation, development and growth of our business. In addition, the terms of any debt or credit agreements may preclude us from paying dividends. For example, the terms of our term loan facility with Oxford Finance, LLC precludes us from paying cash dividends to our stockholders without the lender's consent. As a result, capital appreciation, if any, of our common stock will be your sole source of gain for the foreseeable future.

Sales of substantial amounts of our common stock in the public markets, or the perception that such sale might occur, could reduce the price that our common stock might otherwise attain.

Sales of a substantial amount of shares of our common stock in the public market, particularly sales by our directors, executive officers and significant stockholders, or the perception that these sales could occur, could cause the market price of our common stock to decline and may make it more difficult for you to sell your common stock at a time and price that you deem appropriate.

Our executive officers, directors and certain of our significant stockholders have entered into lock-up agreements with the underwriters under which they have agreed, subject to specific exceptions, not to sell, directly or indirectly, any shares of common stock without the permission of Cowen and Company, LLC and Piper Sandler & Co. for a period of 60 days after the date of the pricing of the offering. We refer to such period as the lock-up period. When the lock-up period expires, we and our executive officers, directors and stockholders who are subject to lock-up agreements will be able to sell shares in the public market. Sales of a substantial number of such shares upon expiration of the lock-up agreements, the perception that such sales may occur, or early release of these agreements, could cause the market price of our common stock to fall or make it more difficult for you to sell your common stock at a time and price that you deem appropriate.

There is no public market for the pre-funded warrants being offered in this offering.

There is no public trading market for the pre-funded warrants being offered in this offering, and we do not expect a market to develop. In addition, we do not intend to apply to list the pre-funded warrants on any securities exchange or nationally recognized trading system, including The Nasdaq Global Select Market. Without an active market, the liquidity of the pre-funded warrants will be limited.

Holders of any pre-funded warrants purchased in this offering will have no rights as holders of our common stock with respect to the shares of common stock underlying such pre-funded warrants until such holders exercise their pre-funded warrants and acquire our common stock.

Until holders of pre-funded warrants acquire shares of our common stock upon exercise of the pre-funded warrants, holders of pre-funded warrants will have no rights with respect to the shares of our common stock underlying such pre-funded warrants including with respect to dividends and voting rights. Upon exercise of the pre-funded warrants, the holders will be entitled to exercise the rights of a holder of our common stock with respect to the shares of common stock underlying such pre-funded warrants only as to matters for which the record date occurs after the exercise date.

Significant holders or beneficial holders of our common stock may not be permitted to exercise pre-funded warrants that they hold.

A holder of a pre-funded warrant will not be entitled to exercise any portion of any pre-funded warrant which, upon giving effect to such exercise, would cause the aggregate number of shares of our common stock beneficially owned by the holder (together with its affiliates) to exceed either 4.99%, 9.99% or 19.99%, as selected by the holder of such pre-funded warrants, of the number of shares of our common stock outstanding immediately after giving effect to the exercise, as such percentage ownership is determined in accordance with the terms of the pre-funded warrants. Such percentage may be increased by the holder of the pre-funded warrant to any other percentage not in excess of 19.99% upon at least 61 days' prior notice from the holder to us. As a result, you may not be able to exercise your pre-funded warrants for shares of our common stock at a time when it would be financially beneficial for you to do so. In such circumstance you could seek to sell your pre-funded warrants to realize value, but you may be unable to do so in the absence of an established trading market for the pre-funded warrants.

Cautionary note regarding forward-looking statements and industry data

This prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein and therein contain forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this prospectus supplement, the accompanying prospectus or the documents incorporated by reference herein and therein, including statements regarding our strategy, future operations, future financial position, future revenue, projected costs, prospects, plans and objectives of management and expected market growth, are forward-looking statements. The words “anticipate,” “believe,” “continue,” “could,” “estimate,” “expect,” “intend,” “may,” “plan,” “potential,” “predict,” “project,” “should,” “target,” “would” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. In addition, statements that “we believe” and similar statements reflect our beliefs and opinions on the relevant subject. The forward-looking statements and opinions contained in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein and therein are based upon information available to us as of the date such statements are made and, while we believe such information forms a reasonable basis for such statements at the time made, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information.

These forward-looking statements include, among other things, statements about:

- our plans to initiate and expand clinical trials of tamibarotene and our expectations for the timing, quantity and quality of information to be reported from our clinical trials of tamibarotene;
- our planned clinical trials for tamibarotene or for any other product candidates, whether conducted by us or by any collaborators, including the timing of these trials and of the anticipated results;
- our ability to replicate in any clinical trial of a product candidate the results we observed in preclinical or earlier clinical studies of such product candidate;
- our plans to research, develop, seek approval for, manufacture and commercialize tamibarotene or any future product candidates;
- our plans to develop and seek approval of companion diagnostic tests for use in identifying patients who may benefit from treatment with tamibarotene or any future product candidates;
- our ability to enter into, and the terms and timing of, any collaborations, license agreements, or other arrangements;
- our plans related to the potential to further develop SY-2101 in the future subject to additional capital availability;
- the potential benefits of any collaboration;
- developments relating to our competitors and our industry;
- the impact of government laws and regulations;
- the timing of and our ability to file new drug applications and obtain and maintain regulatory approvals for tamibarotene or any future product candidates;
- the rate and degree of market acceptance and clinical utility of any products for which we receive marketing approval;
- our commercialization, marketing and manufacturing capabilities and strategy;
- our intellectual property position and strategy;
- our ability to identify additional products or product candidates with significant commercial potential;
- our expectations related to the use of our current cash and cash equivalents and the period of time in which such capital will be sufficient to fund our planned operations;

Table of Contents

- our intended use of the net proceeds from this offering;
- our estimates regarding expenses, future revenue, capital requirements and need for additional financing; and
- general economic conditions, including inflation, recession risk and increasing interest rates.

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. New risks and uncertainties emerge from time to time, and it is not possible for us to predict all risks and uncertainties that could have an impact on the forward-looking statements contained or incorporated by reference in this prospectus supplement and the accompanying prospectus. We have included important factors in the cautionary statements included or incorporated by reference in this prospectus supplement and the accompanying prospectus, particularly in the "Risk factors" section of this prospectus supplement and those described in the risk factors contained in our most recent Annual Report on Form 10-K, our subsequent Quarterly Reports on Form 10-Q, and other filings we make with the SEC, that could cause actual results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements also do not reflect the potential impact of any future acquisitions, mergers, dispositions, collaborations, joint ventures or investments that we may make or enter into. In addition, statements that "we believe" and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this prospectus supplement, and while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete. Our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain and investors are cautioned not to unduly rely upon these statements.

You should read this prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein and therein and the documents that we have filed as exhibits to the registration statement of which this prospectus supplement is a part completely and with the understanding that our actual future results may be materially different from what we expect. We do not assume any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

This prospectus supplement and the accompanying prospectus includes and incorporates by reference certain statistical and other industry and market data that we obtained from industry publications and research, surveys and studies conducted by third parties. All of the market data used or incorporated by reference in this prospectus supplement and the accompanying prospectus involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such data. We believe that the information from these industry publications, surveys and studies is reliable. The industry in which we operate is subject to a high degree of uncertainty and risk due to a variety of important factors, including those described in the "Risk factors" section of this prospectus supplement and those described in the risk factors contained in our most recent Annual Report on Form 10-K, our subsequent Quarterly Reports on Form 10-Q, and other filings we make with the SEC. These and other factors could cause results to differ materially from those expressed in the estimates made by the independent parties and by us.

Use of proceeds

We estimate that the net proceeds to us of the sale of the 4,939,591 shares of our common stock and the pre-funded warrants to purchase 5,242,588 shares of our common stock that we are offering will be approximately \$42.0 million, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us. We will receive nominal proceeds, if any, upon exercise of the pre-funded warrants.

We intend to use the net proceeds from this offering to fund the ongoing development of tamibarotene and related regulatory and commercial preparation activities, as well as for working capital and other general corporate purposes. We believe that our current cash and cash equivalents, without giving effect to the net proceeds to us from this offering, will enable us to fund our planned operating expense and capital expenditure requirements into 2025. Based on our current plans, we believe that the net proceeds to us from this offering, together with our existing cash and cash equivalents, will be sufficient to fund our operations further into 2025 for at least one additional quarter. We have based this estimate on assumptions that may prove to be incorrect, and we could use our available capital resources sooner than we currently expect. The expected net proceeds from this offering, together with our existing cash and cash equivalents, will not be sufficient for us to fund any of our product candidates through regulatory approval, and we will need to raise additional capital to complete the development and commercialization of our product candidates. We may satisfy our future cash needs through the sale of equity securities, additional borrowings under our loan and security agreement with Oxford Finance LLC, other debt financings, working capital lines of credit, corporate collaborations or license agreements, grant funding, interest income earned on invested cash balances or a combination of one or more of these or other sources.

This expected use of net proceeds from this offering represents our intentions based upon our current plans and business conditions, which could change in the future as our plans and business conditions evolve. The amounts and timing of our actual expenditures may vary significantly depending on numerous factors, including the progress of our development, the status of, and results from, clinical trials, the potential need to conduct additional clinical trials to obtain approval of our product candidates for all intended indications, as well as any additional collaborations that we may enter into with third parties for our product candidates and any unforeseen cash needs. As a result, our management will retain broad discretion over the allocation of the net proceeds from this offering.

Pending use of the proceeds as described above, we intend to invest the proceeds in short-term, interest-bearing, investment-grade securities.

Dilution

If you invest in our common stock or pre-funded warrants in this offering, your ownership interest will be diluted to the extent of the difference between the price per share you pay in this offering and the as adjusted net tangible book value per share of our common stock immediately after this offering.

Our net tangible book value as of September 30, 2023 was \$36.3 million, or \$1.75 per share of common stock based upon 20,720,447 shares outstanding. Net tangible book value per share is equal to our total tangible assets less our total liabilities, divided by the total number of shares of common stock outstanding as of September 30, 2023.

After giving further effect to our sale of 4,939,591 shares of common stock and pre-funded warrants to purchase up to 5,242,588 shares of our common stock in this offering at the public offering price of \$4.42 per share and \$4.419 per pre-funded warrant, which equals the offering price per share of the common stock less the \$0.001 per share exercise price of each such pre-funded warrant (and excluding shares of common stock issued or any resulting accounting associated with the pre-funded warrants), and after deducting underwriting discounts and commissions and estimated offering expenses payable by us and excluding the proceeds, if any, from the exercise of the pre-funded warrants issued pursuant to this offering or any resulting accounting associated with the pre-funded warrants, our as adjusted net tangible book value as of September 30, 2023 would have been \$78.3 million, or 3.05 per share. This represents an immediate increase in net tangible book value of \$1.30 per share to existing stockholders and an immediate dilution in net tangible book value of \$1.37 per share of common stock to investors participating in this offering.

The following table illustrates this dilution on a per share basis:

Public offering price per share	\$4.42
Net tangible book value per share as of September 30, 2023	\$1.75
Increase in net tangible book value per share attributable to new investors in this offering	<u>\$1.30</u>
As adjusted net tangible book value per share immediately after this offering	<u>\$3.05</u>
Dilution in net tangible book value per share to new investors	<u>\$1.37</u>

The table above is based on 20,720,447 shares of common stock outstanding as of September 30, 2023 and does not include:

- 1,746,177 shares of common stock issuable upon exercise of stock options outstanding as of September 30, 2023 at a weighted-average exercise price of \$36.43 per share;
- 2,393,891 shares of common stock issuable upon the vesting of restricted stock units outstanding as of September 30, 2023;
- 14,142,298 shares of common stock issuable upon exercise of warrants outstanding as of September 30, 2023 at a weighted-average exercise price of \$12.06 per share;
- 7,279,819 shares of common stock issuable upon exercise of pre-funded warrants outstanding as of September 30, 2023;
- 731,107 shares of common stock reserved as of September 30, 2023 for future issuance under our 2022 Equity Incentive Plan, as amended;
- 661,622 shares of common stock reserved as of September 30, 2023 for future issuance under our 2022 Inducement Stock Incentive Plan, as amended;
- 385,715 shares of common stock reserved as of September 30, 2023 for future issuance under our 2016 Employee Stock Purchase Plan;

[Table of Contents](#)

- 350,000 shares of our common stock issued and sold pursuant to our “at the market offering” program with Cowen and Company, LLC subsequent to September 30, 2023; and
- 5,242,588 shares of common stock issuable upon exercise of the pre-funded warrants being offered hereby.

If holders of the pre-funded warrants purchased in this offering exercise those pre-funded warrants in full, the immediate dilution in as adjusted net tangible book value per share to investors purchasing shares in this offering would be \$0.52 per share.

To the extent that any options or warrants are exercised, new equity awards are granted under our equity incentive plans, additional shares of common stock are issued pursuant to the Sales Agreement with Cowen and Company, LLC or we otherwise issue additional shares of common stock in the future, there may be further dilution to investors.

Description of the pre-funded warrants

The following is a brief summary of certain terms and conditions of the pre-funded warrants being offered by us. The following description is subject in all respects to the provisions contained in the pre-funded warrants.

Form

The pre-funded warrants will be issued as individual warrant agreements to the investors that elect to purchase pre-funded warrants. The form of pre-funded warrant will be filed as an exhibit to a Current Report on Form 8-K that we will file with the SEC in connection with this offering and will be incorporated by reference into the registration statement of which this prospectus supplement forms a part. Prospective investors should carefully review the terms and provisions of the form of pre-funded warrant for a complete description of the terms and conditions of the pre-funded warrants.

Term

The pre-funded warrants will not expire.

Exercisability

The pre-funded warrants will be exercisable at any time after their original issuance. The pre-funded warrants will be exercisable, at the option of each holder, in whole or in part by delivering to us a duly executed exercise notice and by payment in full in immediately available funds for the number of shares of common stock purchased upon such exercise. As an alternative to payment in immediately available funds, the holder may, in its sole discretion, elect to exercise the pre-funded warrant through a cashless exercise, in which case the holder would receive upon such exercise the net number of shares of common stock determined according to the formula set forth in the pre-funded warrant. No fractional shares of common stock will be issued in connection with the exercise of a pre-funded warrant. In lieu of fractional shares, we will pay the holder an amount in cash equal to the fractional amount multiplied by the fair market value of any such fractional shares.

Exercise limitations

Under the pre-funded warrants, neither we nor the holder may effect the exercise of any pre-funded warrant, and a holder will not be entitled to exercise any portion of any pre-funded warrant, which, upon giving effect to such exercise, would cause the aggregate number of shares of our common stock beneficially owned by the holder (together with its affiliates and certain related persons) to exceed 4.99%, 9.99% or 19.99%, as selected by the holder of such pre-funded warrants, of the number of shares of our common stock outstanding immediately after giving effect to the exercise, as such percentage ownership is determined in accordance with the terms of the pre-funded warrants. However, any holder may increase or decrease such percentage, but not in excess of 19.99%, upon at least 61 days' prior notice from the holder to us.

Exercise price and certain distributions

The exercise price per whole share of our common stock purchasable upon the exercise of the pre-funded warrants is \$0.001 per share of common stock. The exercise price of the pre-funded warrants is subject to appropriate adjustment in the event of certain stock dividends and distributions, stock splits, stock combinations, reclassifications or similar events affecting our common stock. Also, upon exercise of the pre-funded warrants, holders will be entitled to certain distributions, if any, of assets, including cash, stock or other property, to our stockholders while the pre-funded warrants are outstanding.

Transferability

Subject to applicable laws, the pre-funded warrants may be offered for sale, sold, transferred or assigned without our consent. The pre-funded warrants will be held in definitive form by the warrant

[Table of Contents](#)

agent. The ownership of the pre-funded warrants and any transfers of the pre-funded warrants will be registered in a warrant register maintained by the warrant agent. We will initially act as warrant agent.

Exchange listing

There is no established public trading market for the pre-funded warrants, and we do not plan to apply to list the pre-funded warrants on The Nasdaq Global Select Market, any other national securities exchange or any other nationally recognized trading system.

