

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

**FORM S-3
REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933
SYROS PHARMACEUTICALS, INC.
(Exact Name of Registrant as Specified in Its Charter)**

Delaware
(State or Other Jurisdiction of
Incorporation or Organization)

45-3772460
(I.R.S. Employer
Identification Number)

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

(Address, Including Zip Code, and Telephone Number, Including Area Code, of Registrant's Principal Executive Offices)

Nancy Simonian, M.D.
President and Chief Executive Officer
Syros Pharmaceuticals, Inc.
35 CambridgePark Drive, 4th Floor
Cambridge, Massachusetts 02140
(617) 744-1340

(Name, Address, Including Zip Code, and Telephone Number, Including Area Code, of Agent for Service)

Copies to:

Nancy A. Simonian, M.D.
President and Chief Executive Officer
Syros Pharmaceuticals, Inc.
35 CambridgePark Drive, 4th Floor
Cambridge, Massachusetts 02140
Telephone: (617) 744-1340

Cynthia T. Mazareas
Wilmer Cutler Pickering Hale and Dorr LLP
60 State Street
Boston, Massachusetts 02109
Telephone: (617) 526-6000
Fax: (617) 526-5000

Approximate date of commencement of proposed sale to the public: From time to time after this registration statement becomes effective.

If the only securities being registered on this Form are being offered pursuant to dividend or interest reinvestment plans, please check the following box.

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, other than securities offered only in connection with dividend or interest reinvestment plans, check the following box.

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this Form is a registration statement pursuant to General Instruction I.D. or a post-effective amendment thereto that shall become effective upon filing with the Commission pursuant to Rule 462(e) under the Securities Act, check the following box.

If this Form is a post-effective amendment to a registration statement filed pursuant to General Instruction I.D. filed to register additional securities or additional classes of securities pursuant to Rule 413(b) under the Securities Act, check the following box.

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company" and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer
Non-accelerated filer

Accelerated filer
Smaller reporting company
Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 7(a)(2)(B) of the Securities Act.

The registrant hereby amends this registration statement on such date or dates as may be necessary to delay its effective date until the registrant shall file a further amendment which specifically states that this registration statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933 or until this registration statement shall become effective on such date as the Commission, acting pursuant to said Section 8(a), may determine.

The information in this prospectus is not complete and may be changed. The selling stockholders named in this prospectus may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities and the selling stockholders named in this prospectus are not soliciting offers to buy these securities in any state or other jurisdiction where the offer or sale is not permitted.

Subject to completion, dated October 14, 2022

PROSPECTUS

27,627,824 Shares



Common Stock

This prospectus relates to the resale from time to time of up to 27,627,824 shares of common stock of Syros Pharmaceuticals, Inc. by the selling stockholders listed on page 8, including their pledgees, assignees, donees, transferees or their respective successors-in-interest, which consist of 6,387,173 outstanding shares of our common stock held by the selling stockholders, 7,426,739 shares of our common stock issuable upon the exercise of outstanding pre-funded warrants held by the selling stockholders to purchase shares of our common stock and 13,813,912 shares of our common stock issuable upon the exercise of outstanding warrants held by the selling stockholders to purchase shares of our common stock (the “Warrants”) (or issuable upon exercise of pre-funded warrants to purchase shares of our common stock that are issuable to holders of Warrants upon exercise of such Warrants for pre-funded warrants in lieu of common stock). We will not receive any proceeds from the sale of the shares offered by this prospectus.

We have agreed, pursuant to a registration rights agreement that we have entered into with the selling stockholders, to bear all of the expenses incurred in connection with the registration of these shares. The selling stockholders will pay or assume discounts, commissions, fees of underwriters, selling brokers or dealer managers and similar expenses, if any, incurred for the sale of these shares of our common stock.

The selling stockholders identified in this prospectus, or their pledgees, assignees, donees, transferees or their respective successors-in-interest, may offer the shares from time to time on terms to be determined at the time of sale through ordinary brokerage transactions or through any other means described in this prospectus under the caption “Plan of Distribution.” The shares may be sold at fixed prices, at prevailing market prices, at prices related to prevailing market prices or at negotiated prices. For a list of the selling stockholders, see the section entitled “Selling Stockholders” on page 8.

We may amend or supplement this prospectus from time to time by filing amendments or supplements as required. You should read the entire prospectus and any amendments or supplements carefully before you make your investment decision.

Our common stock is traded on the Nasdaq Global Select Market (“Nasdaq”) under the symbol “SYRS.” On October 13, 2022, the last reported closing sale price of our common stock on Nasdaq was \$6.18 per share. You are urged to obtain current market quotations for our common stock.

Investing in our common stock involves a high degree of risk. See “[Risk Factors](#)” beginning on page 3 of this prospectus.

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 _____, 2022.

TABLE OF CONTENTS

	<u>Page</u>
PROSPECTUS SUMMARY	1
THE OFFERING	2
RISK FACTORS	3
SELECTED FINANCIAL DATA	4
CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS AND INDUSTRY DATA	5
USE OF PROCEEDS	7
SELLING STOCKHOLDERS	8
PLAN OF DISTRIBUTION	16
LEGAL MATTERS	18
EXPERTS	18
WHERE YOU CAN FIND MORE INFORMATION	18
INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE	18

You should rely only on the information contained or incorporated by reference in this prospectus. We have not authorized any other person to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. This prospectus may only be used where it is legal to offer and sell shares of our common stock. If it is against the law in any jurisdiction to make an offer to sell these shares, or to solicit an offer from someone to buy these shares, then this prospectus does not apply to any person in that jurisdiction, and no offer or solicitation is made by this prospectus to any such person. You should assume that the information appearing in this prospectus is accurate only as of the date on the front cover of this prospectus, regardless of the time of delivery of this prospectus or of any sale of common stock. Our business, financial condition, results of operations and prospects may have changed since such date.

PROSPECTUS SUMMARY

This summary highlights, and is qualified in its entirety by, the more detailed information included elsewhere in this prospectus or incorporated by reference in this prospectus. This summary does not contain all of the information that you should consider before investing. You should read and carefully consider the entire prospectus, especially the "Risk Factors" section of this prospectus, before deciding to invest in our common stock.

Overview

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

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 incorporated by reference into and is not a part of this prospectus. We have included our website address in this prospectus solely as an inactive textual reference.

Except as otherwise indicated herein or as the context otherwise requires, references in this prospectus to "Syros," "the company," "we," "us" and "our" refer to Syros Pharmaceuticals, Inc. and our wholly owned subsidiaries, Syros Securities Corporation, a Massachusetts corporation, Syros Pharmaceuticals (Ireland) Limited, an Irish limited liability company, and Tyme Technologies, Inc., a Delaware corporation.

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.

THE OFFERING

Common stock offered by selling stockholders	27,627,824 shares, consisting of 6,387,173 outstanding shares of our common stock, 7,426,739 shares of our common stock issuable upon the exercise of outstanding pre-funded warrants and 13,813,912 shares of our common stock issuable upon the exercise of Warrants (or issuable upon exercise of pre-funded warrants to purchase shares of our common stock that are issuable to holders of Warrants upon exercise of such Warrants for pre-funded warrants in lieu of common stock).
Use of proceeds	We will not receive any proceeds from the sale of shares in this offering.
Risk factors	You should read the “Risk Factors” section on page 3 of this prospectus for a discussion of factors to consider carefully before deciding to invest in shares of our common stock.
Nasdaq Global Select Market symbol	“SYRS”

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, our most recent Quarterly Report on Form 10-Q and other filings we make with the Securities and Exchange Commission (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, our most recent Quarterly Report on Form 10-Q 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, our most recent Quarterly Report on Form 10-Q 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.

SELECTED FINANCIAL DATA**Reverse Stock Split**

On September 16, 2022, we effected a 1-for-10 reverse stock split of our common stock. The number of authorized shares was also proportionately adjusted. The par value per common share remained unchanged. The consolidated financial statements of Syros Pharmaceuticals, Inc. included in the Annual Report on Form 10-K for the year ended December 31, 2021 that are incorporated by reference into this prospectus are presented without giving effect to the reverse stock split. Except where the context otherwise requires, share numbers in this prospectus reflect the 1-for-10 reverse stock split of our common stock.

The following selected financial data has been derived from our audited financial statements included in our Annual Report on Form 10-K filed with the SEC on March 15, 2022. Our historical results are not indicative of the results that may be expected in the future and results of interim periods are not indicative of the results for the entire year.