Fundamental transactions

In the event of a fundamental transaction, as described in the pre-funded warrants and generally including any reorganization, recapitalization or reclassification of our common stock, the sale of all or substantially all of our assets, our consolidation or merger with or into another person, the acquisition of more than 50% of our outstanding shares of common stock, or any person or group becoming the beneficial owner of 50% of the voting power of our capital stock, the holders of the pre-funded warrants will be entitled to receive upon exercise of the pre-funded warrants the kind and amount of securities, cash or other property that the holders would have received had they exercised the pre-funded warrants immediately prior to such fundamental transaction without regard to any limitations on exercise contained in the pre-funded warrants.

No rights as a stockholder

Except by virtue of such holder's ownership of shares of our common stock, the holder of a pre-funded warrant does not have the rights or privileges of a holder of our common stock, including any voting rights, until the holder exercises the pre-funded warrant.

Material U.S. federal income and estate tax considerations for non-U.S. holders of our common stock and pre-funded warrants

The following is a discussion of the material U.S. federal income and estate tax considerations applicable to non-U.S. holders with respect to their purchase, ownership and disposition of shares of our common stock and pre-funded warrants. This discussion is for informational purposes only and is not tax advice. Accordingly, all prospective non-U.S. holders of our common stock and pre-funded warrants should consult their own tax advisors with respect to the U.S. federal, state, and local and non-U.S. tax consequences of the purchase, ownership and disposition of our common stock and pre-funded warrants. For purposes of this discussion, a “non-U.S. holder” means a beneficial owner (other than a partnership or other entity or arrangement classified as a partnership for U.S. federal income tax purposes) of our common stock or pre-funded warrants that is not, for U.S. federal income tax purposes:

- an individual who is a citizen or resident of the United States;
- a corporation or any other organization taxable as a corporation for U.S. federal income tax purposes, created or organized in the United States or under the laws of the United States or of any state thereof or the District of Columbia;
- an estate, the income of which is subject to U.S. federal income tax regardless of its source; or
- a trust if (1) a U.S. court is able to exercise primary supervision over the trust’s administration and one or more United States persons (as defined in the Code) have the authority to control all of the trust’s substantial decisions or (2) the trust has a valid election in effect under applicable U.S. Treasury Regulations to be treated as a United States person.

This discussion is based on current provisions of the U.S. Internal Revenue Code of 1986, as amended, which we refer to as the Code, U.S. Treasury Regulations promulgated thereunder, current administrative rulings and judicial decisions, all as in effect as of the date of this prospectus supplement, all of which are subject to change or to differing interpretation, possibly with retroactive effect. Any change or differing interpretation could alter the tax consequences to non-U.S. holders described in this prospectus supplement. In addition, there can be no assurance that the Internal Revenue Service, which we refer to as the IRS, will not challenge one or more of the tax consequences described herein. We assume in this discussion that a non-U.S. holder holds shares of our common stock or pre-funded warrants as a capital asset, generally property held for investment.

This discussion does not address all aspects of U.S. federal income and estate taxation that may be relevant to a particular non-U.S. holder in light of that non-U.S. holder’s individual circumstances, nor does it address the alternative minimum tax, the gift tax, the estate tax (except to the limited extent specifically set forth below), the Medicare contribution tax on net investment income, the special tax accounting rules under Section 451(b), or any aspects of U.S. state or local or non-U.S. taxes. This discussion also does not consider any specific facts or circumstances that may apply to a non-U.S. holder and does not address the special tax rules applicable to particular non-U.S. holders, such as:

- insurance companies;
- tax-exempt organizations;
- financial institutions;
- brokers, dealers or traders in securities;
- pension plans;
- controlled foreign corporations;
- passive foreign investment companies;

Table of Contents

- owners that hold our common stock or pre-funded warrants as part of a straddle, hedge, conversion transaction, synthetic security or other integrated investment or that are deemed to sell our common stock or pre-funded warrants under the constructive sale provisions of the Code;
- persons who acquired our common stock pursuant to the exercise of any employee stock option or otherwise as compensation;
- certain former citizens or long-term residents of the United States; and
- holders that own or are deemed to own more than 5% of our capital stock (except to the limited extent specifically set forth below).

In addition, this discussion does not address the tax treatment of partnerships or other pass-through entities or arrangements classified as partnerships for U.S. federal income tax purposes or persons who hold our common stock or pre-funded warrants through such partnerships or other entities or arrangements. A partner in a partnership or other pass-through entity or arrangement classified as a partnership for U.S. federal income tax purposes that holds our common stock or pre-funded warrants should consult his, her or its own tax advisor regarding the tax consequences of acquiring, holding and disposing of our common stock or pre-funded warrants through a partnership or other pass-through entity or arrangement, as applicable.

Treatment of pre-funded warrants

Although it is not entirely free from doubt, a pre-funded warrant should be treated as a share of our common stock for U.S. federal income tax purposes and a holder of pre-funded warrants generally should be taxed in the same manner as a holder of common stock as described below. Accordingly, upon exercise, the holding period of a pre-funded warrant should carry over to the share of common stock received. Similarly, the tax basis of the pre-funded warrant should carry over to the share of common stock received upon exercise increased by the exercise price of \$0.001. If a pre-funded warrant expires without being exercised, the holder should recognize a capital loss in an amount equal to such holder's tax basis in the pre-funded warrant. This loss will be long-term capital loss if, at the time of the expiration, the holder's holding period in the pre-funded warrant is more than one year. The deductibility of capital losses is subject to limitations.

Our characterization is not binding on the IRS, and the IRS may treat our pre-funded warrants as warrants to acquire our common stock. In that case, the amount and character of your gain with respect to an investment in our pre-funded warrants could be materially different than the discussion set forth below. Each holder should consult his, her or its own tax advisor regarding the risks associated with the acquisition of a pre-funded warrant pursuant to this offering (including potential alternative characterizations). The balance of this discussion generally assumes that the characterization described above is respected for U.S. federal income tax purposes.

Distributions on our common stock or pre-funded warrants

As discussed under "Dividend Policy" above, we do not expect to make cash dividends to holders of our common stock or pre-funded warrants in the foreseeable future. Distributions, if any, on our common stock generally will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. If a distribution exceeds our current and accumulated earnings and profits, the excess will be treated as a tax-free return of the non-U.S. holder's investment, up to such holder's tax basis in the common stock or pre-funded warrants. Any remaining excess will be treated as capital gain, subject to the tax treatment described below in "Gain on Sale, Exchange or Other Taxable Disposition of Our Common Stock or Pre-Funded Warrants." Any such distributions will also be subject to the discussion below under the section titled "Withholding and Information Reporting Requirements—FATCA."

[Table of Contents](#)

Dividends paid to a non-U.S. holder generally will be subject to withholding of U.S. federal income tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder's country of residence.

Dividends that are treated as effectively connected with a trade or business conducted by a non-U.S. holder within the United States and, if an applicable income tax treaty so provides, that are attributable to a permanent establishment or a fixed base maintained by the non-U.S. holder within the United States, are generally exempt from the 30% withholding tax if the non-U.S. holder satisfies applicable certification and disclosure requirements (generally including provision of a valid IRS Form W-8ECI (or applicable successor form) certifying that the dividends are effectively connected with the non-U.S. holder's conduct of a trade or business within the United States). However, such U.S. effectively connected income, net of specified deductions and credits, generally is taxed at the same U.S. federal income tax rates applicable to United States persons (as defined in the Code). Any U.S. effectively connected income received by a non-U.S. holder that is a corporation also may be subject, under certain circumstances, to an additional "branch profits tax" at a 30% rate or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder's country of residence.

A non-U.S. holder of our common stock or pre-funded warrants who claims the benefit of an applicable income tax treaty between the United States and such holder's country of residence generally will be required to provide a properly executed IRS Form W-8BEN or W-8BEN-E (or successor form) and satisfy applicable certification and other requirements. Non-U.S. holders are urged to consult their tax advisors regarding their entitlement to benefits under a relevant income tax treaty.

A non-U.S. holder that is eligible for a reduced rate of U.S. withholding tax under an income tax treaty may obtain a refund or credit of any excess amounts withheld by timely filing the required information with the IRS.

Gain on sale, exchange or other taxable disposition of our common stock or pre-funded warrants

In general, a non-U.S. holder will not be subject to any U.S. federal income tax on any gain realized upon such holder's sale, exchange or other taxable disposition of shares of our common stock or pre-funded warrants unless:

- the gain is effectively connected with the non-U.S. holder's conduct of a trade or business within the United States and, if an applicable income tax treaty so provides, is attributable to a permanent establishment or a fixed base maintained by such non-U.S. holder in the United States, in which case the non-U.S. holder generally will be taxed at the U.S. federal income tax rates applicable to United States persons (as defined in the Code) and, if the non-U.S. holder is a foreign corporation, the branch profits tax described above in "Distributions on Our Common Stock or Pre-Funded Warrants" also may apply
- the non-U.S. holder is a nonresident alien individual who is present in the United States for 183 days or more in the taxable year of the taxable disposition and certain other conditions are met, in which case the non-U.S. holder will be subject to a 30% tax (or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder's country of residence) on the net gain derived from the taxable disposition, which may be offset by certain U.S. source capital losses of the non-U.S. holder, if any (even through the individual is not considered a resident of the United States), provided that the non-U.S. holder has timely filed U.S. federal income tax returns with respect to such losses; or
- we are, or have been, at any time during the five-year period preceding such taxable disposition (or the non-U.S. holder's holding period, if shorter) a "U.S. real property holding

corporation," unless our common stock is regularly traded on an established securities market and the non-U.S. holder holds no more than 5% of our outstanding common stock, directly or indirectly, during the shorter of the five-year period ending on the date of the taxable disposition or the period that the non-U.S. holder held our common stock. Special rules may apply to a holder of a pre-funded warrant. Non-U.S. holders are urged to consult their own tax advisors regarding the application of these rules to pre-funded warrants. If we are determined to be a U.S. real property holding corporation and the foregoing exception does not apply, then the non-U.S. holder generally will be taxed on its net gain derived from the disposition at the U.S. federal income tax rates applicable to United States persons (as defined in the Code). Generally, a corporation is a U.S. real property holding corporation only if the fair market value of its U.S. real property interests equals or exceeds 50% of the sum of the fair market value of its worldwide real property interests plus its other assets used or held for use in a trade or business. Although there can be no assurance, we do not believe that we are, or have been, a U.S. real property holding corporation, or that we are likely to become one in the future. No assurance can be provided that our common stock will be regularly traded on an established securities market for purposes of the rules described above.

U.S. federal estate tax

Shares of our common stock or pre-funded warrants that are owned or treated as owned at the time of death by an individual who is not a citizen or resident of the United States, as specifically defined for U.S. federal estate tax purposes, are considered U.S. situs assets and will be included in the individual's gross estate for U.S. federal estate tax purposes. Such shares, therefore, may be subject to U.S. federal estate tax, unless an applicable estate tax or other treaty provides otherwise.

Backup withholding and information reporting

We must report annually to the IRS and to each non-U.S. holder the gross amount of the distributions on our common stock or pre-funded warrants paid to such holder and the tax withheld, if any, with respect to such distributions. Non-U.S. holders may have to comply with specific certification procedures to establish that the holder is not a United States person (as defined in the Code) in order to avoid backup withholding at the applicable rate with respect to dividends on our common stock or pre-funded warrants. Generally, a non-U.S. holder will comply with such procedures if it provides a properly executed IRS Form W-8BEN or W-8BEN-E (or other applicable Form W-8) or otherwise meets the documentary evidence requirements for establishing that it is not a United States person or otherwise establishes an exemption. Dividends paid to non-U.S. holders subject to the U.S. withholding tax, as described above in "Distributions on Our Common Stock," generally will be exempt from U.S. backup withholding.

Information reporting and backup withholding will generally apply to the proceeds of a disposition of our common stock or pre-funded warrants by a non-U.S. holder effected by or through the U.S. office of any broker, U.S. or foreign, unless the holder certifies its status as a non-U.S. holder and satisfies certain other requirements, or otherwise establishes an exemption. Generally, information reporting and backup withholding will not apply to a payment of disposition proceeds to a non-U.S. holder where the transaction is effected outside the United States through a non-U.S. office of a broker. However, for information reporting purposes, dispositions effected through a non-U.S. office of a broker with substantial U.S. ownership or operations generally will be treated in a manner similar to dispositions effected through a U.S. office of a broker. Non-U.S. holders should consult their own tax advisors regarding the application of the information reporting and backup withholding rules to them.

Copies of information returns may be made available to the tax authorities of the country in which the non-U.S. holder resides or is incorporated under the provisions of a specific treaty or agreement.

Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules from a payment to a non-U.S. holder can be refunded or credited against the non-U.S. holder's U.S. federal income tax liability, if any, provided that an appropriate claim is timely filed with the IRS.

Withholding and information reporting requirements—FATCA

Provisions of the Code commonly referred to as the Foreign Account Tax Compliance Act, or FATCA, generally impose a U.S. federal withholding tax at a rate of 30% on certain payments to foreign entities, unless (i) if the foreign entity is a “foreign financial institution,” such foreign entity undertakes certain due diligence, reporting, withholding, and certification obligations, (ii) if the foreign entity is not a “foreign financial institution,” such foreign entity identifies certain of its U.S. investors, if any, or (iii) the foreign entity is otherwise exempt under FATCA.

Withholding under FATCA generally will apply to payments of dividends on our common stock or pre-funded warrants. While withholding under FATCA may apply to payments of gross proceeds from a sale or other disposition of our common stock or pre-funded warrants, under proposed U.S. Treasury Regulations, withholding on payments of gross proceeds is not required. Although such regulations are not final, applicable withholding agents may rely on the proposed regulations until final regulations are issued.

If withholding under FATCA is required on any payment related to our common stock or pre-funded warrants, investors not otherwise subject to withholding (or that otherwise would be entitled to a reduced rate of withholding) on such payment may be required to seek a refund or credit from the IRS. An intergovernmental agreement between the United States and an applicable foreign country may modify these rules. Non-U.S. holders should consult their own tax advisors regarding the possible implications of FATCA on their investment in our common stock or pre-funded warrants and the entities through which they hold our common stock or pre-funded warrants.

The preceding discussion of material U.S. federal tax considerations is for informational purposes only. It is not legal or tax advice. Prospective investors should consult their own tax advisors regarding the particular U.S. federal, state, local and non-U.S. tax consequences of purchasing, holding and disposing of our common stock or pre-funded warrants, including the consequences of any proposed changes in applicable laws.

Underwriting

We and the underwriters for the offering named below have entered into an underwriting agreement with respect to the common stock and pre-funded warrants being offered. Subject to the terms and conditions of the underwriting agreement, each underwriter has severally agreed to purchase from us the number of shares of our common stock and number of pre-funded warrants set forth opposite its name below. Cowen and Company, LLC and Piper Sandler & Co. are the representatives of the underwriters.

<u>Underwriter</u>	<u>Number of Shares</u>	<u>Number of Pre-Funded Warrants</u>
Cowen and Company, LLC	2,617,983	2,778,572
Piper Sandler & Co.	2,321,608	2,464,016
Total	4,939,591	5,242,588

The underwriting agreement provides that the obligations of the underwriters are subject to certain conditions precedent and that the underwriters have agreed, severally and not jointly, to purchase all of the shares of common stock and pre-funded warrants sold under the underwriting agreement if any of these shares and pre-funded warrants are purchased. If an underwriter defaults, the underwriting agreement provides that the purchase commitments of the non-defaulting underwriters may be increased or the underwriting agreement may be terminated.

We have agreed to indemnify the underwriters against specified liabilities, including liabilities under the Securities Act of 1933, and to contribute to payments the underwriters may be required to make in respect thereof.

The underwriters are offering the shares and pre-funded warrants, subject to prior sale, when, as and if issued to and accepted by them, subject to approval of legal matters by their counsel and other conditions specified in the underwriting agreement. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

Discounts and Commissions. The following table shows the public offering price, underwriting discounts and commissions and proceeds, before expenses, to us.

We estimate that the total expenses of the offering, excluding underwriting discounts and commissions, will be approximately \$350,000 and are payable by us. We also have agreed to reimburse the underwriters for up to \$30,000 for their FINRA counsel fee. In accordance with FINRA Rule 5110, this reimbursed fee is deemed underwriting compensation for this offering.

	<u>Per Share</u>	<u>Per Pre-Funded Warrant</u>	<u>Total</u>
Offering price	\$ 4.4200	\$ 4.41900	\$ 44,999,988.59
Underwriting discounts and commissions	\$ 0.2652	\$ 0.26514	\$ 2,699,999.32
Proceeds, before expenses, to Syros	\$ 4.1548	\$ 4.15386	\$ 42,299,989.27

The underwriters propose to offer the shares of common stock and pre-funded warrants at the offering price set forth on the cover of this prospectus. The underwriters may offer the shares of common stock and pre-funded warrants to securities dealers at the offering price less a concession not in excess of \$0.15912 per share and of \$0.15912 per pre-funded warrant. If all of the shares and/or pre-funded warrants are not sold at the offering price, the underwriters may change the offering price and other selling terms.

Discretionary Accounts. The underwriters do not intend to confirm sales of the shares to any accounts over which they have discretionary authority.

Passive Market Making. In connection with this offering, underwriters and selling group members may engage in passive market making transactions in our common stock on the Nasdaq Stock Market in accordance with Rule 103 of Regulation M under the Securities Exchange Act of 1934, as amended, during a period before the commencement of offers or sales of common stock and extending through the completion of the distribution. A passive market maker must display its bid at a price not in excess of the highest independent bid of that security. However, if all independent bids are lowered below the passive market maker's bid, such bid must then be lowered when specified purchase limits are exceeded.

Lock-Up Agreements. Pursuant to certain "lock-up" agreements, we and our executive officers, directors, and certain of our other stockholders, have agreed, subject to certain exceptions, not to offer, sell, assign, transfer, pledge, contract to sell, lend or otherwise dispose of, or announce the intention to otherwise dispose of, or enter into, or announce the intention to enter into, any swap, hedge or similar agreement or arrangement that transfers, is designed to transfer or reasonably could be expected to transfer in whole or in part, directly or indirectly the economic risk of ownership of, or engage in, or announce the intention to engage in, any short selling of, or make any demand or request or exercise any right with respect to the registration of, or file with the SEC a registration statement under the Securities Act relating to, any common stock or securities convertible into or exchangeable or exercisable for any common stock without the prior written consent of Cowen and Company, LLC and Piper Sandler & Co., for a period of 60 days after the date of the pricing of the offering.

This lock-up provision applies to common stock and to securities convertible into or exchangeable or exercisable for common stock. It also applies to common stock owned now or acquired later by the person executing the agreement or for which the person executing the agreement later acquires the power of disposition. The exceptions permit parties to the "lock-up" agreements, among other things and subject to restrictions, to: (a) make certain gifts, make transfers to immediate family members or to a trust, the beneficiaries of which are exclusively the person executing the "lock-up" agreement or its immediate family, make transfers by will or intestate succession upon the death of the signatory to the "lock-up" agreement or make transfers by operation of law, (b) if the party is a corporation, partnership, limited liability company or other business entity, make transfers to any stockholder, partner or member of, or owner of similar equity interest in, the party, or to an affiliate of the party, if such transfer is not for value, (c) if the party is a corporation, partnership, limited liability company or other business entity, make transfers in connection with the sale or other bona fide transfer in a single transaction of all or substantially all of the party's capital stock, partnership interests, membership interests or other similar equity interests, as the case may be, or all or substantially all of the party's assets, in any such case not undertaken for the purpose of avoiding the restrictions imposed by the "lock-up" agreement (d) establish a 10b5-1 trading plan, provided that such plan does not permit the sale of any common stock during the 60-day lock-up period and no public announcement or filing is made regarding such plan during the 60-day lock-up period, provided further that if any filing under the Exchange Act or other public announcement shall be legally required during the lock-up period, such filing or public announcement shall clearly indicate that no transfers under such trading plans are permitted to take place during the lock-up period, (e) transfer or dispose of shares of common stock or other securities pursuant to any 10b5-1 trading plan, provided, however, that no public announcement or filing is voluntarily made regarding such transaction during the lock-up period and provided that to the extent a public announcement or filing is required under the Exchange Act reporting such transaction during the lock-up period, such announcement or filing shall include a statement in such report to the effect that the disposition was effected in accordance with the terms of a trading plan pursuant to Rule 10b5-1 under the Exchange Act, and (f) the transfer of shares of common stock or any security convertible into or exercisable or exchangeable for common stock pursuant to a bona fide third party tender offer, merger, consolidation or other similar transaction made to all holders involving a change of control (as

Table of Contents

defined in the “lock-up” agreement) of the Company that is approved by its board of directors. The exceptions permit us, among other things and subject to restrictions, to: (a) issue common stock or options pursuant to stock-based compensation plans, (b) issue common stock upon exercise of outstanding options or warrants, (c) file registration statements on Form S-8 or a successor form thereto relating to the shares of common stock granted pursuant to or reserved for issuance under our stock-based compensation plans or (d) issue securities in connection with a transaction that includes a commercial relationship or any acquisition of assets or not less than a majority or controlling portion of the equity of another entity provided that the aggregate number of shares of common stock issued pursuant to this exception shall not exceed 5.0% of the total number of outstanding shares of common stock immediately following the issuance and sale of the shares in this offering. In addition, the lock-up provision will not restrict broker-dealers from engaging in market making and similar activities conducted in the ordinary course of their business.

Cowen and Company, LLC and Piper Sandler & Co., in their sole discretion, may release our common stock and other securities subject to the lock-up agreements described above in whole or in part at any time. When determining whether or not to release our common stock and other securities from lock-up agreements, Cowen and Company, LLC and Piper Sandler & Co. will consider, among other factors, the holder’s reasons for requesting the release, the number of shares for which the release is being requested and market conditions at the time of the request.

Canada. The common stock may be sold only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106 *Prospectus Exemptions or subsection 73.3(1) of the Securities Act (Ontario)*, and are permitted clients, as defined in National Instrument 31-103 *Registration Requirements, Exemptions and Ongoing Registrant Obligations*. Any resale of the common stock must be made in accordance with an exemption from, or in a transaction not subject to, the prospectus requirements of applicable securities laws.

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if this prospectus supplement (including any amendment thereto) contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser’s province or territory. The purchaser should refer to any applicable provisions of the securities legislation of the purchaser’s province or territory for particulars of these rights or consult with a legal advisor.

Pursuant to section 3A.3 of National Instrument 33-105 *Underwriting Conflicts* (NI 33-105), the underwriters are not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

United Kingdom. In addition, in the United Kingdom, this document is being distributed only to, and is directed only at, and any offer subsequently made may only be directed at persons who are “qualified investors” (as defined in the Prospectus Regulation) (i) who have professional experience in matters relating to investments falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, as amended (the “Order”) and/or (ii) who are high net worth companies (or persons to whom it may otherwise be lawfully communicated) falling within Article 49(2)(a) to (d) of the Order and/or (iii) to whom it may otherwise be lawfully communicated (all such persons together being referred to as “relevant persons”) in circumstances which have not resulted and will not result in an offer to the public of the securities in the United Kingdom within the meaning of the Financial Services and Markets Act 2000.

Any person in the United Kingdom that is not a relevant person should not act or rely on the information included in this document or use it as basis for taking any action. In the United Kingdom, any investment or investment activity that this document relates to may be made or taken exclusively by relevant persons.

Switzerland. The securities will not be offered, directly or indirectly, to the public in Switzerland and this prospectus does not constitute a public offering prospectus as that term is understood pursuant to article 652a or 1156 of the Swiss Federal Code of Obligations.

European Economic Area. In relation to each Member State of the European Economic Area (each, a “Member State”), no securities have been offered or will be offered pursuant to the offering to the public in that Member State prior to the publication of a prospectus in relation to the securities which has been approved by the competent authority in that Member State or, where appropriate, approved in another Member State and notified to the competent authority in that Member State, all in accordance with the Prospectus Regulation, except that offers of securities may be made to the public in that Member State at any time under the following exemptions under the Prospectus Regulation:

(a) to any legal entity which is a qualified investor as defined under the Prospectus Regulation;

(b) to fewer than 150 natural or legal persons (other than qualified investors as defined under the Prospectus Regulation), subject to obtaining the prior consent of the underwriters; or

(c) in any other circumstances falling within Article 1(4) of the Prospectus Regulation,

provided that no such offer of securities shall require the Company or any underwriter to publish a prospectus pursuant to Article 3 of the Prospectus Regulation or supplement a prospectus pursuant to Article 23 of the Prospectus Regulation and each person who initially acquires any securities or to whom any offer is made will be deemed to have represented, acknowledged and agreed to and with each of the underwriters and the Company that it is a “qualified investor” within the meaning of Article 2(e) of the Prospectus Regulation.

In the case of any securities being offered to a financial intermediary as that term is used in Prospectus Regulation, each such financial intermediary will be deemed to have represented, acknowledged and agreed that the securities acquired by it in the offer have not been acquired on a non-discretionary basis on behalf of, nor have they been acquired with a view to their offer or resale to, persons in circumstances which may give rise to an offer of any securities to the public other than their offer or resale in a Member State to qualified investors as so defined or in circumstances in which the prior consent of the underwriters have been obtained to each such proposed offer or resale.

For the purposes of this provision, the expression an “offer to the public” in relation to securities in any Member State means the communication in any form and by any means of sufficient information on the terms of the offer and any securities to be offered so as to enable an investor to decide to purchase or subscribe for any securities, and the expression “Prospectus Regulation” means Regulation (EU) 2017/1129.

Hong Kong. The securities have not been offered or sold and will not be offered or sold in Hong Kong, by means of any document, other than (a) to “professional investors” as defined in the Securities and Futures Ordinance (Cap. 571 of the Laws of Hong Kong) (the “SFO”) of Hong Kong and any rules made thereunder; or (b) in other circumstances which do not result in the document being a “prospectus” as defined in the Companies (Winding Up and Miscellaneous Provisions) Ordinance (Cap. 32) of Hong Kong) (the “CO”), or which do not constitute an offer to the public within the meaning of the CO. No advertisement, invitation or document relating to the securities has been or may be issued or has been or may be in the possession of any person for the purposes of issue, whether in Hong Kong or elsewhere, which is directed at, or the contents of which are likely to be accessed or read by, the public of Hong Kong (except if permitted to do so under the securities laws of Hong Kong) other than with respect to securities which are or are intended to be disposed of only to persons outside Hong Kong or only to “professional investors” as defined in the SFO and any rules made thereunder.

Table of Contents

Singapore. Each underwriter has acknowledged that this prospectus has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, each underwriter has represented and agreed that it has not offered or sold any securities or caused the securities to be made the subject of an invitation for subscription or purchase and will not offer or sell any securities or cause the securities to be made the subject of an invitation for subscription or purchase, and has not circulated or distributed, nor will it circulate or distribute, this prospectus or any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the securities, whether directly or indirectly, to any person in Singapore other than:

A. to an institutional investor (as defined in Section 4A of the Securities and Futures Act (Chapter 289) of Singapore, as modified or amended from time to time (the "SFA")) pursuant to Section 274 of the SFA;

B. to a relevant person (as defined in Section 275(2) of the SFA) pursuant to Section 275(1) of the SFA, or any person pursuant to Section 275(1A) of the SFA, and in accordance with the conditions specified in Section 275 of the SFA; or

C. otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA.

Where the securities are subscribed or purchased under Section 275 of the SFA by a relevant person which is:

A. a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or

B. a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary of the trust is an individual who is an accredited investor,

securities or securities-based derivatives contracts (each term as defined in Section 2(1) of the SFA) of that corporation or the beneficiaries' rights and interest (however described) in that trust shall not be transferred within six months after that corporation or that trust has acquired the securities pursuant to an offer made under Section 275 of the SFA except:

(i) to an institutional investor or to a relevant person, or to any person arising from an offer referred to in Section 275(1A) or Section 276(4)(i)(B) of the SFA;

(ii) where no consideration is or will be given for the transfer;

(iii) where the transfer is by operation of law;

(iv) as specified in Section 276(7) of the SFA; or

(v) as specified in Regulation 37A of the Securities and Futures (Offers of Investments) (Securities and Securities-based Derivatives Contracts) Regulations 2018.

Singapore SFA Product Classification — In connection with Section 309B of the SFA and the CMP Regulations 2018, unless otherwise specified before an offer of securities, we have determined, and hereby notify all relevant persons (as defined in Section 309A(1) of the SFA), that the securities are "prescribed capital markets products" (as defined in the CMP Regulations 2018) and Excluded Investment Products (as defined in MAS Notice SFA 04-N12: Notice on the Sale of Investment Products and MAS Notice FAA-N16: Notice on Recommendations on Investment Products).

Table of Contents

Israel. In the State of Israel this prospectus shall not be regarded as an offer to the public to purchase securities under the Israeli Securities Law, 5728—1968, which requires a prospectus to be published and authorized by the Israel Securities Authority, if it complies with certain provisions of Section 15 of the Israeli Securities Law, 5728—1968, including, inter alia, if: (i) the offer is made, distributed or directed to not more than 35 investors, subject to certain conditions (the “Addressed Investors”); or (ii) the offer is made, distributed or directed to certain qualified investors defined in the First Addendum of the Israeli Securities Law, 5728—1968, subject to certain conditions (the “Qualified Investors”). The Qualified Investors shall not be taken into account in the count of the Addressed Investors and may be offered to purchase securities in addition to the 35 Addressed Investors. The company has not and will not take any action that would require it to publish a prospectus in accordance with and subject to the Israeli Securities Law, 5728—1968. We have not and will not distribute this prospectus or make, distribute or direct an offer to subscribe for our securities to any person within the State of Israel, other than to Qualified Investors and up to 35 Addressed Investors.

Qualified Investors may have to submit written evidence that they meet the definitions set out in of the First Addendum to the Israeli Securities Law, 5728—1968. In particular, we may request, as a condition to be offered securities, that Qualified Investors will each represent, warrant and certify to us and/or to anyone acting on our behalf: (i) that it is an investor falling within one of the categories listed in the First Addendum to the Israeli Securities Law, 5728—1968; (ii) which of the categories listed in the First Addendum to the Israeli Securities Law, 5728—1968 regarding Qualified Investors is applicable to it; (iii) that it will abide by all provisions set forth in the Israeli Securities Law, 5728—1968 and the regulations promulgated thereunder in connection with the offer to be issued common stock; (iv) that the securities that it will be issued are, subject to exemptions available under the Israeli Securities Law, 5728—1968: (a) for its own account; (b) for investment purposes only; and (c) not issued with a view to resale within the State of Israel, other than in accordance with the provisions of the Israeli Securities Law, 5728—1968; and (v) that it is willing to provide further evidence of its Qualified Investor status. Addressed Investors may have to submit written evidence in respect of their identity and may have to sign and submit a declaration containing, inter alia, the Addressed Investor’s name, address and passport number or Israeli identification number.

We have not authorized and do not authorize the making of any offer of securities through any financial intermediary on our behalf, other than offers made by the underwriters and their respective affiliates, with a view to the final placement of the securities as contemplated in this document. Accordingly, no purchaser of the securities, other than the underwriters, is authorized to make any further offer of securities on our behalf or on behalf of the underwriters.

Electronic Offer, Sale and Distribution of Securities. A prospectus in electronic format may be made available on the websites maintained by one or more of the underwriters or selling group members, if any, participating in this offering and one or more of the underwriters participating in this offering may distribute prospectuses electronically. The representatives may agree to allocate a number of shares to underwriters and selling group members for sale to their online brokerage account holders. Internet distributions will be allocated by the underwriters and selling group members that will make internet distributions on the same basis as other allocations. Other than the prospectus in electronic format, the information on these websites is not part of this prospectus or the registration statement of which this prospectus forms a part, has not been approved or endorsed by us or any underwriter in its capacity as underwriter, and should not be relied upon by investors.