AS REPORTED (in thousands, except per share amounts):

	For the years ended December 31,		
	2019	2020	2021
Net loss	\$ (75,438)	\$ (84,038)	\$ (86,558)
Net loss per share, basic and diluted	\$ (1.88)	\$ (1.82)	\$ (1.38)
Weighted-average shares outstanding, basic and diluted	40,222,182	46,051,617	62,534,978
Common shares outstanding at period end	43,367,801	56,222,746	62,024,035

AS ADJUSTED FOR 1-FOR-10 REVERSE STOCK SPLIT (unaudited, in thousands, except per share amounts):

	For the years ended December 31,		
	2019	2020	2021
Net loss	\$ (75,438)	\$ (84,038)	\$ (86,558)
Net loss per share, basic and diluted	\$ (18.76)	\$ (18.25)	\$ (13.84)
Weighted-average shares outstanding, basic and diluted	4,022,218	4,605,161	6,253,497
Common shares outstanding at period end	4,336,780	5,622,274	6,202,403

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS AND INDUSTRY DATA

This prospectus and the documents incorporated by reference herein contain forward-looking statements that involve substantial risks and uncertainties. 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 future 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 expectations regarding the potential benefits of our gene control platform and our approach;
- 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 investigational new drug application-enabling studies under our sickle cell disease collaboration with Global Blood Therapeutics, Inc. (“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 (“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 future 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 and cash equivalents and the period of time in which such capital will be sufficient to fund our planned operations;
- conditions and events that raise doubt about our ability to continue as a going concern;
- our estimates regarding expenses, future revenue, capital requirements and need for additional financing; and
- other risks and uncertainties, including those listed under the caption “Risk Factors” in our most recent Annual Report on Form 10-K, our most recent Quarterly Report on Form 10-Q, and other filings we make with the SEC.

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, particularly in the “Risk Factors” section, that could cause actual results or events to differ materially from the forward-looking statements that we make. In particular, the extent to which the COVID-19 pandemic continues to impact our operations and those of the third parties on which we rely will depend on future developments, which are highly uncertain and cannot be predicted with confidence, including the duration and severity of the pandemic, additional or modified government actions, and the actions that may be required to contain the coronavirus or treat its impact. COVID-19 has and may continue to adversely impact our operations and workforce, including our discovery research, supply chain and clinical trial operations activities, which in turn could have an adverse impact on our business and financial results.

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 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 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.

USE OF PROCEEDS

We are filing the registration statement of which this prospectus forms a part to permit the holders of the shares of our common stock described in the section entitled “Selling Stockholders” to resell such shares. We are not selling any securities under this prospectus and we will not receive any proceeds from the sale or other disposition of shares of our common stock held by the selling stockholders.

The selling stockholders will pay any underwriting discounts and commissions and expenses incurred by the selling stockholders for brokerage, accounting, tax or legal services or any other expenses incurred by the selling stockholders in disposing of these shares. We will bear all other costs, fees and expenses incurred in effecting the registration of the shares covered by this prospectus, including, without limitation, all registration and filing fees, Nasdaq listing fees and fees and expenses of our counsel and our accountants.

SELLING STOCKHOLDERS

On July 3, 2022, we entered into a securities purchase agreement (the “Purchase Agreement”) with certain institutional and accredited investors (the “Investors”), pursuant to which we issued and sold in a private placement (the “Private Placement”) an aggregate of 6,387,173 shares of our common stock and, in lieu of shares of common stock, pre-funded warrants to purchase an aggregate of 7,426,739 shares of our common stock, and accompanying Warrants to purchase an aggregate of up to 13,813,912 additional shares of common stock (or pre-funded warrants to purchase common stock in lieu thereof) at a price of \$9.40 per unit, consisting of a share of our common stock and an accompanying Warrant to purchase one share of our common stock (a “Common Stock Unit”), or \$9.399 per unit, consisting of a pre-funded warrant to purchase a share of our common stock and an accompanying Warrant to purchase one share of our common stock (a “Pre-Funded Warrant Unit”). The price per Pre-Funded Warrant Unit represents the price of \$9.40 per Common Stock Unit sold in the Private Placement, minus the \$0.001 per share exercise price of each pre-funded warrant included in a Pre-Funded Warrant Unit. The exercise price of the Warrants is \$10.34 per share, or if exercised for a pre-funded warrant in lieu thereof, \$10.339 per pre-funded warrant (representing the Warrant exercise price of \$10.34 per share minus the \$0.001 per share exercise price of each such pre-funded warrant). The closing of the issuance and sale of these securities was consummated on September 16, 2022 (the “Private Placement Closing Date”). The Warrants are exercisable at any time during the period beginning on March 16, 2023 and ending on September 16, 2027. The pre-funded warrants are exercisable at any time after their original issuance and will not expire. The shares issuable upon exercise of the Warrants and pre-funded warrants will become eligible for sale by the selling stockholders under this prospectus only when the Warrants or pre-funded warrants are exercised. We cannot predict when or whether any of the selling stockholders will exercise their Warrants or pre-funded warrants.

The Warrants and pre-funded warrants issued or issuable in the Private Placement provide that a holder of Warrants or pre-funded warrants does not have the right to exercise any portion of its Warrants or pre-funded warrants if such holder, together with its affiliates, would beneficially own in excess of 4.99%, 9.99% or 19.99%, as selected by the holder of such Warrants or pre-funded warrants, of the number of shares of our common stock outstanding immediately after giving effect to such exercise (the “Beneficial Ownership Limitation”); provided, however, that each holder may increase or decrease the Beneficial Ownership Limitation by giving notice to the Company, but not to any percentage in excess of 19.99%.

In connection with the Private Placement, we entered into a registration rights agreement with the Investors, dated as of July 3, 2022 (the “Registration Rights Agreement”), pursuant to which we agreed to file a registration statement with the SEC covering the resale of the shares of common stock sold in the Private Placement and the shares of common stock underlying the Warrants and pre-funded warrants described above. We agreed to file such registration statement within 30 days following the Private Placement Closing Date. The Registration Rights Agreement includes customary indemnification rights in connection with the registration statement. The registration statement of which this prospectus forms a part has been filed in accordance with the Registration Rights Agreement.

We received gross proceeds of approximately \$130 million from the Private Placement, before deducting offering expenses, and excluding any proceeds that we may receive upon exercise of any pre-funded warrants and Warrants.

The foregoing summary descriptions of the Purchase Agreement and the Registration Rights Agreement do not purport to be complete and are qualified in their entirety by reference to the full text of such documents, which are filed as exhibits to the registration statement of which this prospectus forms a part, and are incorporated by reference herein.

This prospectus covers the sale or other disposition by the selling stockholders of up to the total number of shares of our common stock that were issued to the Investors pursuant to the Purchase Agreement, plus the total number of shares of our common stock issuable upon exercise of the Warrants and pre-funded warrants issued or

Table of Contents

issuable to the selling stockholders, without giving effect to the Beneficial Ownership Limitation described above. The table below sets forth, to our knowledge, information concerning the beneficial ownership of shares of our common stock by the selling stockholders as of September 30, 2022. The information in the table below with respect to the selling stockholders has been obtained from the respective selling stockholders. When we refer to the “selling stockholders” in this prospectus, or, if required, a post-effective amendment to the registration statement of which this prospectus is a part, we mean the selling stockholders listed in the table below as offering shares, as well as their respective pledgees, assignees, donees, transferees or successors-in-interest. Throughout this prospectus, when we refer to the shares of our common stock being registered on behalf of the selling stockholders, we are referring to the shares of our common stock and the shares underlying the Warrants and pre-funded warrants issued or issuable to the selling stockholders pursuant to the Purchase Agreement (or issuable upon exercise of pre-funded warrants to purchase shares of our common stock that are issuable to holders of Warrants upon exercise of such Warrants for pre-funded warrants in lieu of common stock), without giving effect to the Beneficial Ownership Limitation described above. The selling stockholders may sell all, some or none of the shares of common stock subject to this prospectus. See “Plan of Distribution” below as it may be supplemented and amended from time to time.

The number of shares of common stock beneficially owned prior to the offering for each selling stockholder includes all shares of our common stock beneficially held by such selling stockholder as of September 30, 2022, which includes (i) all shares of our common stock purchased by such selling stockholder in the Private Placement and (ii) all shares of common stock issuable upon exercise of the pre-funded warrants purchased by such selling stockholder in the Private Placement. The percentages of shares owned before and after the offering are based on 20,236,215 shares of common stock outstanding as of September 30, 2022, which includes the outstanding shares of common stock offered by this prospectus but does not include any shares of common stock offered by this prospectus that are issuable pursuant to warrants and are deemed outstanding in the table below because they are beneficially owned by a person.

Beneficial ownership is determined in accordance with the rules of the SEC and includes voting or investment power with respect to our common stock. Generally, a person “beneficially owns” shares of our common stock if the person has or shares with others the right to vote those shares or to dispose of them, or if the person has the right to acquire voting or disposition rights within 60 days. In computing the number of shares of our common stock beneficially owned by a person and the percentage ownership of that person, we deemed outstanding shares of common stock issuable upon the exercise of pre-funded warrants held by that selling stockholder described above because all are exercisable within 60 days of September 30, 2022. We did not deem these shares outstanding, however, for the purpose of computing the percentage ownership of any other person. In computing the number of shares of our common stock beneficially owned by each selling stockholder, we did not deem outstanding any shares of common stock issuable upon the exercise of Warrants because the Warrants are not exercisable until March 16, 2023. The inclusion of any shares in this table does not constitute an admission of beneficial ownership for any selling stockholder named below.

Name of Selling Stockholder	Shares of Common Stock Beneficially Owned Prior to Offering		Number of Shares of Common Stock Being Offered(1)	Shares of Common Stock to be Beneficially Owned After Offering(2)	
	Number	Percentage		Number	Percentage
Entities affiliated with Baker Brothers Advisors(3)	2,659,799	11.62%	5,319,598	—	—
Entities affiliated with Avidity Capital Partners LP(4)	2,120,000	9.88%	4,240,000	—	—
Entities affiliated with Flagship Pioneering(5)	2,413,848	11.15%	4,240,000	293,848	1.45%
Deep Track Biotechnology Master Fund, Ltd.(6)	1,595,000	7.31%	3,190,000	—	—
Invus Public Equities, L.P.(7)	1,413,829	6.99%	2,127,658	350,000	1.73%
BCLS II Equity Opportunities, LP(8)	1,063,880	5.12%	2,127,760	—	—
Samsara BioCapital, L.P.(9)	910,408	4.49%	1,382,978	218,919	1.08%
CHI IV Public Investments LP(10)	531,914	2.63%	1,063,828	—	—

Table of Contents

Adage Capital Partners, L.P.(11)	531,914	2.63%	1,063,828	—	—
Ally Bridge MedAlpha Master Fund L.P.(12)	907,465	4.48%	1,063,828	375,551	1.86%
CVI Investments, Inc.(13)	425,500	2.10%	851,000	—	—
Altium Growth Fund, LP(14)	319,100	1.58%	638,200	—	—
Entities affiliated with Dafna Capital Management LLC(15)	132,978	*	265,956	—	—
JALAA Equities, LP(16)	26,595	*	53,190	—	—

* Less than one percent

- (1) The number of shares of our Common Stock in the column “Number of Shares of Common Stock Being Offered” represents all of the shares of our common stock that a selling stockholder may offer and sell from time to time under this prospectus, including shares issuable upon the exercise of Warrants and pre-funded warrants issued in the Private Placement.
- (2) We do not know when or in what amounts a selling stockholder may offer shares for sale. The selling stockholders might not sell any or might sell all of the shares offered by this prospectus. Because the selling stockholders may offer all or some of the shares pursuant to this offering, and because there are currently no agreements, arrangements or understandings with respect to the sale of any of the shares, we cannot estimate the number of the shares that will be held by the selling stockholders after completion of the offering. However, for purposes of this table, we have assumed that, after completion of the offering, none of the shares covered by this prospectus will be held by the selling stockholders, including common stock issuable upon exercise of the Warrants and pre-funded warrants issued or issuable in the Private Placement.
- (3) The shares reported under “Shares of Common Stock Beneficially Owned Prior to the Offering” consist of (i) 2,419,127 shares of common stock issuable upon exercise of pre-funded warrants held by Baker Brothers Life Sciences, L.P. and (ii) 240,672 shares of common stock issuable upon exercise of pre-funded warrants held 667, L.P. Baker Brothers Life Sciences, L.P. and 667, L.P. (the “Funds”) are prohibited from exercising such pre-funded warrants, if, as a result of such exercise, the Funds would beneficially own more than 4.99% of the total number of shares of common stock then issued and outstanding immediately after giving effect to the exercise. The beneficial ownership amounts in the table above do not give effect to the Beneficial Ownership Limitation solely for illustrative purposes. The Funds and their affiliates disclaim beneficial ownership of any shares of common stock the issuance of which would violate such Beneficial Ownership Limitation. In addition to the foregoing shares, as of September 30, 2022, (i) Baker Brothers Life Sciences, L.P. held Warrants to purchase 2,419,127 shares of common stock and (ii) 667, L.P. held Warrants to purchase 240,672 shares of common stock that are not included in the shares reported under “Shares of Common Stock Beneficially Owned Prior to the Offering” because they are not exercisable until March 16, 2023. The shares reported under “Number of Shares of Common Stock Being Offered” consist of (i) the shares reported as beneficially owned by the Funds under “Shares of Common Stock Beneficially Owned Prior to the Offering” and (ii) the shares issuable upon exercise of Warrants held by the Funds described above, in each case, without giving effect to the Beneficial Ownership Limitation. Baker Bros. Advisors LP (“Adviser”) is the management company and investment adviser to the Funds and has sole voting and investment power with respect to the shares held by the Funds. Baker Bros. Advisors (GP) LLC (“Adviser GP”) is the sole general partner of Adviser. Julian C. Baker and Felix J. Baker are managing members of Adviser GP. Adviser GP, Felix J. Baker, Julian C. Baker and Adviser may be deemed to be beneficial owners of the securities directly held by the Funds. Julian C. Baker, Felix J. Baker, the Adviser and the Adviser GP disclaim beneficial ownership of all shares held by the Funds, except to the extent of their indirect pecuniary interest therein. The address for the above referenced entities and persons is 860 Washington Street, 3rd Floor, New York, NY 10014.
- (4) The shares reported under “Shares of Common Stock Beneficially Owned Prior to the Offering” consist of (i) 331,970 shares of common stock and 450,000 shares of common stock issuable upon exercise of pre-funded warrants, in each case held by Avidity Master Fund LP (“Avidity Master”), (ii) 40,940 shares of common stock and 55,500 shares of common stock issuable upon exercise of pre-funded warrants, in each case held by Avidity Capital Fund II LP (“Avidity II”), (iii) 30,560 shares of common stock and 41,420 shares of common stock issuable upon exercise of pre-funded warrants, in each case held by Avidity

Table of Contents

Capital HL Sub Fund III LLC (“Avidity III”), and (iv) 496,530 shares of common stock and 673,080 shares of common stock issuable upon exercise of pre-funded warrants, in each case held Avidity Private Master Fund I LP (“Avidity Private”). In addition to the foregoing shares, as of September 30, 2022, (i) Avidity Master held Warrants to purchase 781,970 shares of common stock, (ii) Avidity II held Warrants to purchase 96,440 shares of common stock, (iii) Avidity III held Warrants to purchase 71,980 shares of common stock and (iv) Avidity Private held Warrants to purchase 1,169,610 shares of common stock that are not included in the shares reported under “Shares of Common Stock Beneficially Owned Prior to the Offering” because they are not exercisable until March 16, 2023. The shares reported under “Number of Shares of Common Stock Being Offered” consist of (i) the shares reported as beneficially owned by the Avidity entities (as defined below) under “Shares of Common Stock Beneficially Owned Prior to the Offering” and (ii) the shares issuable upon exercise of Warrants held by the Avidity entities described above. Avidity Master is a Cayman exempted limited partnership, Avidity II is a Delaware limited partnership, Avidity III is a Delaware limited liability company, and Avidity Private is a Cayman exempted limited partnership. Avidity Master, Avidity II, Avidity III and Avidity Private are collectively referred to as the Avidity entities. The general partner of each of the Avidity entities is Avidity Capital Partners Fund (GP) LP, a Delaware limited partnership, whose general partner is Avidity Capital Partners (GP) LLC, a Delaware limited liability company. Avidity Partners Management LP, is the investment manager of the Avidity entities. Avidity Partners Management (GP) LLC is the general partner of Avidity Partners Management LP. David Witzke and Michael Gregory are the managing members of Avidity Capital Partners (GP) LLC and Avidity Partners Management (GP) LLC. Each of the entities and individuals referenced in this paragraph may be deemed to beneficially own the shares held by the Avidity entities. Certain affiliates of the Avidity entities, which are not selling stockholders, may also own shares. The address of the selling stockholders is 2828 N. Harwood Street, Suite 1220, Dallas, TX 75201.

- (5) The shares reported under “Shares of Common Stock Beneficially Owned Prior to the Offering” consist of (i) 21,333 shares of common stock held by Flagship VentureLabs IV, LLC (“VentureLabs IV”), (ii) 216,590 shares of common stock held by Flagship Ventures Fund IV, L.P. (“Flagship Fund IV”), (iii) 55,925 shares of common stock held by Flagship Ventures Fund IV-Rx, L.P. (“Flagship Fund IV-Rx”), (iv) 700,000 shares of common stock held Flagship Pioneering Fund VII, L.P. (“Flagship Fund VII”), and (v) 1,420,000 shares of common stock issuable upon the exercise of pre-funded warrants held by Flagship Fund VII. VentureLabs IV, Flagship Fund IV, Flagship Fund IV-Rx and Flagship Fund VII are together referred to as the Flagship Funds. The Flagship Funds are prohibited from exercising such pre-funded warrants, if, as a result of such exercise, the Flagship Funds would beneficially own more than 4.99% of the total number of shares of common stock then issued and outstanding immediately after giving effect to the exercise. The beneficial ownership amounts in the table above do not give effect to the Beneficial Ownership Limitation solely for illustrative purposes. The Flagship Funds and their affiliates disclaim beneficial ownership of any shares of common stock the issuance of which would violate such Beneficial Ownership Limitation. In addition to the foregoing shares, as of September 30, 2022, Flagship Fund VII held Warrants to purchase 2,120,000 shares of common stock that are not included in the shares reported under “Shares of Common Stock Beneficially Owned Prior to the Offering” because they are not exercisable until March 16, 2023. The shares reported under “Number of Shares of Common Stock Being Offered” consist of (i) the shares reported as beneficially owned by Flagship Fund VII under “Shares of Common Stock Beneficially Owned Prior to the Offering” and (ii) the shares issuable upon exercise of Warrants held by Flagship Fund VII described above, in each case, without giving effect to the Beneficial Ownership Limitation. Flagship Fund IV is a member of VentureLabs IV and also serves as its manager. The general partner of each of Flagship Fund IV and Flagship Fund IV-Rx is Flagship Ventures Fund IV General Partner LLC (“Flagship Fund IV GP”). Noubar B. Afeyan, Ph.D. is the sole manager of Flagship Fund IV GP. Flagship Fund IV GP and Noubar B. Afeyan, Ph.D. may be deemed to share voting, investment and dispositive power with respect to all shares held by the Flagship Funds. Each of the foregoing disclaims beneficial ownership of the shares except to the extent of any pecuniary interest therein. The address of such stockholder is 55 Cambridge Parkway, Suite 800E, Cambridge, Massachusetts 02142.
- (6) The shares reported under “Shares of Common Stock Beneficially Owned Prior to the Offering” consist of 1,595,000 shares of common stock issuable upon the exercise of pre-funded warrants held by Deep Track