Other Relationships. Certain of the underwriters and their affiliates have provided, and may in the future provide, various investment banking, commercial banking and other financial services for us and our affiliates for which they have received, and may in the future receive, customary fees. Cowen and Company, LLC is the sales agent under the Sales Agreement. Under the Sales Agreement, we may offer and sell, from time to time, shares of our common stock through Cowen and Company, LLC through an “at the market offering,” as defined in Rule 415(a)(4) promulgated under the Securities Act.

Legal matters

The validity of the shares of common stock and pre-funded warrants offered hereby will be passed upon for us by Wilmer Cutler Pickering Hale and Dorr LLP, Boston, Massachusetts. Cooley LLP, New York, New York, has acted as counsel for the underwriters in connection with certain legal matters related to this offering.

Experts

The consolidated financial statements of Syros Pharmaceuticals, Inc. appearing in Syros Pharmaceuticals, Inc.'s Annual Report (Form 10-K) for the year ended December 31, 2022, have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their report thereon included therein, and incorporated herein by reference. Such financial statements are, and audited financial statements to be included in subsequently filed documents will be, incorporated herein in reliance upon the reports of Ernst & Young LLP pertaining to such financial statements (to the extent covered by consents filed with the Securities and Exchange Commission) given on the authority of such firm as experts in accounting and auditing.

Where you can find more information

We file reports, proxy statements and other documents with the SEC. Our SEC filings are available to you on the SEC's Internet site at www.sec.gov.

This prospectus supplement is part of a registration statement that we filed with the SEC. The registration statement contains more information than this prospectus supplement regarding us and our common stock, including certain exhibits and schedules. You can obtain a copy of the registration statement from the SEC's Internet site.

Incorporation of certain documents by reference

The SEC requires us to "incorporate" into this prospectus supplement information that we file with the SEC in other documents. This means that we can disclose important information to you by referring to other documents that contain that information. The information incorporated by reference is considered to be part of this prospectus supplement and the accompanying prospectus. Information contained in this prospectus supplement and the accompanying prospectus and information that we file with the SEC in the future and incorporate by reference in this prospectus supplement automatically updates and supersedes previously filed information. We incorporate by reference the documents listed below and any future filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act after the date of this prospectus supplement and prior to the sale of all the shares covered by this prospectus supplement.

- Our Annual Report on Form 10-K for the year ended December 31, 2022, filed with the SEC on [March 2, 2023](#), including the information specifically incorporated by reference therein from our definitive proxy statement for our 2023 Annual Meeting of Stockholders, as filed with the SEC on [April 21, 2023](#);
- Our Quarterly Report on [Form 10-Q](#) for the quarter ended March 31, 2023, filed with the SEC on May 10, 2023;
- Our Quarterly Report on [Form 10-Q](#) for the quarter ended June 30, 2023, filed with the SEC on August 8, 2023;
- Our Quarterly Report on [Form 10-Q](#) for the quarter ended September 30, 2023, filed with the SEC on November 14, 2023;
- Our Current Reports on Form 8-K filed with the SEC on [January 9, 2023](#) (other than the information furnished under Item 7.01 therein), [May 25, 2023](#) (other than the information furnished under Item 7.01 therein), [June 2, 2023](#), [July 21, 2023](#), [August 11, 2023](#), [October 2, 2023](#) and [December 6, 2023](#) (other than the information furnished under Item 7.01 therein); and
- The description of our common stock contained in our Registration Statement on [Form 8-A/A](#) filed on July 20, 2017, including any amendments or reports filed for the purpose of updating such description.

A statement contained in a document incorporated by reference into this prospectus supplement shall be deemed to be modified or superseded for purposes of this prospectus supplement to the extent that a statement contained in this prospectus supplement, the accompanying prospectus or in any other subsequently filed document which is also incorporated in this prospectus supplement modifies or replaces such statement. Any statements so modified or superseded shall not be deemed, except as so modified or superseded, to constitute a part of this prospectus supplement.

[Table of Contents](#)

You may request a copy of these documents, which will be provided to you at no cost, by writing or telephoning us using the following contact information:

Syros Pharmaceuticals, Inc.
35 CambridgePark Drive, 4th Floor
Cambridge, Massachusetts, 02140
Attention: Gerald E. Quirk, Chief Legal and Compliance Officer & Secretary
Telephone: (617) 744-1340

PROSPECTUS

SYROS PHARMACEUTICALS, INC.



\$250,000,000
of
Debt Securities
Common Stock
Preferred Stock
Units
Warrants

We may offer and sell securities from time to time in one or more offerings of up to \$250,000,000 in aggregate offering price. This prospectus describes the general terms of these securities and the general manner in which these securities will be offered. We will provide the specific terms of these securities in supplements to this prospectus. The prospectus supplements will also describe the specific manner in which these securities will be offered and may also supplement, update or amend information contained in this document. You should read this prospectus and any applicable prospectus supplement before you invest.

We may offer these securities in amounts, at prices and on terms determined at the time of offering. The securities may be sold directly to you, through agents, or through underwriters and dealers. If agents, underwriters or dealers are used to sell the securities, we will name them and describe their compensation in a prospectus supplement.

Our common stock is listed on The Nasdaq Global Select Market under the symbol "SYRS." The applicable prospectus supplement will contain information, where applicable, as to any other listing on the Nasdaq Global Select Market or any securities market or other exchange of the securities, if any, covered by the prospectus supplement.

Investing in these securities involves certain risks. See "[Risk Factors](#)" on page 6 of this prospectus and in any accompanying prospectus supplement and in the documents incorporated by reference in this prospectus for a discussion of the factors you should carefully consider before deciding to purchase these securities.

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

The date of this prospectus is April 28, 2023

TABLE OF CONTENTS

ABOUT THIS PROSPECTUS	1
WHERE YOU CAN FIND MORE INFORMATION	2
INCORPORATION BY REFERENCE	2
CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS AND INDUSTRY DATA	3
SYROS PHARMACEUTICALS, INC.	5
RISK FACTORS	6
USE OF PROCEEDS	7
DESCRIPTION OF DEBT SECURITIES	8
DESCRIPTION OF CAPITAL STOCK	18
DESCRIPTION OF WARRANTS	26
DESCRIPTION OF UNITS	27
FORMS OF SECURITIES	28
PLAN OF DISTRIBUTION	30
LEGAL MATTERS	33
EXPERTS	33

ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission, which we refer to as the SEC, utilizing a “shelf” registration process. Under this shelf registration process, we may from time to time sell any combination of the securities described in this prospectus in one or more offerings for an aggregate initial offering price of up to \$250,000,000.

This prospectus provides you with a general description of the securities we may offer. Each time we sell securities, we will provide one or more prospectus supplements that will contain specific information about the terms of the offering. The prospectus supplement may also add, update or change information contained in this prospectus. You should read both this prospectus and the accompanying prospectus supplement together with the additional information described under the heading “Where You Can Find More Information” beginning on page 2 of this prospectus.

You should rely only on the information contained in or incorporated by reference in this prospectus, in any accompanying prospectus supplement or in any related free writing prospectus filed by us with the SEC. We have not authorized anyone to provide you with different information. This prospectus and any accompanying prospectus supplement do not constitute an offer to sell or the solicitation of an offer to buy any securities other than the securities described in this prospectus or such accompanying prospectus supplement or an offer to sell or the solicitation of an offer to buy such securities in any circumstances in which such offer or solicitation is unlawful. You should assume that the information appearing in this prospectus, any prospectus supplement, the documents incorporated by reference and any related free writing prospectus is accurate only as of their respective dates. Our business, financial condition, results of operations and prospects may have changed materially since those dates.

Unless the context otherwise indicates, references in this prospectus to “we,” “our” and “us” refer, collectively, to Syros Pharmaceuticals, Inc., a Delaware corporation, and its consolidated subsidiaries.

The Syros logo, “Syros” and “Syros Pharmaceuticals” are our trademarks. Solely for convenience, the trademarks and trade names in this prospectus are referred to without the ® and ™ symbols, but such references should not be construed as any indicator that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto. The trademarks, trade names and service marks appearing in this prospectus are the property of their respective owners.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and current reports, proxy statements and other information with the SEC. Our SEC filings are available to the public over the Internet at the SEC's website at <http://www.sec.gov>. Copies of certain information filed by us with the SEC are also available on our website at www.syros.com. Our website is not a part of this prospectus and is not incorporated by reference in this prospectus.

This prospectus is part of a registration statement we filed with the SEC. This prospectus omits some information contained in the registration statement in accordance with SEC rules and regulations. You should review the information and exhibits in the registration statement for further information about us and our consolidated subsidiaries and the securities we are offering. Statements in this prospectus concerning any document we filed as an exhibit to the registration statement or that we otherwise filed with the SEC are not intended to be comprehensive and are qualified by reference to these filings and the exhibits attached thereto. You should review the complete document to evaluate these statements.

INCORPORATION BY REFERENCE

The SEC allows us to incorporate by reference much of the information we file with the SEC, which means that we can disclose important information to you by referring you to those publicly available documents. The information that we incorporate by reference in this prospectus is considered to be part of this prospectus. Because we are incorporating by reference future filings with the SEC, this prospectus is continually updated and those future filings may modify or supersede some of the information included or incorporated in this prospectus. This means that you must look at all of the SEC filings that we incorporate by reference to determine if any of the statements in this prospectus or in any document previously incorporated by reference have been modified or superseded. This prospectus incorporates by reference the documents listed below (File No. 001-37813) and any future filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act (in each case, other than those documents or the portions of those documents not deemed to be filed) between the date of the initial registration statement and the effectiveness of the registration statement and following the effectiveness of the registration statement, until the offering of the securities under the registration statement is terminated or completed:

- Annual Report on [Form 10-K](#) for the fiscal year ended December 31, 2022, as filed with SEC on March 2, 2023, including the information specifically incorporated by reference into the Annual Report on Form 10-K from our definitive proxy statement for the 2023 Annual Meeting of Stockholders;
- Current Report on Form 8-K filed [January 9, 2023](#) (other than the information furnished under Item 7.01 therein; and
- The description of our common stock contained in our Registration Statement on [Form 8-A/A](#) filed on July 20, 2017, as updated by [Exhibit 4.1](#) to our Annual Report on Form 10-K for the fiscal year ended December 31, 2022, and including any amendments and reports filed for the purpose of updating such description.

You may request a copy of these filings, at no cost, by writing or telephoning us at the following address or telephone number:

Syros Pharmaceuticals, Inc.
35 CambridgePark Drive, 4th Floor
Cambridge, Massachusetts, 02140
Attention: Gerald E. Quirk, Chief Legal Officer
Telephone: (617) 744-1340

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS AND INDUSTRY DATA

This prospectus and the information incorporated by reference in this prospectus include “forward-looking statements” within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Exchange Act. All statements, other than statements of historical facts, contained in this prospectus or incorporated by reference herein, including statements regarding our strategy, future operations, future financial position, future revenue, projected costs, prospects, plans and objectives of management and expected market growth are forward-looking statements. The words “anticipate,” “believe,” “continue,” “could,” “estimate,” “expect,” “intend,” “may,” “plan,” “potential,” “predict,” “project,” “should,” “target,” “would” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. In addition, statements that “we believe” and similar statements reflect our beliefs and opinions on the relevant subject. The forward-looking statements and opinions contained in this prospectus and incorporated by reference herein are based upon information available to us as of the date such statements are made and, while we believe such information forms a reasonable basis for such statements at the time made, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information. These forward-looking statements include, among other things, statements about:

- our plans to initiate and expand clinical trials of our product candidates and our expectations for the timing, quantity and quality of information to be reported from our clinical trials of tamibarotene, SY-2101 and SY-5609;
- our planned clinical trials for our product candidates, whether conducted by us or by any collaborators, including the timing of these trials and of the anticipated results;
- our ability to discover and develop compounds suitable for clinical development and the timing for designation of future development candidates;
- our ability to replicate in any clinical trial of one of our product candidates the results we observed in preclinical or earlier clinical studies of such product candidate;
- our plans to research, develop, seek approval for, manufacture and commercialize our current and future product candidates;
- our plans to develop and seek approval of companion diagnostic tests for use in identifying patients who may benefit from treatment with our products and product candidates;
- our ability to enter into, and the terms and timing of, any collaborations, license agreements, or other arrangements;
- whether a drug candidate will be nominated to enter into investigational new drug application-enabling studies under our sickle cell disease collaboration with Global Blood Therapeutics, Inc., or GBT, whether GBT will exercise its option to exclusively license intellectual property arising from the collaboration, whether and when any option exercise fees, milestone payments or royalties under the collaboration agreement with GBT will ever be paid, and whether we exercise our U.S. co-promotion option under the GBT agreement;
- whether our target discovery collaboration with Incyte Corporation, or Incyte, will yield any validated targets, whether Incyte will exercise any of its options to exclusively license intellectual property directed to such targets, and whether and when any of the target validation fees, option exercise fees, milestone payments or royalties under the Incyte collaboration will ever be paid;
- the potential benefits of any collaboration;
- developments relating to our competitors and our industry;
- the impact of government laws and regulations;

Table of Contents

- the timing of and our ability to file new drug applications and obtain and maintain regulatory approvals for our product candidates;
- the rate and degree of market acceptance and clinical utility of any products for which we receive marketing approval;
- our commercialization, marketing and manufacturing capabilities and strategy;
- our intellectual property position and strategy;
- our ability to identify additional products or product candidates with significant commercial potential;
- our expectations related to the use of our current cash, cash equivalents and marketable securities and the period of time in which such capital will be sufficient to fund our planned operations;
- our estimates regarding expenses, future revenue, capital requirements and need for additional financing; and
- general economic conditions, including inflation, recession risk and increasing interest rates.

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. New risks and uncertainties emerge from time to time, and it is not possible for us to predict all risks and uncertainties that could have an impact on the forward-looking statements contained or incorporated by reference in this prospectus.

We have included important factors in the cautionary statements included or incorporated by reference in this prospectus that could cause actual results or events to differ materially from the forward-looking statements that we make, particularly the factors discussed below under “Risk Factors”.

Our forward-looking statements also do not reflect the potential impact of any future acquisitions, mergers, dispositions, collaborations, joint ventures or investments that we may make or enter into.

You should read this prospectus, the documents incorporated by reference in this prospectus and the documents that we have filed as exhibits to the registration statement of which this prospectus is a part completely and with the understanding that our actual future results may be materially different from what we expect. We do not assume any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

This prospectus includes and incorporates by reference certain statistical and other industry and market data that we obtained from industry publications and research, surveys and studies conducted by third parties. All of the market data used or incorporated by reference in this prospectus involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such data. We believe that the information from these industry publications, surveys and studies is reliable. The industry in which we operate is subject to a high degree of uncertainty and risk due to a variety of important factors, including those described in the section titled “Risk Factors.” These and other factors could cause results to differ materially from those expressed in the estimates made by the independent parties and by us.

SYROS PHARMACEUTICALS, INC.

Overview

We are a biopharmaceutical company committed to developing new standards of care for the frontline treatment of patients with hematologic malignancies. Driven by the motivation to help patients with blood disorders that have largely eluded other targeted approaches, we are advancing a late-stage clinical pipeline which includes product candidates targeting multiple hematology indications.

Corporate Information

We were incorporated under the laws of the State of Delaware on November 9, 2011 under the name LS22, Inc. We changed our name to Syros Pharmaceuticals, Inc. on August 15, 2012. Our principal executive offices are located at 35 CambridgePark Drive, 4th Floor, Cambridge, Massachusetts 02140, and our telephone number is (617) 744-1340. Our internet address is www.syros.com. The information on our web site is not incorporated by reference into this prospectus and should not be considered to be a part of this prospectus. Our internet address is included in this prospectus as an inactive textual reference only.

RISK FACTORS

Investing in our common stock involves a high degree of risk. Before you decide to invest in our common stock, you should carefully consider the risks and uncertainties described in the section captioned “Risk Factors” in our most recent Annual Report on Form 10-K and other filings we make with the SEC, from time to time, which are incorporated by reference herein in their entirety, together with the other information in this prospectus and documents incorporated by reference in this prospectus. The risks described in our most recent Annual Report on Form 10-K and the other filings incorporated by reference herein are not the only ones facing our company. Additional risks and uncertainties may also impair our business operations. If any of the risks described in our most recent Annual Report on Form 10-K and the other filings incorporated by reference herein occurs, our business, financial condition, results of operations and future growth prospects could be harmed. In these circumstances, the market price of our common stock could decline, and you may lose all or part of your investment.