Table of Contents

Biotechnology Master Fund, Ltd. (“Deep Track Master Fund”). In addition to the foregoing shares, as of September 30, 2022, Deep Track Master Fund held Warrants to purchase 1,595,000 shares of common stock that are not included in the shares reported under “Shares of Common Stock Beneficially Owned Prior to the Offering” because they are not exercisable until March 16, 2023. The shares reported under “Number of Shares of Common Stock Being Offered” consist of (i) the shares reported as beneficially owned by Deep Track Master Fund under “Shares of Common Stock Beneficially Owned Prior to the Offering” and (ii) the shares issuable upon exercise of Warrants held by Deep Track Master Fund described above. The address of Deep Track Master Fund is 200 Greenwich Ave., 3rd Floor, Greenwich, CT 06830.

- (7) Invus Public Equities, L.P. (“Invus PE”) directly holds the 1,413,829 shares of common stock reported under “Shares of Common Stock Beneficially Owned Prior to the Offering”. In addition to the foregoing shares, as of September 30, 2022, Invus PE held Warrants to purchase 1,063,829 shares of common stock that are not included in the shares reported under “Shares of Common Stock Beneficially Owned Prior to the Offering” because they are not exercisable until March 16, 2023. The shares reported under “Number of Shares of Common Stock Being Offered” consist of (i) 1,063,829 shares of common stock purchased by Invus PE in the Private Placement and (ii) the shares issuable upon exercise of Warrants held by Invus PE described above. Invus Public Equities Advisors, LLC (“Invus PE Advisors”) controls Invus PE, as its general partner and accordingly, may be deemed to beneficially own the shares held by Invus PE. The Geneva branch of Artal International S.C.A. (“Artal International”) controls Invus PE Advisors, as its managing member and accordingly, may be deemed to beneficially own the shares held by Invus PE. Artal International Management S.A. (“Artal International Management”), as the managing partner of Artal International, controls Artal International and accordingly, may be deemed to beneficially own the shares that Artal International may be deemed to beneficially own. Artal Group S.A., as the sole stockholder of Artal International Management, controls Artal International Management and accordingly, may be deemed to beneficially own the shares that Artal International Management may be deemed to beneficially own. Westend S.A. (“Westend”), as the parent company of Artal Group S.A. (“Artal Group”), controls Artal Group and accordingly, may be deemed to beneficially own the shares that Artal Group may be deemed to beneficially own. Stichting Administratiekantoor Westend (the “Stichting”), as majority shareholder of Westend, controls Westend and accordingly, may be deemed to beneficially own the shares that Westend may be deemed to beneficially own. Mr. Amaury Wittouck, as the sole member of the board of the Stichting, controls the Stichting and accordingly, may be deemed to beneficially own the Shares that the Stichting may be deemed to beneficially own. The address for Invus PE and Invus PE Advisors is 750 Lexington Avenue, 30th Floor, New York, NY 10022. The address for Artal International, Artal International Management, Artal Group, Westend and Mr. Wittouck is Valley Park, 44, Rue de la Vallée, L-2661, Luxembourg. The address for the Stichting is Claude Debussylaan, 46, 1082 MD Amsterdam, The Netherlands.
- (8) The shares reported under “Shares of Common Stock Beneficially Owned Prior to the Offering” consist of 531,940 shares of common stock and 531,940 shares of common stock issuable upon exercise of pre-funded warrants, in each case held by BCLS II Equity Opportunities, LP (“BCLS II Equity”). In addition to the foregoing shares, as of September 30, 2022, BCLS II Equity held Warrants to purchase 1,063,880 shares of common stock that are not included in the shares reported under “Shares of Common Stock Beneficially Owned Prior to the Offering” or “Shares of Common Stock to be Beneficially Owned After Offering” because they are not exercisable until March 16, 2023. The shares reported under “Number of Shares of Common Stock Being Offered” consist of (i) the shares reported as beneficially owned by BCLS II Equity under “Shares of Common Stock Beneficially Owned Prior to the Offering” and (ii) the shares issuable upon exercise of Warrants held by BCLS II Equity described above. Bain Capital Life Sciences Investors, LLC (“BCLSI”) is the manager of Bain Capital Life Sciences Investors II, LLC, which is the general partner of Bain Capital Life Sciences Fund II, L.P. (“BCLS Fund II”), which is the manager of BCLS II Equity Opportunities GP, LLC, which is the general partner of BCLS II Equity. As a result, BCLSI may be deemed to share beneficial ownership with respect to the securities held by BCLS II Equity. The shares of common stock, including the shares of common stock issuable upon exercise of pre-funded warrants and Warrants, held by BCLS II Equity are required to be aggregated for purposes of the Beneficial Ownership Limitation with the following shares of common stock, which are held by certain affiliates of BCLS II Equity and may

Table of Contents

be deemed to be beneficially owned by BCLSI: 490,701 shares of common stock, warrants to purchase 111,428 shares of common stock and 89,142 shares of common stock issuable upon exercise of pre-funded warrants, in each case held by BCLS Fund II, and 59,765 shares of common stock, warrants to purchase 13,571 shares of common stock and 10,857 shares of common stock issuable upon exercise of pre-funded warrants, in each case held by BCIP Life Sciences Associates, LP. The address of BCLS II Equity is c/o Bain Capital Life Sciences, LP, 200 Clarendon Street, Boston, MA 02116.

- (9) The shares reported under “Shares of Common Stock Beneficially Owned Prior to the Offering” consist of 881,450 shares of common stock and warrants to purchase 28,958 shares of common stock, in each case owned by Samsara BioCapital, L.P. (“Samsara LP”). In addition to the foregoing shares, as of September 30, 2022, Samsara LP held Warrants to purchase 691,489 shares of common stock that are not included in the shares reported under “Shares of Common Stock Beneficially Owned Prior to the Offering” because they are not exercisable until March 16, 2023. The shares reported under “Number of Shares of Common Stock Being Offered” consist of (i) 691,489 shares of common stock purchased by Samsara in the Private Placement and (ii) the shares issuable upon exercise of Warrants held by Samsara LP described above. The general partner of Samsara LP is Samsara BioCapital GP, LLC (“Samsara LLC”). The managers of Samsara LLC are Srinivas Akkaraju and Michael Dybbs. These individuals may be deemed to have shared voting and investment power of the shares held by Samsara LP and may be deemed to beneficially own certain shares held by Samsara LP. Dr. Akkaraju disclaims beneficial ownership of these shares, except to the extent of his pecuniary interest therein. The address for Samsara LP is 628 Middlefield Road, Palo Alto, CA 94301.
- (10) CHI IV Public Investments LP (“CHI IV”) directly holds the 531,914 shares of common stock reported under “Shares of Common Stock Beneficially Owned Prior to the Offering”. In addition to the foregoing shares, as of September 30, 2022, CHI IV held Warrants to purchase 531,914 shares of common stock that are not included in the shares reported under “Shares of Common Stock Beneficially Owned Prior to the Offering” because they are not exercisable until March 16, 2023. The shares reported under “Number of Shares of Common Stock Being Offered” consist of (i) the shares reported as beneficially owned by CHI IV under “Shares of Common Stock Beneficially Owned Prior to the Offering” and (ii) the shares issuable upon exercise of Warrants held by CHI IV described above. CHI Advisors LLC, the investment adviser of CHI IV has sole voting and investment power with respect to the shares owned by CHI IV. The address for CHI Advisors, LLC and CHI IV is 599 Lexington Avenue, 19th Floor, New York, NY 10022.
- (11) Adage Capital Partners, L.P. directly holds the 531,914 shares of common stock reported under “Shares of Common Stock Beneficially Owned Prior to the Offering”. In addition to the foregoing shares, as of September 30, 2022, Adage Capital Partners, L.P. held Warrants to purchase 531,914 shares of common stock that are not included in the shares reported under “Shares of Common Stock Beneficially Owned Prior to the Offering” because they are not exercisable until March 16, 2023. The shares reported under “Number of Shares of Common Stock Being Offered” consist of (i) the shares reported as beneficially owned by Adage Capital Partners, L.P. under “Shares of Common Stock Beneficially Owned Prior to the Offering” and (ii) the shares issuable upon exercise of Warrants held by Adage Capital Partners, L.P. described above. Bob Atchinson and Phillip Gross are the managing members of Adage Capital Advisors, L.L.C., which is the managing member of Adage Capital Partners GP, L.L.C., which is the general partner of Adage Capital Partners, L.P., and each such person or entity, as the case may be, may be deemed the beneficial owner of such shares. The address of Adage Capital Partners, L.P. is 200 Clarendon Street, 52nd Floor, Boston MA 02116.
- (12) The shares reported under “Shares of Common Stock Beneficially Owned Prior to the Offering” consist of 868,403 shares of common stock and warrants to purchase 39,062 shares of common stock, in each case held by Ally Bridge MedAlpha Master Fund L.P. (“Ally Bridge”). In addition to the foregoing shares, as of September 30, 2022, Ally Bridge held Warrants to purchase 531,914 shares of common stock that are not included in the shares reported under “Shares of Common Stock Beneficially Owned Prior to the Offering” because they are not exercisable until March 16, 2023. The shares reported under “Number of Shares of Common Stock Being Offered” consist of (i) 531,914 shares of common stock purchased by Ally Bridge in the Private Placement and (ii) the shares issuable upon exercise of Warrants held by Ally Bridge described above. Mr. Fan Yu is the sole shareholder of ABG Management Ltd., which is the sole member of Ally