USE OF PROCEEDS

Except as described in any applicable prospectus supplement or in any free writing prospectuses that we may authorize to be provided to you in connection with a specific offering, we intend to use the net proceeds from the sale of any securities offered under this prospectus for general corporate purposes unless otherwise indicated in the applicable prospectus supplement. General corporate purposes may include research and development expenditures, acquisitions or in-licenses of complementary companies, products, product candidates or technologies, expenditures to build out our development and commercial capabilities, repayment and refinancing of debt, working capital and capital expenditures. We may temporarily invest such net proceeds in investment-grade, interest-bearing securities until they are used for their stated purpose. We have not determined the amount of net proceeds to be used specifically for such purposes. As a result, management will retain broad discretion over the allocation of the net proceeds of any offering.

DESCRIPTION OF DEBT SECURITIES

The following description summarizes the general terms and provisions of the debt securities that we may offer and sell from time to time. We will describe in a prospectus supplement the specific terms of the debt securities offered through that prospectus supplement, as well as any general terms and provisions described in this section that will not apply to those debt securities. As used in this “Description of Debt Securities”, the term “debt securities” means the senior and subordinated debt securities that we issue and the trustee authenticates and delivers under the applicable indenture. When we refer to “the Company,” “we,” “our,” and “us” in this section, we mean Syros Pharmaceuticals, Inc., excluding, unless the context otherwise requires or as otherwise expressly stated, its subsidiaries.

We may issue senior debt securities from time to time, in one or more series under a senior indenture to be entered into between us and a senior trustee to be named in a prospectus supplement, which we refer to as the senior trustee. We may issue subordinated debt securities from time to time, in one or more series under a subordinated indenture to be entered into between us and a subordinated trustee to be named in a prospectus supplement, which we refer to as the subordinated trustee. The forms of senior indenture and subordinated indenture are filed as exhibits to the registration statement of which this prospectus forms a part. The senior indenture and the subordinated indenture are referred to individually as an indenture and together as the indentures and the senior trustee and the subordinated trustee are referred to individually as a trustee and together as the trustees. This section summarizes some of the provisions of the indentures and is qualified in its entirety by the specific text of the indentures, including definitions of terms used in the indentures. Wherever we refer to particular sections of, or defined terms in, the indentures, those sections or defined terms are incorporated by reference in this prospectus or the applicable prospectus supplement. You should review the indentures that are filed as exhibits to the registration statement of which this prospectus forms a part for additional information.

Neither indenture will limit the amount of debt securities that we may issue. The applicable indenture will provide that debt securities may be issued up to an aggregate principal amount authorized from time to time by us and may be payable in any currency or currency unit designated by us or in amounts determined by reference to an index.

General

The senior debt securities will constitute our unsecured and unsubordinated general obligations and will rank equally in right of payment with our other unsecured and unsubordinated obligations. The subordinated debt securities will constitute our unsecured and subordinated general obligations and will be junior in right of payment to our senior indebtedness (including senior debt securities), as described under the heading “—Certain Terms of the Subordinated Debt Securities—Subordination.” The debt securities will be structurally subordinated to all existing and future indebtedness and other liabilities of our subsidiaries unless such subsidiaries expressly guarantee such debt securities.

The debt securities will be our unsecured obligations. Any secured debt or other secured obligations will be effectively senior to the debt securities to the extent of the value of the assets securing such debt or other obligations.

The applicable prospectus supplement and/or free writing prospectus will include any additional or different terms of the debt securities of any series being offered, including the following terms:

- the title and type of the debt securities;
- whether the debt securities will be senior or subordinated debt securities, and, with respect to any subordinated debt securities the terms on which they are subordinated;
- the initial aggregate principal amount of the debt securities;
- the price or prices at which we will sell the debt securities;

Table of Contents

- the maturity date or dates of the debt securities and the right, if any, to extend such date or dates;
- the rate or rates, if any, at which the debt securities will bear interest, or the method of determining such rate or rates;
- the date or dates from which such interest will accrue, the interest payment dates on which such interest will be payable or the method of determination of such dates;
- the right, if any, to extend the interest payment periods and the duration of that extension;
- the manner of paying principal and interest and the place or places where principal and interest will be payable;
- the denominations of the debt securities;
- provisions for a sinking fund, purchase fund or other analogous fund, if any;
- any redemption dates, prices, obligations and restrictions on the debt securities;
- the currency, currencies or currency units in which the debt securities will be denominated and the currency, currencies or currency units in which principal and interest, if any, on the debt securities may be payable;
- any conversion or exchange features of the debt securities;
- whether the debt securities will be subject to the defeasance provisions in the indenture;
- whether the debt securities will be issued in definitive or global form or in definitive form only upon satisfaction of certain conditions;
- whether the debt securities will be guaranteed as to payment or performance;
- any special tax implications of the debt securities;
- any events of defaults or covenants in addition to or in lieu of those set forth in the indenture; and
- any other material terms of the debt securities.

When we refer to “principal” in this section with reference to the debt securities, we are also referring to “premium, if any.”

We may from time to time, without notice to or the consent of the holders of any series of debt securities, create and issue further debt securities of any such series ranking equally with the debt securities of such series in all respects (or in all respects other than (1) the payment of interest accruing prior to the issue date of such further debt securities or (2) the first payment of interest following the issue date of such further debt securities). Such further debt securities may be consolidated and form a single series with the debt securities of such series and have the same terms as to status, redemption or otherwise as the debt securities of such series.

You may present debt securities for exchange and you may present debt securities for transfer in the manner, at the places and subject to the restrictions set forth in the debt securities and the applicable prospectus supplement. We will provide you those services without charge, although you may have to pay any tax or other governmental charge payable in connection with any exchange or transfer, as set forth in the indenture.

Debt securities may bear interest at a fixed rate or a floating rate. Debt securities bearing no interest or interest at a rate that at the time of issuance is below the prevailing market rate (original issue discount securities) may be sold at a discount below their stated principal amount. U.S. federal income tax considerations applicable to any such discounted debt securities or to certain debt securities issued at par which are treated as having been issued at a discount for U.S. federal income tax purposes will be described in the applicable prospectus supplement.

Table of Contents

We may issue debt securities with the principal amount payable on any principal payment date, or the amount of interest payable on any interest payment date, to be determined by reference to one or more currency exchange rates, securities or baskets of securities, commodity prices or indices. You may receive a payment of principal on any principal payment date, or a payment of interest on any interest payment date, that is greater than or less than the amount of principal or interest otherwise payable on such dates, depending on the value on such dates of the applicable currency, security or basket of securities, commodity or index. Information as to the methods for determining the amount of principal or interest payable on any date, the currencies, securities or baskets of securities, commodities or indices to which the amount payable on such date is linked and certain related tax considerations will be set forth in the applicable prospectus supplement.

Certain Terms of the Senior Debt Securities

Covenants. Unless we indicate otherwise in a prospectus supplement with respect to a particular series of senior debt securities, the senior debt securities will not contain any financial or restrictive covenants, including covenants restricting either us or any of our subsidiaries from incurring, issuing, assuming or guaranteeing any indebtedness secured by a lien on any of our or our subsidiaries' property or capital stock, or restricting either us or any of our subsidiaries from entering into sale and leaseback transactions.

Consolidation, Merger and Sale of Assets. Unless we indicate otherwise in a prospectus supplement with respect to a particular series of senior debt securities, we may not consolidate with or merge into any other person, in a transaction in which we are not the surviving corporation, or convey, transfer or lease our properties and assets substantially as an entirety to any person, in either case, unless:

- the successor entity, if any, is a U.S. corporation, limited liability company, partnership or trust;
- the successor entity assumes our obligations on the senior debt securities and under the senior indenture;
- immediately after giving effect to the transaction, no default or event of default shall have occurred and be continuing; and
- we have delivered to the senior trustee an officer's certificate and an opinion of counsel, each stating that the consolidation, merger, conveyance, transfer or lease and, if a supplemental indenture is required in connection with such transaction, such supplemental indenture, comply with the senior indenture and all conditions precedent provided for in the senior indenture relating to such transaction have been complied with.

The restrictions described in the bullets above do not apply (1) to our consolidation with or merging into one of our affiliates, if our board of directors determines in good faith that the purpose of the consolidation or merger is principally to change our state of incorporation or our form of organization to another form or (2) if we merge with or into a single direct or indirect wholly-owned subsidiary of ours.

The surviving business entity will succeed to, and be substituted for, us under the senior indenture and the senior debt securities and, except in the case of a lease, we shall be released from all obligations under the senior indenture and the senior debt securities.

No Protection in the Event of a Change in Control. Unless we indicate otherwise in a prospectus supplement with respect to a particular series of senior debt securities, the senior debt securities will not contain any provisions that may afford holders of the senior debt securities protection in the event we have a change in control or in the event of a highly leveraged transaction (whether or not such transaction results in a change in control).

Table of Contents

Events of Default. Unless we indicate otherwise in a prospectus supplement with respect to a particular series of senior debt securities, the following are events of default under the senior indenture with respect to senior debt securities of each series:

- failure to pay interest on any senior debt securities of such series when due and payable, if that default continues for a period of 30 days (or such other period as may be specified for such series);
- failure to pay principal on the senior debt securities of such series when due and payable whether at maturity, upon redemption, by declaration or otherwise (and, if specified for such series, the continuance of such failure for a specified period);
- default in the performance of or breach of any of our covenants or agreements in the senior indenture applicable to senior debt securities of such series, other than a covenant breach which is specifically dealt with elsewhere in the senior indenture, and that default or breach continues for a period of 90 days after we receive written notice from the trustee or from the holders of 25% or more in aggregate principal amount of the senior debt securities of such series;
- certain events of bankruptcy or insolvency, whether or not voluntary; and
- any other event of default provided for in such series of senior debt securities as may be specified in the applicable prospectus supplement.

Unless we indicate otherwise in a prospectus supplement with respect to a particular series of senior debt securities, the default by us under any other debt, including any other series of debt securities, is not a default under the senior indenture.

If an event of default other than an event of default specified in the fourth bullet point above occurs with respect to a series of senior debt securities and is continuing under the senior indenture, then, and in each such case, either the trustee or the holders of not less than 25% in aggregate principal amount of such series then outstanding under the senior indenture (each such series voting as a separate class) by written notice to us and to the trustee, if such notice is given by the holders, may, and the trustee at the request of such holders shall, declare the principal amount of and accrued interest on such series of senior debt securities to be immediately due and payable, and upon this declaration, the same shall become immediately due and payable.

If an event of default specified in the fourth bullet point above occurs and is continuing, the entire principal amount of and accrued interest on each series of senior debt securities then outstanding shall automatically become immediately due and payable.

Unless otherwise specified in the prospectus supplement relating to a series of senior debt securities originally issued at a discount, the amount due upon acceleration shall include only the original issue price of the senior debt securities, the amount of original issue discount accrued to the date of acceleration and accrued interest, if any.

Upon certain conditions, declarations of acceleration may be rescinded and annulled and past defaults may be waived by the holders of a majority in aggregate principal amount of all the senior debt securities of such series affected by the default, each series voting as a separate class. Furthermore, subject to various provisions in the senior indenture, the holders of a majority in aggregate principal amount of a series of senior debt securities, by notice to the trustee, may waive a continuing default or event of default with respect to such senior debt securities and its consequences, except a default in the payment of principal of or interest on such senior debt securities (other than any such default in payment resulting solely from an acceleration of the senior debt securities) or in respect of a covenant or provision of the senior indenture which cannot be modified or amended without the consent of the holders of each such senior debt security. Upon any such waiver, such default shall cease to exist, and any event of default with respect to such senior debt securities shall be deemed to have been cured, for every purpose of the senior indenture; but no such waiver shall extend to any subsequent or other default or event of default or impair any right consequent thereto.

Table of Contents

The holders of a majority in aggregate principal amount of a series of senior debt securities may direct the time, method and place of conducting any proceeding for any remedy available to the trustee or exercising any trust or power conferred on the trustee with respect to such senior debt securities. However, the trustee may refuse to follow any direction that conflicts with law or the senior indenture, that may involve the trustee in personal liability or that the trustee determines in good faith may be unduly prejudicial to the rights of holders of such series of senior debt securities not joining in the giving of such direction and may take any other action it deems proper that is not inconsistent with any such direction received from holders of such series of senior debt securities. A holder may not pursue any remedy with respect to the senior indenture or any series of senior debt securities unless:

- the holder gives the trustee written notice of a continuing event of default;
- the holders of at least 25% in aggregate principal amount of such series of senior debt securities make a written request to the trustee to pursue the remedy in respect of such event of default;
- the requesting holder or holders offer the trustee indemnity satisfactory to the trustee against any costs, liability or expense;
- the trustee does not comply with the request within 60 days after receipt of the request and the offer of indemnity; and
- during such 60-day period, the holders of a majority in aggregate principal amount of such series of senior debt securities do not give the trustee a direction that is inconsistent with the request.

These limitations, however, do not apply to the right of any holder of a senior debt security of any affected series to receive payment of the principal of and interest on such senior debt security in accordance with the terms of such debt security, or to bring suit for the enforcement of any such payment in accordance with the terms of such debt security, on or after the due date for the senior debt securities, which right shall not be impaired or affected without the consent of the holder.

The senior indenture requires certain of our officers to certify, on or before a fixed date in each year in which any senior debt security is outstanding, as to their knowledge of our compliance with all covenants, agreements and conditions under the senior indenture.

Satisfaction and Discharge. We can satisfy and discharge our obligations to holders of any series of debt securities if:

- we have paid or caused to be paid the principal of and interest on all senior debt securities of such series (with certain limited exceptions) when due and payable; or
- we deliver to the senior trustee for cancellation all senior debt securities of such series theretofore authenticated under the senior indenture (with certain limited exceptions); or
- all senior debt securities of such series have become due and payable or will become due and payable within one year (or are to be called for redemption within one year under arrangements satisfactory to the senior trustee) and we deposit in trust an amount of cash or a combination of cash and U.S. government or U.S. government agency obligations (or in the case of senior debt securities denominated in a foreign currency, foreign government securities or foreign government agency securities) sufficient to make interest, principal and any other payments on the debt securities of that series on their various due dates;

and if, in any such case, we also pay or cause to be paid all other sums payable under the senior indenture, as and when the same shall be due and payable and we deliver to the senior trustee an officer's certificate and an opinion of counsel, each stating that these conditions have been satisfied.

Under current U.S. federal income tax law, the deposit and our legal release from the debt securities would be treated as though we took back your debt securities and gave you your share of the cash and debt securities or

Table of Contents

bonds deposited in trust. In that event, you could recognize gain or loss on the debt securities you give back to us. Purchasers of the debt securities should consult their own advisers with respect to the tax consequences to them of such deposit and discharge, including the applicability and effect of tax laws other than the U.S. federal income tax law.

Defeasance. Unless the applicable prospectus supplement provides otherwise, the following discussion of legal defeasance and covenant defeasance will apply to any series of debt securities issued under the indentures.

Legal Defeasance. We can legally release ourselves from any payment or other obligations on the debt securities of any series (called “legal defeasance”) if certain conditions are met, including the following:

- We deposit in trust for your benefit and the benefit of all other direct holders of the debt securities of the same series cash or a combination of cash and U.S. government or U.S. government agency obligations (or, in the case of senior debt securities denominated in a foreign currency, foreign government or foreign government agency obligations) that will generate enough cash to make interest, principal and any other payments on the debt securities of that series on their various due dates.
- There is a change in current U.S. federal income tax law or an IRS ruling that lets us make the above deposit without causing you to be taxed on the debt securities any differently than if we did not make the deposit and instead repaid the debt securities ourselves when due. Under current U.S. federal income tax law, the deposit and our legal release from the debt securities would be treated as though we took back your debt securities and gave you your share of the cash and debt securities or bonds deposited in trust. In that event, you could recognize gain or loss on the debt securities you give back to us.
- We deliver to the trustee a legal opinion of our counsel confirming the tax law change or ruling described above.