Table of Contents

Bridge Group (NY) LLC, which manages Ally Bridge’s investments. As such, each of the foregoing entities and Mr. Fan Yu may be deemed to share beneficial ownership of the shares held of record by Ally Bridge. Each of them disclaims any such beneficial ownership. The principal business address of Ally Bridge is c/o Ally Bridge Group (NY) LLC, 430 Park Avenue, 12th Floor, New York, NY 10022.

- (13) CVI Investments, Inc. directly holds the 425,500 shares of common stock reported under “Shares of Common Stock Beneficially Owned Prior to the Offering”. In addition to the foregoing shares, as of September 30, 2022, CVI Investments, Inc. held Warrants to purchase 425,500 shares of common stock that are not included in the shares reported under “Shares of Common Stock Beneficially Owned Prior to the Offering” because they are not exercisable until March 16, 2023. The shares reported under “Number of Shares of Common Stock Being Offered” consist of (i) the shares reported as beneficially owned by CVI Investments, Inc. under “Shares of Common Stock Beneficially Owned Prior to the Offering” and (ii) the shares issuable upon exercise of Warrants held by CVI Investments, Inc. described above. Heights Capital Management, Inc. is the authorized agent of CVI Investments, Inc. and may be deemed to have investment discretion and voting power over the shares held by CVI Investments, Inc. Martin Kobinger, in his capacity as Investment Manager of Heights Capital Management, Inc., may also be deemed to have investment discretion and voting power over the shares held by CVI Investments, Inc. The business address of Martin Kobinger and the entity is c/o Heights Capital Management, Inc., 101 California Street, Suite 3250, San Francisco, California 94111.
- (14) Altium Growth Fund, LP directly holds the 319,100 shares of common stock reported under “Shares of Common Stock Beneficially Owned Prior to the Offering”. In addition to the foregoing shares, as of September 30, 2022, Altium Growth Fund, LP held Warrants to purchase 319,100 shares of common stock that are not included in the shares reported under “Shares of Common Stock Beneficially Owned Prior to the Offering” because they are not exercisable until March 16, 2023. The shares reported under “Number of Shares of Common Stock Being Offered” consist of (i) the shares reported as beneficially owned by Altium Growth Fund, LP under “Shares of Common Stock Beneficially Owned Prior to the Offering” and (ii) the shares issuable upon exercise of Warrants held by Altium Growth Fund, LP described above. Altium Capital Management, LP, the investment manager of Altium Growth Fund, LP, has voting and investment power over these securities. Jacob Gottlieb is the managing member of Altium Capital Growth GP, LLC, which is the general partner of Altium Growth Fund, LP. Each of Altium Growth Fund, LP and Jacob Gottlieb disclaims beneficial ownership over these securities. The address of Altium Capital Management, LP is 152 West 57th Street, 20th Floor, New York, NY 10019.
- (15) The shares reported under “Shares of Common Stock Beneficially Owned Prior to the Offering” consist of (i) 101,000 shares of common stock held by Dafna Lifescience LP (“Dafna LP”) and (ii) 31,978 shares of common stock held by Dafna Lifescience Select LP (“Dafna Select LP”). In addition to the foregoing shares, as of September 30, 2022, (i) Dafna LP held Warrants to purchase 101,000 shares of common stock and (ii) Dafna Select LP held Warrants to purchase 31,978 shares of common stock that are not included in the shares reported under “Shares of Common Stock Beneficially Owned Prior to the Offering” because they are not exercisable until March 16, 2023. The shares reported under “Number of Shares of Common Stock Being Offered” consist of (i) the shares reported as beneficially owned by Dafna LP and Dafna Select LP under “Shares of Common Stock Beneficially Owned Prior to the Offering” and (ii) the shares issuable upon exercise of Warrants held by Dafna LP and Dafna Select LP described above. DAFNA Capital Management LLC is the sole general partner of DAFNA LP and DAFNA Select LP. The Chief Executive Officer and Chief Investment Officer of DAFNA Capital Management LLC are Dr. Nathan Fischel and Dr. Fariba Ghodsian, respectively. These individuals may be deemed to have shared voting and investment power of the shares held by DAFNA LP and DAFNA Select LP. Each of Dr. Fischel and Dr. Fariba disclaim beneficial ownership of such shares, except to the extent of his or her pecuniary interest therein. The address of DAFNA LP and DAFNA Select LP is 10990 Wilshire Blvd., Suite 1400, Los Angeles, CA 90024.
- (16) JALAA Equities, LP (“JALAA”) directly holds the 26,595 shares of common stock reported under “Shares of Common Stock Beneficially Owned Prior to the Offering”. In addition to the foregoing shares, as of September 30, 2022, JALAA held Warrants to purchase 26,595 shares of common stock that are not included in the shares reported under “Shares of Common Stock Beneficially Owned Prior to the Offering”

[Table of Contents](#)

because they are not exercisable until March 16, 2023. The shares reported under “Number of Shares of Common Stock Being Offered” consist of (i) the shares reported as beneficially owned by JALAA under “Shares of Common Stock Beneficially Owned Prior to the Offering” and (ii) the shares issuable upon exercise of Warrants held by JALAA described above. Jason Aryeh is the managing general partner of JALAA. The address of JALAA is 34 Sumner Road, Greenwich, CT 06831.

PLAN OF DISTRIBUTION

The selling stockholders, which as used herein includes pledgees, assignees, donees, transferees or their respective successors-in-interest selling shares of common stock or interests in shares of common stock received after the date of this prospectus from a selling stockholder as a pledge, assignment, gift, partnership distribution or other transfer, may, from time to time, sell, transfer or otherwise dispose of any or all of their shares of common stock or interests in shares of common stock on any stock exchange, market or trading facility on which the shares are traded or in private transactions. These dispositions may be at fixed prices, at prevailing market prices at the time of sale, at prices related to the prevailing market price, at varying prices determined at the time of sale, or at negotiated prices.

The selling stockholders may use any one or more of the following methods when disposing of shares or interests therein:

- ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers;
- block trades in which the broker-dealer will attempt to sell the shares as agent, but may position and resell a portion of the block as principal to facilitate the transaction;
- purchases by a broker-dealer as principal and resale by the broker-dealer for its account;
- an exchange distribution in accordance with the rules of the applicable exchange;
- privately negotiated transactions;
- short sales;
- through the writing or settlement of options or other hedging transactions, whether through an options exchange or otherwise;
- broker-dealers may agree with the selling stockholders to sell a specified number of such shares at a stipulated price per share;
- a combination of any such methods of sale; and
- any other method permitted by applicable law.

The selling stockholders may, from time to time, pledge or grant a security interest in some or all of the shares of common stock owned by them and, if they default in the performance of their secured obligations, the pledgees or secured parties may offer and sell the shares of common stock, from time to time, under this prospectus, or under an amendment to this prospectus under Rule 424(b)(3) or other applicable provision of the Securities Act of 1933, as amended (the “Securities Act”), amending the list of selling stockholders to include the pledgee, transferee or other successors-in-interest as selling stockholders under this prospectus. The selling stockholders also may transfer the shares of common stock in other circumstances, in which case the transferees, pledgees, donees or other successors-in-interest will be the selling beneficial owners for purposes of this prospectus.

In connection with the sale of our common stock or interests therein, the selling stockholders may enter into hedging transactions with broker-dealers or other financial institutions, which may in turn engage in short sales of the common stock in the course of hedging the positions they assume. The selling stockholders may also sell shares of our common stock short and deliver these securities to close out their short positions, or loan or pledge the common stock to broker-dealers that in turn may sell these securities. The selling stockholders may also enter into option or other transactions with broker-dealers or other financial institutions or the creation of one or more derivative securities which require the delivery to such broker-dealer or other financial institution of shares offered by this prospectus, which shares such broker-dealer or other financial institution may resell pursuant to this prospectus (as supplemented or amended to reflect such transaction).

Table of Contents

The aggregate proceeds to the selling stockholders from the sale of the common stock offered by them will be the purchase price of the common stock less discounts or commissions, if any. Each of the selling stockholders reserves the right to accept and, together with their agents from time to time, to reject, in whole or in part, any proposed purchase of common stock to be made directly or through agents. We will not receive any of the proceeds from this offering. Upon any exercise of the pre-funded warrants or Warrants by payment of cash, however, we will receive the exercise price of the pre-funded warrants or Warrants.

The selling stockholders also may resell all or a portion of the shares in open market transactions in reliance upon Rule 144 under the Securities Act, provided that they meet the criteria and conform to the requirements of that rule.

The selling stockholders and any underwriters, broker-dealers or agents that participate in the sale of the common stock or interests therein may be “underwriters” within the meaning of Section 2(a)(11) of the Securities Act. Any discounts, commissions, concessions or profit they earn on any resale of the shares may be underwriting discounts and commissions under the Securities Act. Selling stockholders who are “underwriters” within the meaning of Section 2(a)(11) of the Securities Act will be subject to the prospectus delivery requirements of the Securities Act.

To the extent required, the shares of our common stock to be sold, the names of the selling stockholders, the respective purchase prices and public offering prices, the names of any agents, dealers or underwriters, and any applicable commissions or discounts with respect to a particular offer will be set forth in an accompanying prospectus supplement or, if appropriate, a post-effective amendment to the registration statement that includes this prospectus.

In order to comply with the securities laws of some states, if applicable, the common stock may be sold in these jurisdictions only through registered or licensed brokers or dealers. In addition, in some states the common stock may not be sold unless it has been registered or qualified for sale or an exemption from registration or qualification requirements is available and is complied with.

We have advised the selling stockholders that the anti-manipulation rules of Regulation M under the Securities Exchange Act of 1934, as amended (the “Exchange Act”), may apply to sales of shares in the market and to the activities of the selling stockholders and their affiliates. In addition, to the extent applicable, we will make copies of this prospectus (as it may be supplemented or amended from time to time) available to the selling stockholders for the purpose of satisfying the prospectus delivery requirements of the Securities Act. The selling stockholders may indemnify any broker-dealer that participates in transactions involving the sale of the shares against certain liabilities, including liabilities arising under the Securities Act.

We have agreed to indemnify the selling stockholders against liabilities, including liabilities under the Securities Act and state securities laws, relating to the registration of the shares offered by this prospectus.

We have agreed with the selling stockholders to use commercially reasonable efforts to cause the registration statement of which this prospectus forms a part to remain continuously effective until the earlier of (1) such time as all of the shares covered by this prospectus have been disposed of pursuant to and in accordance with such registration statement or (2) the date on which all of the shares may be sold without restriction pursuant to Rule 144 of the Securities Act.

LEGAL MATTERS

The validity of the shares of our common stock offered by this prospectus has been passed upon by Wilmer Cutler Pickering Hale and Dorr LLP.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our consolidated financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2021, as set forth in their report, which is incorporated by reference in this prospectus and elsewhere in the registration statement. Our financial statements are incorporated by reference in reliance on Ernst & Young LLP's report, given on their authority 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 also available to you on the SEC's website at www.sec.gov.

We make available, free of charge, through our investor relations website, our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, statements of changes in beneficial ownership of securities and amendments to those reports and statements as soon as reasonably practicable after they are filed with the SEC. The address for our website is <http://www.syros.com>. The contents on our website are not part of this prospectus, and the reference to our website does not constitute incorporation by reference into this prospectus of the information contained at that site.

This prospectus is part of a registration statement that 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 our securities. 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. You should review the complete document to evaluate these statements. You can obtain a copy of the registration statement from the SEC's website.

INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE

The SEC requires us to "incorporate" into this prospectus 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. Information contained in this prospectus and information that we file with the SEC in the future and incorporate by reference in this prospectus 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 and prior to the sale of all the shares covered by this prospectus, other than the portions of those documents not deemed to be filed.

- (1) Our Annual Report on [Form 10-K](#) for the year ended December 31, 2021, filed with the SEC on March 15, 2022 (including information specifically incorporated by reference therein from our Proxy Statement filed with the SEC on April 21, 2022);
- (2) Our Quarterly Report on [Form 10-Q](#) for the quarter ended March 31, 2022, filed with the SEC on May 16, 2022;

Table of Contents

- (3) Our Quarterly Report on [Form 10-Q](#) for the quarter ended June 30, 2022, filed with the SEC on August 9, 2022;
- (4) Our Current Reports on Form 8-K filed with the SEC on [January 10, 2022](#), [March 8, 2022](#), [June 7, 2022](#), [July 5, 2022](#), [July 6, 2022](#), [September 2, 2022](#), [September 15, 2022](#) and [September 16, 2022](#);
- (5) 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, 2021, and including any amendments or reports filed for the purpose of updating such description; and
- (6) Any other filings we make pursuant to the Exchange Act after the date of filing the registration statement of which this prospectus is a part and prior to effectiveness of the registration statement.

A statement contained in a document incorporated by reference into this prospectus shall be deemed to be modified or superseded for purposes of this prospectus to the extent that a statement contained in this prospectus, any prospectus supplement or in any other subsequently filed document which is also incorporated in this prospectus 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.

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: Nancy A. Simonian, M.D., President and Chief Executive Officer
Telephone: (617) 744-1340

27,627,824 Shares



Common Stock

PROSPECTUS

, 2022

PART II

INFORMATION NOT REQUIRED IN PROSPECTUS

Item 14. Other Expenses of Issuance and Distribution.

The following table sets forth the various expenses to be incurred in connection with the sale and distribution of the securities being registered hereby, all of which will be borne by the Registrant (except any underwriting discounts and commissions and expenses incurred by the selling stockholders for brokerage, accounting, tax or legal services or any other expenses incurred by the selling stockholders in disposing of the shares). All amounts shown are estimates except the SEC registration fee.

SEC registration fee	\$ 18,450
Accounting fees and expenses	30,000
Legal fees and expenses	40,000
Miscellaneous fees and expenses	1,550
Total	<u>\$ 90,000</u>

Item 15. Indemnification of Directors and Officers.

Section 145 of the General Corporation Law of the State of Delaware (“DGCL”) provides, generally, that a corporation shall have the power to indemnify any person who was or is a party or is threatened to be made a party to any threatened, pending or completed action, suit or proceeding (except actions by or in the right of the corporation) by reason of the fact that such person is or was a director, officer, employee or agent of the corporation against all expenses, judgments, fines and amounts paid in settlement actually and reasonably incurred by such person in connection with such action, suit or proceeding if such person acted in good faith and in a manner such person reasonably believed to be in or not opposed to the best interests of the corporation and, with respect to any criminal action or proceeding, had no reasonable cause to believe his or her conduct was unlawful. A corporation may similarly indemnify such person for expenses actually and reasonably incurred by such person in connection with the defense or settlement of any action or suit by or in the right of the corporation, *provided* that such person acted in good faith and in a manner he or she reasonably believed to be in or not opposed to the best interests of the corporation, and, in the case of claims, issues and matters as to which such person shall have been adjudged liable to the corporation, *provided* that a court shall have determined, upon application, that, despite the adjudication of liability but in view of all of the circumstances of the case, such person is fairly and reasonably entitled to indemnity for such expenses which such court shall deem proper.

Section 102(b)(7) of the DGCL provides, generally, that our certificate of incorporation may contain a provision eliminating or limiting the personal liability of a director to the corporation or its shareholders for monetary damages for breach of fiduciary duty as a director, *provided* that such provision may not eliminate or limit the liability of a director (i) for any breach of the director’s duty of loyalty to the corporation or its shareholders, (ii) for acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of law, (iii) under section 174 of the DGCL, or (iv) for any transaction from which the director derived an improper personal benefit. No such provision may eliminate or limit the liability of a director for any act or omission occurring prior to the date when such provision became effective.

Our restated certificate of incorporation provides that we will indemnify each person who was or is a party or threatened to be made a party to or is involved in any threatened, pending or completed action, suit or proceeding, whether civil, criminal, administrative or investigative (other than an action by or in the right of us) by reason of the fact that he or she is or was, or has agreed to become, our director or officer, or is or was serving, or has agreed to serve, at our request as a director, officer, partner, employee or trustee of, or in a similar capacity with, another corporation, partnership, joint venture, trust or other enterprise (all such persons being referred to as an “Indemnitee”), or by reason of any action alleged to have been taken or omitted in such

Table of Contents

capacity, against all expenses (including attorneys' fees), judgments, fines and amounts paid in settlement actually and reasonably incurred in connection with such action, suit or proceeding and any appeal therefrom, if such Indemnitee acted in good faith and in a manner he or she reasonably believed to be in, or not opposed to, our best interests, and, with respect to any criminal action or proceeding, he or she had no reasonable cause to believe his or her conduct was unlawful. Our restated certificate of incorporation also provides that we will indemnify any Indemnitee who was or is a party to an action or suit by or in the right of us to procure a judgment in our favor by reason of the fact that the Indemnitee is or was, or has agreed to become, our director or officer, or is or was serving, or has agreed to serve, at our request as a director, officer, partner, employee or trustee of, or in a similar capacity with, another corporation, partnership, joint venture, trust or other enterprise, or by reason of any action alleged to have been taken or omitted in such capacity, against all expenses (including attorneys' fees) and, to the extent permitted by law, amounts paid in settlement actually and reasonably incurred in connection with such action, suit or proceeding, and any appeal therefrom, if the Indemnitee acted in good faith and in a manner he or she reasonably believed to be in, or not opposed to, our best interests, except that no indemnification shall be made with respect to any claim, issue or matter as to which such person shall have been adjudged to be liable to us, unless a court determines that, despite such adjudication but in view of all of the circumstances, he or she is entitled to indemnification of such expenses. Notwithstanding the foregoing, to the extent that any Indemnitee has been successful, on the merits or otherwise, he or she will be indemnified by us against all expenses (including attorneys' fees) actually and reasonably incurred by him or her or on his or her behalf in connection therewith. If we do not assume the defense, expenses must be advanced to an Indemnitee under certain circumstances.