If we accomplish legal defeasance, as described above, you would have to rely solely on the trust deposit for repayment of the debt securities. You could not look to us for repayment in the event of any shortfall.

Covenant Defeasance. Without any change in current U.S. federal tax law, we can make the same type of deposit described above and be released from some of the covenants in the debt securities (called “covenant defeasance”). In that event, you would lose the protection of those covenants but would gain the protection of having money and securities set aside in trust to repay the debt securities. In order to achieve covenant defeasance, we must do the following (among other things):

- deposit in trust for your benefit and the benefit of all other direct holders of the debt securities of the same series cash or a combination of cash and U.S. government or U.S. government agency obligations (or, in the case of senior debt securities denominated in a foreign currency, foreign government or foreign government agency obligations) that will generate enough cash to make interest, principal and any other payments on the debt securities of that series on their various due dates.
- deliver to the trustee a legal opinion of our counsel confirming that under current U.S. federal income tax law we may make the above deposit without causing you to be taxed on the debt securities any differently than if we did not make the deposit and instead repaid the debt securities ourselves when due.

If we accomplish covenant defeasance, you could still look to us for repayment of the debt securities if there were a shortfall in the trust deposit. In fact, if one of the events of default occurred (such as our bankruptcy) and the debt securities become immediately due and payable, there may be such a shortfall. Depending on the events causing the default, you may not be able to obtain payment of the shortfall.

Table of Contents

Modification and Waiver. We and the trustee may amend or supplement the senior indenture or the senior debt securities of any series without the consent of any holder:

- to convey, transfer, assign, mortgage or pledge any assets as security for the senior debt securities of one or more series;
- to evidence the succession of a corporation, limited liability company, partnership or trust to us, and the assumption by such successor of our covenants, agreements and obligations under the senior indenture or to otherwise comply with the covenant relating to mergers, consolidations and sales of assets;
- to comply with the requirements of the SEC in order to effect or maintain the qualification of the senior indenture under the Trust Indenture Act of 1939, as amended, or the Trust Indenture Act;
- to add to our covenants such new covenants, restrictions, conditions or provisions for the protection of the holders, and to make the occurrence, or the occurrence and continuance, of a default in any such additional covenants, restrictions, conditions or provisions an event of default;
- to cure any ambiguity, defect or inconsistency in the senior indenture or in any supplemental indenture or to conform the senior indenture or the senior debt securities to the description of senior debt securities of such series set forth in this prospectus or any applicable prospectus supplement;
- to provide for or add guarantors with respect to the senior debt securities of any series;
- to establish the form or forms or terms of the senior debt securities as permitted by the senior indenture;
- to evidence and provide for the acceptance of appointment under the senior indenture by a successor trustee, or to make such changes as shall be necessary to provide for or facilitate the administration of the trusts in the senior indenture by more than one trustee;
- to add to, change or eliminate any of the provisions of the senior indenture in respect of one or more series of senior debt securities, provided that any such addition, change or elimination shall (a) neither (1) apply to any senior debt security of any series created prior to the execution of such supplemental indenture and entitled to the benefit of such provision nor (2) modify the rights of the holder of any such senior debt security with respect to such provision or (b) become effective only when there is no senior debt security described in clause (a)(1) outstanding;
- to make any change to the senior debt securities of any series so long as no senior debt securities of such series are outstanding; or
- to make any change that does not adversely affect the rights of any holder in any material respect.

Other amendments and modifications of the senior indenture or the senior debt securities issued may be made, and our compliance with any provision of the senior indenture with respect to any series of senior debt securities may be waived, with the consent of the holders of a majority of the aggregate principal amount of the outstanding senior debt securities of each series affected by the amendment or modification (voting as separate series); provided, however, that each affected holder must consent to any modification, amendment or waiver that:

- extends the final maturity of any senior debt securities of such series;
- reduces the principal amount of any senior debt securities of such series;
- reduces the rate, or extends the time for payment of, interest on any senior debt securities of such series;
- reduces the amount payable upon the redemption of any senior debt securities of such series;
- changes the currency of payment of principal of or interest on any senior debt securities of such series;

Table of Contents

- reduces the principal amount of original issue discount securities payable upon acceleration of maturity or the amount provable in bankruptcy;
- waives a continuing default in the payment of principal of or interest on the senior debt securities (other than any such default in payment resulting solely from an acceleration of the senior debt securities);
- changes the provisions relating to the waiver of past defaults or impairs the right of holders to receive payment or to institute suit for the enforcement of any payment or conversion of any senior debt securities of such series on or after the due date therefor;
- modifies any of the provisions of these restrictions on amendments and modifications, except to increase any required percentage or to provide that certain other provisions cannot be modified or waived without the consent of the holder of each senior debt security of such series affected by the modification;
- adversely affects the right to convert or exchange senior debt securities into common stock or other property in accordance with the terms of the senior debt securities; or
- reduces the above-stated percentage of outstanding senior debt securities of such series whose holders must consent to a supplemental indenture or modifies or amends or waives certain provisions of or defaults under the senior indenture.

It shall not be necessary for the holders to approve the particular form of any proposed amendment, supplement or waiver, but it shall be sufficient if the holders' consent approves the substance thereof. After an amendment, supplement or waiver of the senior indenture in accordance with the provisions described in this section becomes effective, the trustee must give to the holders affected thereby certain notice briefly describing the amendment, supplement or waiver. Any failure by the trustee to give such notice, or any defect therein, shall not, however, in any way impair or affect the validity of any such amendment, supplemental indenture or waiver.

Notice of Redemption. Notice of any redemption of senior debt securities will be mailed at least 10 days but not more than 60 days before the redemption date to each holder of senior debt securities of a series to be redeemed. Any notice may, at our discretion, be subject to the satisfaction or waiver of one or more conditions precedent. In that case, such notice shall state the nature of such condition precedent. If we elect to redeem a portion but not all of such senior debt securities, the trustee will select the senior debt securities to be redeemed in a manner that complies with applicable legal and stock exchange requirements, if any. Interest on such debt securities or portions of senior debt securities will cease to accrue on and after the date fixed for redemption, unless we default in the payment of such redemption price and accrued interest with respect to any such senior debt security or portion thereof.

If any date of redemption of any senior debt security is not a business day, then payment of principal and interest may be made on the next succeeding business day with the same force and effect as if made on the nominal date of redemption and no interest will accrue for the period after such nominal date.

Conversion Rights. We will describe the terms upon which senior debt securities may be convertible into our common stock or other securities in a prospectus supplement. These terms will include the type of securities the senior debt securities are convertible into, the conversion price or manner of calculation thereof, the conversion period, provisions as to whether conversion will be at our option or the option of the holders, the events requiring an adjustment of the conversion price and provisions affecting conversion in the event of the redemption of the senior debt securities and any restrictions on conversion. They may also include provisions adjusting the number of shares of our common stock or other securities issuable upon conversion.

No Personal Liability of Incorporators, Stockholders, Officers, Directors. The senior indenture provides that no recourse shall be had under any obligation, covenant or agreement of ours in the senior indenture or any

Table of Contents

supplemental indenture, or in any of the senior debt securities or because of the creation of any indebtedness represented thereby, against any of our incorporators, stockholders, officers or directors, past, present or future, or of any predecessor or successor entity thereof under any law, statute or constitutional provision or by the enforcement of any assessment or by any legal or equitable proceeding or otherwise. Each holder, by accepting the senior debt securities, waives and releases all such liability.

Concerning the Trustee. The senior indenture provides that, except during the continuance of an event of default, the trustee will not be liable except for the performance of such duties as are specifically set forth in the senior indenture. If an event of default has occurred and is continuing, the trustee will exercise such rights and powers vested in it under the senior indenture and will use the same degree of care and skill in its exercise as a prudent person would exercise under the circumstances in the conduct of such person's own affairs.

The senior indenture and the provisions of the Trust Indenture Act incorporated by reference therein contain limitations on the rights of the trustee thereunder, should it become a creditor of ours or any of our subsidiaries, to obtain payment of claims in certain cases or to realize on certain property received by it in respect of any such claims, as security or otherwise. The trustee is permitted to engage in other transactions, provided that if it acquires any conflicting interest (as defined in the Trust Indenture Act), it must eliminate such conflict or resign.

We may have normal banking relationships with the senior trustee in the ordinary course of business.

Unclaimed Funds. All funds deposited with the trustee or any paying agent for the payment of principal, premium, interest or additional amounts in respect of the senior debt securities that remain unclaimed for two years after the date upon which such amounts became due and payable will be repaid to us. Thereafter, any right of any holder of senior debt securities to such funds shall be enforceable only against us, and the trustee and paying agents will have no liability therefor.

Governing Law. The senior indenture and the senior debt securities will be governed by, and construed in accordance with, the internal laws of the State of New York.

Certain Terms of the Subordinated Debt Securities

Other than the terms of the subordinated indenture and subordinated debt securities relating to subordination or otherwise as described in the prospectus supplement relating to a particular series of subordinated debt securities, the terms of the subordinated indenture and subordinated debt securities are identical in all material respects to the terms of the senior indenture and senior debt securities.

Additional or different subordination terms may be specified in the prospectus supplement applicable to a particular series.

Subordination. The indebtedness evidenced by the subordinated debt securities is subordinate to the prior payment in full of all of our senior indebtedness, as defined in the subordinated indenture. During the continuance beyond any applicable grace period of any default in the payment of principal, premium, interest or any other payment due on any of our senior indebtedness, we may not make any payment of principal or interest on the subordinated debt securities (except for certain sinking fund payments). In addition, upon any payment or distribution of our assets upon any dissolution, winding-up, liquidation or reorganization, the payment of the principal of and interest on the subordinated debt securities will be subordinated to the extent provided in the subordinated indenture in right of payment to the prior payment in full of all our senior indebtedness. Because of this subordination, if we dissolve or otherwise liquidate, holders of our subordinated debt securities may receive less, ratably, than holders of our senior indebtedness. The subordination provisions do not prevent the occurrence of an event of default under the subordinated indenture.

Table of Contents

The term “senior indebtedness” of a person means with respect to such person the principal of, premium, if any, interest on, and any other payment due pursuant to any of the following, whether outstanding on the date of the subordinated indenture or incurred by that person in the future:

- all of the indebtedness of that person for money borrowed;
- all of the indebtedness of that person evidenced by notes, debentures, bonds or other securities sold by that person for money;
- all of the lease obligations that are capitalized on the books of that person in accordance with generally accepted accounting principles;
- all indebtedness of others of the kinds described in the first two bullet points above and all lease obligations of others of the kind described in the third bullet point above that the person, in any manner, assumes or guarantees or that the person in effect guarantees through an agreement to purchase, whether that agreement is contingent or otherwise; and
- all renewals, extensions or refundings of indebtedness of the kinds described in the first, second or fourth bullet point above and all renewals or extensions of leases of the kinds described in the third or fourth bullet point above;

unless, in the case of any particular indebtedness, renewal, extension or refunding, the instrument creating or evidencing it or the assumption or guarantee relating to it expressly provides that such indebtedness, renewal, extension or refunding is not superior in right of payment to the subordinated debt securities. Our senior debt securities constitute senior indebtedness for purposes of the subordinated indenture.

DESCRIPTION OF CAPITAL STOCK

General

Our authorized capital stock consists of 70,000,000 shares of common stock, par value \$0.001 per share, and 10,000,000 shares of preferred stock, par value \$0.001 per share. The following description of our capital stock and provisions of our restated certificate of incorporation and second amended and restated by-laws are summaries and are qualified by reference to our restated certificate of incorporation and our second amended and restated by-laws, copies of which are filed with the SEC as exhibits to our registration statement of which this prospectus forms a part.

Common Stock

Annual Meeting. Annual meetings of our stockholders are held on the date designated in accordance with our second amended and restated by-laws. Notice must be given to each stockholder entitled to vote not less than ten nor more than 60 days before the date of the meeting. The presence in person, by means of remote communication in a manner authorized by the board of directors, or by proxy of the holders of a majority in voting power of the shares of our capital stock issued and outstanding and entitled to vote at the meeting constitutes a quorum for the transaction of business at meetings of the stockholders. Special meetings of stockholders may be called at any time by the board of directors, the chair of the board of directors or our Chief Executive Officer. Business transacted at any special meeting of stockholders shall be limited to matters relating to the purpose or purposes stated in the notice of meeting.

Voting Rights. Holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of stockholders and do not have cumulative voting rights. An election of directors by our stockholders is determined by a plurality of the votes cast by the stockholders entitled to vote on the election. Other matters are decided by the affirmative vote of our stockholders having a majority in voting power of the votes cast by the stockholders present or represented and voting on such matter, except as otherwise disclosed below.

Dividends. Subject to the rights, powers and preferences of any outstanding preferred stock, and except as provided by law or in our restated certificate of incorporation, dividends may be declared and paid or set aside for payment on the common stock out of legally available assets or funds when and as declared by the board of directors. The payment of dividends is contingent upon our revenue and earnings, capital requirements, and general financial condition, as well as contractual restrictions and other considerations deemed to be relevant by our board of directors.

Liquidation. In the event of our liquidation or dissolution, the holders of common stock are entitled to receive proportionately all assets available for distribution to stockholders after the payment of all debts and other liabilities and subject to the prior rights of any outstanding preferred stock. Holders of common stock have no preemptive, subscription, redemption or conversion rights, and there are no sinking fund provisions applicable to our common stock. The rights, preferences and privileges of holders of common stock are subject to and may be adversely affected by the rights of the holders of shares of any series of preferred stock that we may designate and issue in the future.

Preferred Stock

We are authorized to issue "blank check" preferred stock, which may be issued in one or more series upon authorization of our board of directors. Our board of directors is authorized to fix the designations, powers, preferences and the relative, participating, optional or other special rights and any qualifications, limitations and restrictions of the shares of each series of preferred stock. The purpose of authorizing our board of directors to issue preferred stock and determine its rights and preferences is to eliminate delays associated with a stockholder vote on specific issuances. The authorized shares of our preferred stock are available for issuance without further

Table of Contents

action by our stockholders, unless such action is required by applicable law or the rules of any stock exchange on which our securities may be listed. If the approval of our stockholders is not required for the issuance of shares of our preferred stock, our board of directors may determine not to seek stockholder approval. The specific terms of any series of preferred stock offered pursuant to this prospectus will be described in the prospectus supplement relating to that series of preferred stock.

A series of our preferred stock could, depending on the terms of such series, impede the completion of a merger, tender offer or other takeover attempt. Our board of directors will make any determination to issue preferred shares based upon its judgment as to the best interests of our stockholders. Our directors, in so acting, could issue preferred stock having terms that could discourage an acquisition attempt through which an acquirer may be able to change the composition of our board of directors, including a tender offer or other transaction that some, or a majority, of our stockholders might believe to be in their best interests or in which stockholders might receive a premium for their stock over the then-current market price of the stock. There are no shares of preferred stock currently outstanding.

Any preferred stock offered pursuant to this prospectus will have the terms described below unless otherwise provided in the prospectus supplement relating to a particular series of preferred stock. You should read the prospectus supplement relating to the particular series of preferred stock being offered for specific terms, including:

- the designation and stated value per share of the preferred stock and the number of shares offered;
- the amount of liquidation preference per share;
- the price at which the preferred stock will be issued;
- the dividend rate, or method of calculation of dividends, the dates on which dividends will be payable, whether dividends will be cumulative or noncumulative and, if cumulative, the dates from which dividends will commence to accumulate;
- any redemption or sinking fund provisions;
- if other than the currency of the United States, the currency or currencies including composite currencies in which the preferred stock is denominated and/or in which payments will or may be payable;
- any conversion provisions; and
- any other rights, preferences, privileges, limitations and restrictions on the preferred stock.

The preferred stock will, when issued, be fully paid and non-assessable. Unless otherwise specified in the prospectus supplement, each series of preferred stock will rank equally as to dividends and liquidation rights in all respects with each other series of preferred stock. The rights of holders of shares of each series of preferred stock will be subordinate to those of our general creditors.