We have entered into indemnification agreements with our directors and executive officers. In general, these agreements provide that we will indemnify the director or executive officer to the fullest extent permitted by law for claims arising in his or her capacity as a director or officer of our company or in connection with their service at our request for another corporation or entity. The indemnification agreements also provide for procedures that will apply in the event that a director or executive officer makes a claim for indemnification and establish certain presumptions that are favorable to the director or executive officer.

We maintain a general liability insurance policy that covers certain liabilities of our directors and officers arising out of claims based on acts or omissions in their capacities as directors or officers.

Certain of our non-employee directors may, through their relationships with their employers, be insured and/or indemnified against certain liabilities in their capacity as members of our board of directors.

The underwriting agreement we entered into in connection with the initial public offering of our common stock provides that the underwriters will indemnify, under certain conditions, our directors and officers (as well as certain other persons) against certain liabilities arising in connection with such offering.

Insofar as the foregoing provisions permit indemnification of directors, executive officers, or persons controlling us for liability arising under the Securities Act of 1933, as amended (the "Securities Act"), we have been informed that, in the opinion of the Securities and Exchange Commission, such indemnification is against public policy as expressed in the Securities Act and is therefore unenforceable.

Item 16. Exhibits

<u>Exhibit No.</u>	<u>Description</u>
4.1	<u>Restated Certificate of Incorporation of the Registrant, including the Certificate of Designation of Preferences, Rights and Limitations of Series A Convertible Preferred Stock of the Registrant (incorporated by reference to Exhibit 3.1 to the Registrant's Quarterly Report on Form 10-Q for the quarter ended March 31, 2019 filed with the SEC on May 1, 2019 (FileNo. 001-37813)).</u>

Table of Contents

4.2	<u>Certificate of Amendment to the Restated Certificate of Incorporation of the Company related to the Share Increase Amendment, dated September 15, 2022 (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K filed with the SEC on September 16, 2022 (File No. 001-37813)).</u>
4.3	<u>Certificate of Amendment to the Restated Certificate of Incorporation of the Company related to the Stock Split Amendment, dated September 16, 2022 (incorporated by reference to Exhibit 3.2 to the Registrant's Current Report on Form 8-K filed with the SEC on September 16, 2022 (File No. 001-37813)).</u>
4.4	<u>Second Amended and Restated By-laws of the Registrant (incorporated by reference to Exhibit 3.2 to the Registrant's Quarterly Report on Form 10-Q for the quarter ended June 30, 2021 filed with the SEC on August 5, 2021 (FileNo. 001-37813)).</u>
4.5	<u>Form of Common Stock Certificate (incorporated by reference to Exhibit 4.1 to the Registrant's FormS-1 filed with the SEC on June 3, 2016 (File No. 333-211818)).</u>
4.6	<u>Form of Warrant to Purchase Common Stock or Pre-Funded Warrants (incorporated by reference to Exhibit 4.1 to the Registrant's Current Report on Form 8-K filed with the SEC on July 5, 2022 (FileNo. 001-37813)).</u>
4.7	<u>Form of Pre-Funded Warrant (incorporated by reference to Exhibit 4.2 to the Registrant's Current Report on Form 8-K filed with the SEC on July 5, 2022 (File No. 001-37813)).</u>
4.8	<u>Securities Purchase Agreement, dated July 3, 2022, by and among the Registrant and the persons party thereto (incorporated by reference to Exhibit 10.4 to the Registrant's Current Report on Form 8-K filed with the SEC on July 5, 2022 (File No. 001-37813)).</u>
4.9	<u>Registration Rights Agreement, dated July 3, 2022, by and among the Registrant and the persons party thereto (incorporated by reference to Exhibit 10.5 to the Registrant's Current Report on Form 8-K filed with the SEC on July 5, 2022 (File No. 001-37813)).</u>
5.1	<u>Opinion of Wilmer Cutler Pickering Hale and Dorr LLP.</u>
23.1	<u>Consent of Ernst & Young LLP, independent registered public accounting firm for the Registrant.</u>
23.2	<u>Consent of Wilmer Cutler Pickering Hale and Dorr LLP (included in Exhibit 5.1).</u>
24.1	<u>Powers of Attorney (included in the signature pages to the Registration Statement).</u>
107	<u>Filing Fee Table</u>

Item 17. Undertakings.

The undersigned Registrant hereby undertakes:

- (a)(1) To file, during any period in which offers or sales are being made, a post-effective amendment to this registration statement:
 - (i) To include any prospectus required by Section 10(a)(3) of the Securities Act of 1933, as amended (the "Securities Act");
 - (ii) To reflect in the prospectus any facts or events arising after the effective date of this registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in this registration statement. Notwithstanding the foregoing, any increase or decrease in the volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the Commission pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than a

Table of Contents

20 percent change in the maximum aggregate offering price set forth in the “Calculation of Registration Fee” table in the effective registration statement; and

- (iii) To include any material information with respect to the plan of distribution not previously disclosed in this registration statement or any material change to such information in this registration statement;

provided, however, that paragraphs (a)(1)(i), (a)(1)(ii) and (a)(1)(iii) do not apply if the information required to be included in a post-effective amendment by those paragraphs is contained in reports filed with or furnished to the Commission by the Registrant pursuant to Section 13 or Section 15(d) of the Securities Exchange Act of 1934, as amended (the “Exchange Act”), that are incorporated by reference in this registration statement, or is contained in a form of prospectus filed pursuant to Rule 424(b) that is part of this registration statement.

- (2) That, for the purposes of determining any liability under the Securities Act, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at the time shall be deemed to be the initial *bona fide* offering thereof.
- (3) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.
- (4) That, for the purpose of determining liability under the Securities Act to any purchaser:
 - (i) Each prospectus filed by the Registrant pursuant to Rule 424(b)(3) shall be deemed to be part of the registration statement as of the date the filed prospectus was deemed part of and included in the registration statement; and
 - (ii) Each prospectus required to be filed pursuant to Rule 424(b)(2), (b)(5), or (b)(7) as part of a registration statement in reliance on Rule 430B relating to an offering made pursuant to Rule 415(a)(1)(i), (vii), or (x) for the purpose of providing the information required by section 10(a) of the Securities Act shall be deemed to be part of and included in the registration statement as of the earlier of the date such form of prospectus is first used after effectiveness or the date of the first contract of sale of securities in the offering described in the prospectus. As provided in Rule 430B, for liability purposes of the issuer and any person that is at that date an underwriter, such date shall be deemed to be a new effective date of the registration statement relating to the securities in the registration statement to which that prospectus relates, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof. *Provided, however*, that no statement made in a registration statement or prospectus that is part of the registration statement or made in a document incorporated or deemed incorporated by reference into the registration statement or prospectus that is part of the registration statement will, as to a purchaser with a time of contract of sale prior to such effective date, supersede or modify any statement that was made in the registration statement or prospectus that was part of the registration statement or made in any such document immediately prior to such effective date.
- (b) The Registrant hereby undertakes that, for purposes of determining any liability under the Securities Act, each filing of the Registrant’s annual report pursuant to Section 13(a) or 15(d) of the Exchange Act (and, where applicable, each filing of an employee benefit plan’s annual report pursuant to Section 15(d) of the Exchange Act) that is incorporated by reference in this registration statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof.
- (c) Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers and controlling persons of the Registrant pursuant to the indemnification provisions described herein, or otherwise, the Registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in

[Table of Contents](#)

the Securities Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the Registrant of expenses incurred or paid by a director, officer or controlling person of the Registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the Registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act and will be governed by the final adjudication of such issue.

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, as amended, the Registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and has duly caused this Registration Statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Cambridge, Commonwealth of Massachusetts, on this 14th day of October, 2022.

SYROS PHARMACEUTICALS, INC.

By: /s/ Nancy Simonian
Name: Nancy Simonian, M.D.
Title: President, Chief Executive Officer and Director

SIGNATURES AND POWER OF ATTORNEY

We, the undersigned officers and directors of Syros Pharmaceuticals, Inc. hereby severally constitute and appoint Nancy Simonian and Jason Haas, and each of them singly, our true and lawful attorneys with full power to any of them, and to each of them singly, to sign for us and in our names in the capacities indicated below the Registration Statement on Form S-3 filed herewith and any and all pre-effective and post-effective amendments to said Registration Statement and generally to do all such things in our name and behalf in our capacities as officers and directors to enable Syros Pharmaceuticals, Inc. to comply with the provisions of the Securities Act of 1933, as amended, and all requirements of the Securities and Exchange Commission, hereby ratifying and confirming our signatures as they may be signed by our said attorneys, or any of them, to said Registration Statement and any and all amendments thereto.