Rank. Unless otherwise specified in the prospectus supplement, the preferred stock will, with respect to dividend rights and rights upon our liquidation, dissolution or winding up of our affairs, rank:

- senior to our common stock and to all equity securities ranking junior to such preferred stock with respect to dividend rights or rights upon our liquidation, dissolution or winding up of our affairs;
- on a parity with all equity securities issued by us, the terms of which specifically provide that such equity securities rank on a parity with the preferred stock with respect to dividend rights or rights upon our liquidation, dissolution or winding up of our affairs; and
- junior to all equity securities issued by us, the terms of which specifically provide that such equity securities rank senior to the preferred stock with respect to dividend rights or rights upon our liquidation, dissolution or winding up of our affairs.

Table of Contents

The term “equity securities” does not include convertible debt securities.

Dividends. Holders of preferred stock of each series will be entitled to receive, when, as and if declared by our board of directors, cash dividends at such rates and on such dates described in the prospectus supplement. Different series of preferred stock may be entitled to dividends at different rates or based on different methods of calculation. The dividend rate may be fixed or variable or both. Dividends will be payable to the holders of record as they appear on our stock books on record dates fixed by our board of directors, as specified in the applicable prospectus supplement.

Dividends on any series of preferred stock may be cumulative or noncumulative, as described in the applicable prospectus supplement. If our board of directors does not declare a dividend payable on a dividend payment date on any series of noncumulative preferred stock, then the holders of that noncumulative preferred stock will have no right to receive a dividend for that dividend payment date, and we will have no obligation to pay the dividend accrued for that period, whether or not dividends on that series are declared payable on any future dividend payment dates. Dividends on any series of cumulative preferred stock will accrue from the date we initially issue shares of such series or such other date specified in the applicable prospectus supplement.

No dividends may be declared or paid or funds set apart for the payment of any dividends on any parity securities unless full dividends have been paid or set apart for payment on the preferred stock. If full dividends are not paid, the preferred stock will share dividends pro rata with the parity securities.

No dividends may be declared or paid or funds set apart for the payment of dividends on any junior securities unless full dividends for all dividend periods terminating on or prior to the date of the declaration or payment will have been paid or declared and a sum sufficient for the payment set apart for payment on the preferred stock.

Liquidation Preference. Upon any voluntary or involuntary liquidation, dissolution or winding up of our affairs, then, before we make any distribution or payment to the holders of any common stock or any other class or series of our capital stock ranking junior to the preferred stock in the distribution of assets upon any liquidation, dissolution or winding up of our affairs, the holders of each series of preferred stock shall be entitled to receive out of assets legally available for distribution to stockholders, liquidating distributions in the amount of the liquidation preference per share set forth in the prospectus supplement, plus any accrued and unpaid dividends thereon. Such dividends will not include any accumulation in respect of unpaid noncumulative dividends for prior dividend periods. Unless otherwise specified in the prospectus supplement, after payment of the full amount of their liquidating distributions, the holders of preferred stock will have no right or claim to any of our remaining assets. Upon any such voluntary or involuntary liquidation, dissolution or winding up, if our available assets are insufficient to pay the amount of the liquidating distributions on all outstanding preferred stock and the corresponding amounts payable on all other classes or series of our capital stock ranking on parity with the preferred stock and all other such classes or series of shares of capital stock ranking on parity with the preferred stock in the distribution of assets, then the holders of the preferred stock and all other such classes or series of capital stock ranking on parity with the preferred stock will share ratably in any such distribution of assets in proportion to the full liquidating distributions to which they would otherwise be entitled.

Upon any such liquidation, dissolution or winding up and if we have made liquidating distributions in full to all holders of preferred stock, we will distribute our remaining assets among the holders of any other classes or series of capital stock ranking junior to the preferred stock according to their respective rights and preferences and, in each case, according to their respective number of shares. For such purposes, our consolidation or merger with or into any other corporation, trust or entity, or the sale, lease or conveyance of all or substantially all of our property or assets will not be deemed to constitute a liquidation, dissolution or winding up of our affairs.

Redemption. If so provided in the applicable prospectus supplement, the preferred stock will be subject to mandatory redemption or redemption at our option, as a whole or in part, in each case upon the terms, at the times and at the redemption prices set forth in such prospectus supplement.

Table of Contents

The prospectus supplement relating to a series of preferred stock that is subject to mandatory redemption will specify the number of shares of preferred stock that shall be redeemed by us in each year commencing after a date to be specified, at a redemption price per share to be specified, together with an amount equal to all accrued and unpaid dividends thereon to the date of redemption. Unless the shares have a cumulative dividend, such accrued dividends will not include any accumulation in respect of unpaid dividends for prior dividend periods. We may pay the redemption price in cash or other property, as specified in the applicable prospectus supplement. If the redemption price for preferred stock of any series is payable only from the net proceeds of the issuance of shares of our capital stock, the terms of such preferred stock may provide that, if no such shares of our capital stock shall have been issued or to the extent the net proceeds from any issuance are insufficient to pay in full the aggregate redemption price then due, such preferred stock shall automatically and mandatorily be converted into the applicable shares of our capital stock pursuant to conversion provisions specified in the applicable prospectus supplement.

Notwithstanding the foregoing, we will not redeem any preferred stock of a series unless:

- if that series of preferred stock has a cumulative dividend, we have declared and paid or contemporaneously declare and pay or set aside funds to pay full cumulative dividends on the preferred stock for all past dividend periods and the then current dividend period; or
- if such series of preferred stock does not have a cumulative dividend, we have declared and paid or contemporaneously declare and pay or set aside funds to pay full dividends for the then current dividend period.

In addition, we will not acquire any preferred stock of a series unless:

- if that series of preferred stock has a cumulative dividend, we have declared and paid or contemporaneously declare and pay or set aside funds to pay full cumulative dividends on all outstanding shares of such series of preferred stock for all past dividend periods and the then current dividend period; or
- if that series of preferred stock does not have a cumulative dividend, we have declared and paid or contemporaneously declare and pay or set aside funds to pay full dividends on the preferred stock of such series for the then current dividend period.

However, at any time we may purchase or acquire preferred stock of that series (1) pursuant to a purchase or exchange offer made on the same terms to holders of all outstanding preferred stock of such series or (2) by conversion into or exchange for shares of our capital stock ranking junior to the preferred stock of such series as to dividends and upon liquidation.

If fewer than all of the outstanding shares of preferred stock of any series are to be redeemed, we will determine the number of shares that may be redeemed pro rata from the holders of record of such shares in proportion to the number of such shares held or for which redemption is requested by such holder or by any other equitable manner that we determine. Such determination will reflect adjustments to avoid redemption of fractional shares.

Unless otherwise specified in the prospectus supplement, we will mail notice of redemption at least 10 days but not more than 60 days before the redemption date to each holder of record of preferred stock to be redeemed at the address shown on our stock transfer books. Each notice shall state:

- the redemption date;
- the number of shares and series of preferred stock to be redeemed;
- the redemption price;
- the place or places where certificates for such preferred stock are to be surrendered for payment of the redemption price;

Table of Contents

- that dividends on the shares to be redeemed will cease to accrue on such redemption date;
- the date on which the holder's conversion rights, if any, as to such shares shall terminate; and
- the specific number of shares to be redeemed from each such holder if fewer than all the shares of any series are to be redeemed.

If notice of redemption has been given and we have set aside the funds necessary for such redemption in trust for the benefit of the holders of any shares called for redemption, then from and after the redemption date, dividends will cease to accrue on such shares, and all rights of the holders of such shares will terminate, except the right to receive the redemption price.

Voting Rights. Holders of preferred stock will not have any voting rights, except as required by law or as indicated in the applicable prospectus supplement.

Unless otherwise provided for under the terms of any series of preferred stock, no consent or vote of the holders of shares of preferred stock or any series thereof shall be required for any amendment to our restated certificate of incorporation that would increase the number of authorized shares of preferred stock or the number of authorized shares of any series thereof or decrease the number of authorized shares of preferred stock or the number of authorized shares of any series thereof (but not below the number of authorized shares of preferred stock or such series, as the case may be, then outstanding).

Conversion Rights. The terms and conditions, if any, upon which any series of preferred stock is convertible into shares of our common stock will be set forth in the applicable prospectus supplement relating thereto. Such terms will include the number of shares of common stock into which the shares of preferred stock are convertible, the conversion price, rate or manner of calculation thereof, the conversion period, provisions as to whether conversion will be at our option or at the option of the holders of the preferred stock, the events requiring an adjustment of the conversion price and provisions affecting conversion in the event of the redemption.

Transfer Agent and Registrar. The transfer agent and registrar for the preferred stock will be set forth in the applicable prospectus supplement.

Registration Rights

As further described below, we have entered into three registration rights agreements with certain holders of our common stock, warrants and pre-funded warrants. These holders have the right to require us to register their shares under the Securities Act under specified circumstances. We refer to the shares with these registration rights as registrable securities. After registration pursuant to these rights, as further described below, the registrable securities became freely tradable without restriction under the Securities Act.

Subject to the terms of the respective registration rights agreements, the registration rights agreements contain customary cross-indemnification provisions, pursuant to which we are obligated to indemnify the selling stockholders in the event of material misstatements or omissions in the registration statement attributable to us or any violation or alleged violation whether by action or inaction by us under the Securities Act, the Exchange Act, any state securities law or any rule or regulation promulgated under the Securities Act, the Exchange Act or any state securities law in connection with such registration statement or the qualification or compliance of the offering, and they are obligated to indemnify us for material misstatements or omissions in the registration statement attributable to them.

December 2020 Registration Rights Agreement

On December 4, 2020, in connection with a private placement of our securities, we entered into a registration rights agreement with certain holders of our common stock, warrants and pre-funded warrants. Pursuant to the

Table of Contents

terms of this registration rights agreement, we agreed to file a registration statement within 30 days following the closing of the private placement covering (i) the resale of the shares of our common stock issued in the private placement and (ii) the issuance of the shares of common stock underlying the warrants and pre-funded warrants issued in the private placement. We also agreed to use commercially reasonable efforts to cause such registration statement to become effective as soon as practicable and to keep such registration statement effective until the date the registrable securities covered by such registration statement have been sold or may be resold pursuant to Rule 144 under the Securities Act, or Rule 144, without restriction. We agreed to be responsible for all fees and expenses incurred in connection with the registration of the registrable securities. On January 7, 2021, we filed a Registration Statement on Form S-3 in connection with the registrable securities issued in this private placement, which was declared effective on January 19, 2021.

July 2022 Registration Rights Agreement and Affiliate Registration Rights Agreement

On July 3, 2022, in connection with a private placement of our securities, we entered into a registration rights agreement with certain holders of our common stock, warrants and pre-funded warrants. Pursuant to the terms of this registration rights agreement, we agreed to file a registration statement within 30 days following the closing of the private placement covering (i) the resale of the shares of our common stock issued in the private placement and (ii) the issuance of the shares of common stock underlying the warrants and pre-funded warrants issued in the private placement. We also agreed to use commercially reasonable efforts to cause such registration statement to become effective as soon as practicable and to keep such registration statement effective until the date the registrable securities covered by such registration statement have been sold or may be resold pursuant to Rule 144 without restriction. We agreed to be responsible for all fees and expenses incurred in connection with the registration of the registrable securities.

Also on July 3, 2022, in connection with a private placement of our securities, we entered into an affiliate registration rights agreement with Baker Brothers Life Sciences, L.P. and 667, L.P., which we refer to as the Baker Funds. Pursuant to the terms of this affiliate registration rights agreement, following a request by the Baker Funds, we are obligated to file a resale registration statement on Form S-3, or other appropriate form, covering the issuance of the shares of common stock underlying the warrants and pre-funded warrants issued to the Baker Funds in the private placement. We agreed to file such resale registration statement as promptly as reasonably practicable following such request, and in any event within sixty (60) days of such request. Our obligations to file such registration statement were subject to specified exceptions, and suspension and deferral rights as set forth in this affiliate registration rights agreement. Under specified circumstances, we were permitted to include securities of ours in any such registration statement. Under this affiliate registration rights agreement, the Baker Funds also had the right to one underwritten offering per calendar year, but no more than three underwritten offerings in total and not more than two underwritten offerings or “block trades” in any twelve month period, to effect the sale or distribution of the registrable securities, subject to specified exceptions, conditions and limitations.

On October 14, 2022, we filed a Registration Statement on Form S-3 in connection with the registrable securities issued in this private placement and on December 1, 2022, we filed an amendment to this registration statement, which was declared effective on December 22, 2022.

Anti-Takeover Effects of Delaware Law and Our Charter and By-laws

Delaware law and our restated certificate of incorporation and our second amended and restated by-laws contain provisions that could have the effect of delaying, deferring or discouraging another party from acquiring control of us. These provisions, which are summarized below, are expected to discourage coercive takeover practices and inadequate takeover bids. These provisions are also designed to encourage persons seeking to acquire control of us to first negotiate with our board of directors.

Staggered Board; Removal of Directors

Our restated certificate of incorporation and our second amended and restated by-laws divide our board of directors into three classes with staggered three-year terms. In addition, a director may only be removed for cause and only by the affirmative vote of the holders of at least 75% of the votes that all of our stockholders would be entitled to cast in an annual election of directors. Any vacancy on our board of directors, including a vacancy resulting from an enlargement of our board of directors, may only be filled by vote of a majority of our directors then in office. The classification of our board of directors and the limitations on the removal of directors and filling of vacancies could make it more difficult for a third party to acquire, or discourage a third party from seeking to acquire, control of our company.

Stockholder Action by Written Consent; Special Meetings

Our restated certificate of incorporation provides that any action required or permitted to be taken by our stockholders must be effected at a duly called annual or special meeting of such holders and may not be effected by any consent in writing by such holders. Our restated certificate of incorporation and our second amended and restated by-laws also provide that, except as otherwise required by law, special meetings of our stockholders can only be called by our chairman of the board, our chief executive officer or our board of directors.

Advance Notice Requirements for Stockholder Proposals

Our second amended and restated by-laws establish an advance notice procedure for stockholder proposals to be brought before an annual meeting of stockholders, including proposed nominations of persons for election to our board of directors. Stockholders at an annual meeting may only consider proposals or nominations specified in the notice of meeting or brought before the meeting by or at the direction of our board of directors or by a stockholder of record on the record date for the meeting who is entitled to vote at the meeting and who has delivered timely written notice in proper form to our secretary of the stockholder's intention to bring such business before the meeting. These provisions could have the effect of delaying until the next stockholder meeting stockholder actions that are favored by the holders of a majority of our outstanding voting securities.

Exclusive Forum Selection

Our second amended and restated by-laws provide that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware (or, if the Court of Chancery of the State of Delaware does not have jurisdiction, the federal district court for the District of Delaware) shall, to the fullest extent permitted by law, be the sole and exclusive forum for (1) any derivative action or proceeding brought on our behalf, (2) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers, other employees or stockholders to our company or our stockholders, (3) any action asserting a claim arising pursuant to any provision of the General Corporation Law of the State of Delaware, or the DGCL, or as to which the DGCL confers jurisdiction on the Court of Chancery of the State of Delaware or (4) any action asserting a claim arising pursuant to any provision of our restated certificate of incorporation or second amended and restated by-laws (in each case, as they may be amended from time to time) or governed by the internal affairs doctrine. This choice of forum provision will not apply to actions arising under the Securities Act, the Exchange Act or any other claim for which the federal courts have exclusive jurisdiction. Unless we consent in writing to the selection of an alternative forum, the federal district courts of the United States of America shall, to the fullest extent permitted by law, be the sole and exclusive forum for the resolution of any claims arising under the Securities Act. Although our second amended and restated by-laws contain the choice of forum provisions described above, it is possible that a court could rule that such a provision is inapplicable for a particular claim or action or that such provision is unenforceable.