Pursuant to the requirements of the Securities Act of 1933, as amended, this Registration Statement has been signed by the following persons in the capacities and on the dates indicated.

<u>Signature</u>	<u>Title</u>	<u>Date</u>
<u>/s/ Nancy Simonian</u> Nancy Simonian, M.D.	President, Chief Executive Officer and Director (Principal Executive Officer)	October 14, 2022
<u>/s/ Jason Haas</u> Jason Haas	Chief Financial Officer (Principal Financial and Accounting Officer)	October 14, 2022
<u>/s/ Peter Wirth</u> Peter Wirth	Chair of the Board of Directors	October 14, 2022
<u>/s/ Srinivas Akkaraju</u> Srinivas Akkaraju, M.D., Ph.D.	Director	October 14, 2022
<u>/s/ Mark J. Alles</u> Mark J. Alles	Director	October 14, 2022
<u>/s/ Deborah Dunsire</u> Deborah Dunsire, M.D.	Director	October 14, 2022
<u>/s/ S. Gail Eckhardt</u> S. Gail Eckhardt, M.D.	Director	October 14, 2022

Table of Contents

<u>/s/ Marsha H. Fanucci</u> Marsha H. Fanucci	Director	October 14, 2022
<u>/s/ Andrew M. Oh</u> Andrew M. Oh	Director	October 14, 2022
<u>/s/ Timothy C. Tyson</u> Timothy C. Tyson	Director	October 14, 2022
<u>/s/ Richard A. Young</u> Richard A. Young, Ph.D.	Director	October 14, 2022

October 14, 2022

+1 617 526 6000 (t)
+1 617 526 5000 (f)
wilmerhale.comSyros Pharmaceuticals, Inc.
35 CambridgePark Drive, 4th Floor
Cambridge, MA 02140Registration Statement on Form S-3

Ladies and Gentlemen:

This opinion is furnished to you in connection with a Registration Statement on Form S-3 (the "Registration Statement") filed with the Securities and Exchange Commission (the "Commission") under the Securities Act of 1933, as amended (the "Securities Act"), for the registration of the resale of an aggregate of 27,627,824 shares (the "Shares") of common stock, \$0.001 par value per share (the "Common Stock"), of Syros Pharmaceuticals, Inc., a Delaware corporation (the "Company"). All of the Shares are being registered on behalf of certain stockholders of the Company (the "Selling Stockholders"). The Shares consist of (i) 6,387,173 outstanding shares of Common Stock (the "Outstanding Shares") that are held by the Selling Stockholders, (ii) 7,426,739 shares of Common Stock issuable upon the exercise of outstanding pre-funded warrants to purchase shares of Common Stock and (iii) 13,813,912 shares of Common Stock issuable upon the exercise of outstanding warrants to purchase shares of Common Stock (the "Warrants") (or issuable upon exercise of pre-funded warrants to purchase shares of Common Stock that are issuable to holders of Warrants upon exercise of such warrants for pre-funded warrants in lieu of Common Stock) (collectively, the "Warrant Shares" and any and all pre-funded warrants described in clauses (ii) and (iii), the "Pre-Funded Warrants") that are held by the Selling Stockholders.

We are acting as counsel for the Company in connection with the registration for resale of the Shares. We have examined signed copies of the Registration Statement as filed with the Commission. We have also examined and relied upon minutes of meetings of the stockholders and the Board of Directors of the Company as provided to us by the Company, the Certificate of Incorporation and By-Laws of the Company, each as restated and/or amended to date, and such other documents as we have deemed necessary for purposes of rendering the opinions hereinafter set forth.

In our examination of the foregoing documents, we have assumed the genuineness of all signatures, the authenticity of all documents submitted to us as originals, the conformity to original documents of all documents submitted to us as copies, the authenticity of the originals of such latter documents and the legal competence of all signatories to such documents.

Our opinion below, insofar as it relates to the Outstanding Shares being fully paid, is based solely on a certificate of the Chief Financial Officer of the Company confirming the Company's receipt of the consideration called for by the applicable resolutions authorizing the issuance of such Outstanding Shares.

Wilmer Cutler Pickering Hale and Dorr LLP, 60 State Street, Boston, Massachusetts 02109

Beijing Berlin Boston Brussels Denver Frankfurt London Los Angeles New York Palo Alto San Francisco Washington

We assume that the appropriate action will be taken, prior to the offer and sale of the Shares by the Selling Stockholders, to register and qualify the Shares for sale under all applicable state securities or “blue sky” laws.

We express no opinion herein as to the laws of any state or jurisdiction other than the state laws of the Commonwealth of Massachusetts, the General Corporation Law of the State of Delaware and the federal laws of the United States of America.

Based upon and subject to the foregoing, we are of the opinion that (i) the Outstanding Shares have been duly authorized for issuance and are validly issued, fully paid and nonassessable, and (ii) the Warrant Shares have been duly authorized for issuance and, when issued, delivered and paid for in accordance with the terms of the Pre-Funded Warrants or Warrants, as applicable, including the payment of the exercise price therefor, will be validly issued, fully paid and nonassessable.

It is understood that this opinion is to be used only in connection with the offer and sale of the Shares while the Registration Statement is in effect.

Please note that we are opining only as to the matters expressly set forth herein, and no opinion should be inferred as to any other matters. This opinion is based upon currently existing statutes, rules, regulations and judicial decisions, and we disclaim any obligation to advise you of any change in any of these sources of law or subsequent legal or factual developments which might affect any matters or opinions set forth herein.

We hereby consent to the filing of this opinion with the Commission as an exhibit to the Registration Statement in accordance with the requirements of Item 601(b)(5) of Regulation S-K under the Securities Act and to the use of our name therein and in the related Prospectus under the caption “Legal Matters.” In giving such consent, we do not hereby admit that we are in the category of persons whose consent is required under Section 7 of the Securities Act or the rules and regulations of the Commission.

Very truly yours,

/s/ Wilmer Cutler Pickering Hale and Dorr LLP

WILMER CUTLER PICKERING HALE AND DORR LLP

Consent of Independent Registered Public Accounting Firm

We consent to the reference to our firm under the caption “Experts” in the Registration Statement (FormS-3) and related Prospectus of Syros Pharmaceuticals, Inc. for the registration of 27,627,824 shares of its common stock and to the incorporation by reference therein of our report dated March 15, 2022, with respect to the consolidated financial statements of Syros Pharmaceuticals, Inc. included in its Annual Report for the year ended December 31, 2021, filed with the Securities and Exchange Commission.

/s/ Ernst & Young LLP

Boston, Massachusetts
October 14, 2022

Calculation of Filing Fee Tables

Form S-3
(Form Type)Syros Pharmaceuticals, Inc.
(Exact Name of Registrant as Specified in its Charter)

Table 1: Newly Registered and Carry Forward Securities

	Security Type	Security Class Title	Fee Calculation or Carry Forward Rule	Amount Registered	Proposed Maximum Offering Price Per Unit	Maximum Aggregate Offering Price	Fee Rate	Amount of Registration Fee	Carry Forward Form Type	Carry Forward File Number	Carry Forward Initial Effective Date	Filing Fee Previously Paid In Connection with Unsold Securities to be Carried Forward
Newly Registered Securities												
Fees to Be Paid	Equity	Common Stock, \$0.001 par value per share	Other	27,627,824(1)	\$6.06(2)	\$167,424,614(2)	0.00011020	\$18,450.20				
Fees Previously Paid	—	—	—	—	—	—	—	—				
Carry Forward Securities												
Carry Forward Securities	—	—	—	—	—	—	—	—	—	—	—	—
	Total Offering Amounts					\$167,424,614(2)	—	\$18,450.20				
	Total Fees Previously Paid							—				
	Total Fee Offsets							—				
	Net Fee Due							\$18,450.20				

- (1) The shares of common stock will be offered for resale by the selling stockholders pursuant to the prospectus contained in the registration statement to which this exhibit is attached. The registration statement registers the resale of an aggregate of 27,627,824 shares of the Registrant's common stock, which consists of (i) 6,387,173 outstanding shares of common stock, (ii) 7,426,739 shares of common stock issuable upon the exercise of outstanding pre-funded warrants and (iii) 13,813,912 shares of common stock issuable upon the exercise of outstanding warrants (or issuable upon exercise of pre-funded warrants to purchase shares of common stock that are issuable to holders of warrants upon exercise of such warrants for pre-funded warrants in lieu of common stock). Pursuant to Rule 416 under the Securities Act of 1933, as amended (the "Securities Act"), the shares of common stock being registered hereunder include such indeterminate number of shares of common stock as may be issuable upon stock splits, stock dividends, or other distribution, recapitalization or similar events.
- (2) This estimate is made pursuant to Rule 457(c) of the Securities Act solely for purposes of calculating the registration fee. The price per share and aggregate offering price are based upon the average of the high and low prices of the Registrant's common stock on October 12, 2022, as reported on the Nasdaq Global Select Market.