Delaware Business Combination Statute

We are subject to Section 203 of the DGCL. Subject to certain exceptions, Section 203 prevents a publicly held Delaware corporation from engaging in a "business combination" with any "interested stockholder" for three

Table of Contents

years following the date that the person became an interested stockholder, unless the interested stockholder attained such status with the approval of our board of directors or unless the business combination is approved in a prescribed manner. A “business combination” includes, among other things, a merger or consolidation involving us and the “interested stockholder” and a sale involving us and the “interested stockholder” of 10% or more of our assets. In general, an “interested stockholder” is any entity or person beneficially owning 15% or more of our outstanding voting stock and any entity or person affiliated with or controlling or controlled by such entity or person.

Amendment of Certificate of Incorporation and By-laws

The DGCL provides generally that the affirmative vote of a majority of the shares entitled to vote on any matter is required to amend a corporation’s certificate of incorporation or by-laws, unless a corporation’s certificate of incorporation or by-laws, as the case may be, requires a greater percentage. Our second amended and restated by-laws may be amended or repealed by a majority vote of our board of directors or by the affirmative vote of the holders of at least 75% of the votes that all of our stockholders would be entitled to cast in any annual election of directors. In addition, the affirmative vote of the holders of at least 75% of the votes that all of our stockholders would be entitled to cast in any annual election of directors is required to amend or repeal or to adopt any provisions inconsistent with any of the provisions of our restated certificate of incorporation described above under “—Staggered Board; Removal of Directors” and “—Stockholder Action by Written Consent; Special Meetings.”

Listing on The Nasdaq Global Select Market

Our common stock is listed on The Nasdaq Global Select Market under the symbol “SYRS.”

Authorized but Unissued Shares

The authorized but unissued shares of our common stock and preferred stock are available for future issuance without stockholder approval, subject to any limitations imposed by the listing requirements of The Nasdaq Global Select Market. These additional shares may be used for a variety of corporate finance transactions, acquisitions and employee benefit plans. The existence of authorized but unissued and unreserved common stock and preferred stock could make it more difficult or discourage an attempt to obtain control of us by means of a proxy contest, tender offer, merger or otherwise.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Computershare Trust Company, N.A.

DESCRIPTION OF WARRANTS

We may issue warrants to purchase common stock, preferred stock or debt securities. We may offer warrants separately or together with one or more additional warrants, common stock, preferred stock or debt securities, or any combination of those securities in the form of units, as described in the applicable prospectus supplement. If we issue warrants as part of a unit, the accompanying prospectus supplement will specify whether those warrants may be separated from the other securities in the unit prior to the expiration date of the warrants. The applicable prospectus supplement will also describe the following terms of any warrants:

- the specific designation and aggregate number of, and the offering price at which we will issue, the warrants;
- the currency or currency units in which the offering price, if any, and the exercise price are payable;
- the date on which the right to exercise the warrants will begin and the date on which that right will expire or, if you may not continuously exercise the warrants throughout that period, the specific date or dates on which you may exercise the warrants;
- whether the warrants are to be sold separately or with other securities as parts of units;
- whether the warrants will be issued in definitive or global form or in any combination of these forms, although, in any case, the form of a warrant included in a unit will correspond to the form of the unit and of any security included in that unit;
- any applicable material U.S. federal income tax consequences;
- the identity of the warrant agent for the warrants and of any other depositaries, execution or paying agents, transfer agents, registrars or other agents;
- the proposed listing, if any, of the warrants or any securities purchasable upon exercise of the warrants on any securities exchange;
- the designation and terms of any equity securities purchasable upon exercise of the warrants;
- the designation, aggregate principal amount, currency and terms of any debt securities that may be purchased upon exercise of the warrants;
- if applicable, the designation and terms of the preferred stock with which the warrants are issued and the number of warrants issued with each security;
- if applicable, the date from and after which any warrants issued as part of a unit and the related debt securities, preferred stock or common stock will be separately transferable;
- the number of shares of common stock or preferred stock purchasable upon exercise of a warrant and the price at which those shares may be purchased;
- if applicable, the minimum or maximum amount of the warrants that may be exercised at any one time;
- information with respect to book-entry procedures, if any;
- the anti-dilution provisions of, and other provisions for changes to or adjustment in the exercise price of, the warrants, if any;
- any redemption or call provisions; and
- any additional terms of the warrants, including terms, procedures and limitations relating to the exchange or exercise of the warrants.

DESCRIPTION OF UNITS

We may issue units consisting of one or more of the other securities described in this prospectus in any combination, as described in the applicable prospectus supplement. We may issue units in one or more series, which will be described in the applicable prospectus supplement. The applicable prospectus supplement will also describe the following terms of any units:

- the designation and the terms of the units and of the securities constituting the units, including whether and under what circumstances the securities comprising the units may be traded separately;
- the identity of any unit agent for the units, if applicable, and of any other depositaries, execution or paying agents, transfer agents, registrars or other agents;
- any additional terms of the governing unit agreement, if applicable;
- any additional provisions for the issuance, payment, settlement, transfer or exchange of the units or of the debt securities, common stock, preferred stock, purchase contracts or warrants constituting the units; and
- any applicable material U.S. federal income tax consequences.

FORMS OF SECURITIES

Each debt security, unit and warrant will be represented either by a certificate issued in definitive form to a particular investor or by one or more global securities representing the entire issuance of securities. Unless the applicable prospectus supplement provides otherwise, certificated securities in definitive form and global securities will be issued in registered form. Definitive securities name you or your nominee as the owner of the security, and in order to transfer or exchange these securities or to receive payments other than interest or other interim payments, you or your nominee must physically deliver the securities to the trustee, registrar, paying agent or other agent, as applicable. Global securities name a depositary or its nominee as the owner of the debt securities, units or warrants represented by these global securities. The depositary maintains a computerized system that will reflect each investor's beneficial ownership of the securities through an account maintained by the investor with its broker/dealer, bank, trust company or other representative, as we explain more fully below.

Global Securities

We may issue the debt securities of a particular series, units and warrants in the form of one or more fully registered global securities that will be deposited with a depositary or its nominee identified in the applicable prospectus supplement and registered in the name of that depositary or nominee. In those cases, one or more global securities will be issued in a denomination or aggregate denominations equal to the portion of the aggregate principal or face amount of the securities to be represented by global securities. Unless and until it is exchanged in whole for securities in definitive registered form, a global security may not be transferred except as a whole by and among the depositary for the global security, the nominees of the depositary or any successors of the depositary or those nominees.

If not described below, any specific terms of the depositary arrangement with respect to any securities to be represented by a global security will be described in the prospectus supplement relating to those securities. We anticipate that the following provisions will apply to all depositary arrangements.

Ownership of beneficial interests in a global security will be limited to persons, called participants, that have accounts with the depositary or persons that may hold interests through participants. Upon the issuance of a global security, the depositary will credit, on its book-entry registration and transfer system, the participants' accounts with the respective principal or face amounts of the securities beneficially owned by the participants. Any dealers, underwriters or agents participating in the distribution of the securities will designate the accounts to be credited. Ownership of beneficial interests in a global security will be shown on, and the transfer of ownership interests will be effected only through, records maintained by the depositary, with respect to interests of participants, and on the records of participants, with respect to interests of persons holding through participants. The laws of some states may require that some purchasers of securities take physical delivery of these securities in definitive form. These laws may impair your ability to own, transfer or pledge beneficial interests in global securities.

So long as the depositary, or its nominee, is the registered owner of a global security, that depositary or its nominee, as the case may be, will be considered the sole owner or holder of the securities represented by the global security for all purposes under the applicable indenture, unit agreement or warrant agreement. Except as described below, owners of beneficial interests in a global security will not be entitled to have the securities represented by the global security registered in their names, will not receive or be entitled to receive physical delivery of the securities in definitive form and will not be considered the owners or holders of the securities under the applicable indenture, unit agreement or warrant agreement. Accordingly, each person owning a beneficial interest in a global security must rely on the procedures of the depositary for that global security and, if that person is not a participant, on the procedures of the participant through which the person owns its interest, to exercise any rights of a holder under the applicable indenture, unit agreement or warrant agreement. We understand that under existing industry practices, if we request any action of holders or if an owner of a beneficial interest in a global security desires to give or take any action that a holder is entitled to give or take

Table of Contents

under the applicable indenture, unit agreement or warrant agreement, the depositary for the global security would authorize the participants holding the relevant beneficial interests to give or take that action, and the participants would authorize beneficial owners owning through them to give or take that action or would otherwise act upon the instructions of beneficial owners holding through them.

Principal, premium, if any, and interest payments on debt securities, and any payments to holders with respect to warrants or units, represented by a global security registered in the name of a depositary or its nominee will be made to the depositary or its nominee, as the case may be, as the registered owner of the global security. None of us, or any trustee, warrant agent, unit agent or other agent of ours, or any agent of any trustee, warrant agent or unit agent will have any responsibility or liability for any aspect of the records relating to payments made on account of beneficial ownership interests in the global security or for maintaining, supervising or reviewing any records relating to those beneficial ownership interests.

We expect that the depositary for any of the securities represented by a global security, upon receipt of any payment to holders of principal, premium, interest or other distribution of underlying securities or other property on that registered global security, will immediately credit participants' accounts in amounts proportionate to their respective beneficial interests in that global security as shown on the records of the depositary. We also expect that payments by participants to owners of beneficial interests in a global security held through participants will be governed by standing customer instructions and customary practices, as is now the case with the securities held for the accounts of customers or registered in "street name," and will be the responsibility of those participants.

If the depositary for any of the securities represented by a global security is at any time unwilling or unable to continue as depositary or ceases to be a clearing agency registered under the Exchange Act, and a successor depositary registered as a clearing agency under the Exchange Act is not appointed by us within 90 days, we will issue securities in definitive form in exchange for the global security that had been held by the depositary. Any securities issued in definitive form in exchange for a global security will be registered in the name or names that the depositary gives to the relevant trustee, warrant agent, unit agent or other relevant agent of ours or theirs. It is expected that the depositary's instructions will be based upon directions received by the depositary from participants with respect to ownership of beneficial interests in the global security that had been held by the depositary.

PLAN OF DISTRIBUTION

We may sell securities:

- through underwriters;
- through dealers;
- through agents;
- directly to purchasers; or
- through a combination of any of these methods of sale.

In addition, we may issue the securities as a dividend or distribution or in a subscription rights offering to our existing security holders. This prospectus may be used in connection with any offering of our securities through any of these methods or other methods described in the applicable prospectus supplement.

We may directly solicit offers to purchase securities, or agents may be designated to solicit such offers. We will, in the prospectus supplement relating to such offering, name any agent that could be viewed as an underwriter under the Securities Act, and describe any commissions that we must pay. Any such agent will be acting on a best efforts basis for the period of its appointment or, if indicated in the applicable prospectus supplement, on a firm commitment basis.

The distribution of the securities may be effected from time to time in one or more transactions:

- at a fixed price, or prices, which may be changed from time to time;
- at market prices prevailing at the time of sale;
- at prices related to such prevailing market prices; or
- at negotiated prices.

Each prospectus supplement will describe the method of distribution of the securities and any applicable restrictions.

The prospectus supplement with respect to the securities of a particular series will describe the terms of the offering of the securities, including the following:

- the name of the agent or any underwriters;
- the public offering or purchase price and the proceeds we will receive from the sale of the securities;
- any discounts and commissions to be allowed or re-allowed or paid to the agent or underwriters;
- all other items constituting underwriting compensation;
- any discounts and commissions to be allowed or re-allowed or paid to dealers; and
- any exchanges on which the securities will be listed.

If any underwriters or agents are utilized in the sale of the securities in respect of which this prospectus is delivered, we will enter into an underwriting agreement or other agreement with them at the time of sale to them, and we will set forth in the prospectus supplement relating to such offering the names of the underwriters or agents and the terms of the related agreement with them.

If a dealer is utilized in the sale of the securities in respect of which this prospectus is delivered, we will sell such securities to the dealer, as principal. The dealer may then resell such securities to the public at varying prices to be determined by such dealer at the time of resale.

Table of Contents

If we offer securities in a subscription rights offering to our existing security holders, we may enter into a standby underwriting agreement with dealers, acting as standby underwriters. We may pay the standby underwriters a commitment fee for the securities they commit to purchase on a standby basis. If we do not enter into a standby underwriting arrangement, we may retain a dealer-manager to manage a subscription rights offering for us.

Remarketing firms, agents, underwriters, dealers and other persons may be entitled under agreements which they may enter into with us to indemnification by us against certain civil liabilities, including liabilities under the Securities Act, and may be customers of, engage in transactions with or perform services for us in the ordinary course of business.

If so indicated in the applicable prospectus supplement, we will authorize underwriters or other persons acting as our agents to solicit offers by certain institutions to purchase securities from us pursuant to delayed delivery contracts providing for payment and delivery on the date stated in the prospectus supplement. Each contract will be for an amount not less than, and the aggregate amount of securities sold pursuant to such contracts shall not be less nor more than, the respective amounts stated in the prospectus supplement. Institutions with whom the contracts, when authorized, may be made include commercial and savings banks, insurance companies, pension funds, investment companies, educational and charitable institutions and other institutions, but shall in all cases be subject to our approval. Delayed delivery contracts will not be subject to any conditions except that:

- the purchase by an institution of the securities covered under that contract shall not at the time of delivery be prohibited under the laws of the jurisdiction to which that institution is subject; and
- if the securities are also being sold to underwriters acting as principals for their own account, the underwriters shall have purchased such securities not sold for delayed delivery. The underwriters and other persons acting as our agents will not have any responsibility in respect of the validity or performance of delayed delivery contracts.

Certain agents, underwriters and dealers, and their associates and affiliates may be customers of, have borrowing relationships with, engage in other transactions with, and/or perform services, including investment banking services, for us or one or more of our respective affiliates in the ordinary course of business.

In order to facilitate the offering of the securities, any underwriters may engage in transactions that stabilize, maintain or otherwise affect the price of the securities or any other securities the prices of which may be used to determine payments on such securities. Specifically, any underwriters may overallocate in connection with the offering, creating a short position for their own accounts. In addition, to cover overallocations or to stabilize the price of the securities or of any such other securities, the underwriters may bid for, and purchase, the securities or any such other securities in the open market. Finally, in any offering of the securities through a syndicate of underwriters, the underwriting syndicate may reclaim selling concessions allowed to an underwriter or a dealer for distributing the securities in the offering if the syndicate repurchases previously distributed securities in transactions to cover syndicate short positions, in stabilization transactions or otherwise. Any of these activities may stabilize or maintain the market price of the securities above independent market levels. Any such underwriters are not required to engage in these activities and may end any of these activities at any time.

Under Rule 15c6-1 of the Exchange Act, trades in the secondary market generally are required to settle in two business days, unless the parties to any such trade expressly agree otherwise. The applicable prospectus supplement may provide that the original issue date for your securities may be more than two scheduled business days after the trade date for your securities. Accordingly, in such a case, if you wish to trade securities on any date prior to the second business day before the original issue date for your securities, you will be required, by virtue of the fact that your securities initially are expected to settle in more than two scheduled business days after the trade date for your securities, to make alternative settlement arrangements to prevent a failed settlement.

[Table of Contents](#)

The securities may be new issues of securities and may have no established trading market. The securities may or may not be listed on a national securities exchange. We can make no assurance as to the liquidity of or the existence of trading markets for any of the securities.

LEGAL MATTERS

Unless the applicable prospectus supplement indicates otherwise, the validity of the securities in respect of which this prospectus is being delivered will be passed upon by Wilmer Cutler Pickering Hale and Dorr LLP. Any underwriters will also be advised about the validity of the securities and other legal matters by their own counsel, which will be named in the applicable prospectus supplement.

EXPERTS

The consolidated financial statements of Syros Pharmaceuticals, Inc. appearing in Syros Pharmaceuticals, Inc.'s Annual Report (Form 10-K) for the year ended December 31, 2022, have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their report thereon included therein and incorporated herein by reference. Such financial statements are, and audited financial statements to be included in subsequently filed documents will be, incorporated herein in reliance upon the report of Ernst & Young LLP pertaining to such financial statements (to the extent covered by consents filed with the Securities and Exchange Commission) given on the authority of such firm as experts in accounting and auditing.



4,939,591 shares of common stock
Pre-funded warrants to purchase up to 5,242,588 shares of common stock

Prospectus supplement

TD Cowen

Piper Sandler

December 18, 2023
