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

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

Filed by the Registrant

Filed by a Party other than the Registrant

Check the appropriate box:

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

SYROS PHARMACEUTICALS, INC.

(Name of Registrant as Specified in Its Charter)

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

Payment of Filing Fee (Check the appropriate box):

- No fee required
- Fee paid previously with preliminary materials
- Fee computed on table in exhibit required by Item 25(b) per Exchange Act Rules 14a-6(i)(1) and 0-11
-
-



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

**NOTICE OF 2022 ANNUAL MEETING OF STOCKHOLDERS
To Be Held on June 1, 2022**

Dear Stockholders:

You are cordially invited to attend the 2022 annual meeting of stockholders of Syros Pharmaceuticals, Inc. The meeting will be held virtually via the Internet at www.meetnow.global/M7TXWW9 on Wednesday, June 1, 2022 at 11:00 a.m., Eastern Daylight Time.

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

1. The election of three Class III directors, S. Gail Eckhardt, M.D., Marsha H. Fanucci, and Nancy A. Simonian, M.D., nominated by our board of directors, each to serve for a three-year term expiring at the 2025 annual meeting of stockholders and until her successor has been duly elected and qualified;
2. The ratification of the appointment of Ernst & Young LLP as our independent registered public accounting firm for the fiscal year ending December 31, 2022;
3. The approval, on a non-binding advisory basis, of the compensation of our named executive officers;
4. The recommendation, on a non-binding advisory basis, of the frequency of future advisory votes on the compensation of our named executive officers; and
5. The transaction of any other business that may properly come before the annual meeting or any adjournment or postponement thereof.

As noted above, our annual meeting will be a “virtual meeting” of stockholders, which will be conducted exclusively via the Internet. There will not be a physical meeting location, and stockholders will not be able to attend the annual meeting in person. This means that you can attend the annual meeting online, vote your shares during the online meeting and submit questions for consideration prior to and during the online meeting, all by following the instructions described in the accompanying proxy statement. Stockholders of record at the close of business on April 4, 2022 will be entitled to notice of and to vote at the annual meeting or any adjournment or postponement thereof. We believe that hosting a “virtual meeting” will enable greater stockholder attendance and participation from any location around the world.

This Notice, the accompanying proxy statement and a form of proxy card are being mailed beginning on or about April 21, 2022 to all stockholders entitled to vote at the annual meeting. We have elected to provide access to our proxy materials over the Internet under the Securities and Exchange Commission’s “notice and access” rules. We believe that providing our proxy materials over the Internet expedites stockholders’ receipt of proxy materials, lowers costs and reduces the environmental impact of our annual meeting.

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

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

By Order of the Board of Directors,

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

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

Cambridge, Massachusetts
April 21, 2022

Important Notice Regarding Internet Availability of Proxy Materials: The attached proxy statement and our 2021 annual report to stockholders, which includes our Annual Report on Form 10-K for the fiscal year ended December 31, 2021, are available at www.envisionreports.com/SYRS. These documents are also available to any stockholder who wishes to receive a paper copy by calling (866) 641-4276, by emailing investorvote@computershare.com with “Proxy Materials Syros Pharmaceuticals, Inc.” in the subject line, or by submitting a request over the Internet at www.envisionreports.com/SYRS.

TABLE OF CONTENTS

INFORMATION CONCERNING SOLICITATION AND VOTING	1
IMPORTANT INFORMATION ABOUT THE ANNUAL MEETING AND VOTING	1
BOARD OF DIRECTORS AND CORPORATE GOVERNANCE	7
Election of Directors	7
Corporate Governance Matters	11
EXECUTIVE AND DIRECTOR COMPENSATION	20
Executive Officers	20
Executive Compensation	21
Outstanding Equity Awards at Fiscal Year End 2021	24
Employment Agreements; Potential Payments upon Termination or Change in Control	25
Tax Deductibility	26
Director Compensation	26
Limitation of Liability and Indemnification	27
SECURITIES AUTHORIZED FOR ISSUANCE UNDER EQUITY COMPENSATION PLANS	29
REPORT OF THE AUDIT COMMITTEE OF THE BOARD OF DIRECTORS	30
MATTERS TO BE VOTED ON	31
Proposal 1: Election of Directors	31
Proposal 2: Ratification of the Appointment of Independent Registered Public Accounting Firm	31
Proposal 3: Advisory Vote on Executive Compensation	33
Proposal 4: Advisory Vote on the Frequency of Future Executive Compensation Advisory Votes	34
STOCK OWNERSHIP AND REPORTING	35
Security Ownership of Certain Beneficial Owners and Management	35
OTHER MATTERS	38
Stockholder Proposals for our 2022 Annual Meeting	38
Householding of Annual Meeting Materials	38



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

PROXY STATEMENT
2022 ANNUAL MEETING OF STOCKHOLDERS
To Be Held on June 1, 2022

INFORMATION CONCERNING SOLICITATION AND VOTING

This proxy statement and the enclosed proxy card are being furnished in connection with the solicitation of proxies by the board of directors of Syros Pharmaceuticals, Inc. for use at the annual meeting of stockholders to be held on Wednesday, June 1, 2022 at 11:00 a.m., Eastern Daylight Time, and at any adjournment thereof. The meeting will be held virtually via the Internet at www.meetnow.global/M7TXWW9. You will be able to attend and participate in the annual meeting online, vote your shares electronically and submit your questions prior to and during the meeting, all by following the instructions described in this proxy statement in the section entitled "Important Information About the Annual Meeting and Voting." There will not be a physical meeting location, and stockholders will not be able to attend the annual meeting in person. Except where the context otherwise requires, references to "Syros Pharmaceuticals," "the Company," "we," "us," "our" and similar terms refer to Syros Pharmaceuticals, Inc.

This proxy statement summarizes information about the proposals to be considered at the meeting and other information you may find useful in determining how to vote. The proxy card is how you authorize another person to vote your shares in accordance with your instructions. We are making this proxy statement, the related proxy card and our annual report to stockholders for the fiscal year ended December 31, 2021 available to stockholders for the first time on or about April 21, 2022.

A copy of our Annual Report on Form 10-K for the fiscal year ended December 31, 2021, as filed with the Securities and Exchange Commission, or SEC, except for exhibits, will be furnished without charge to any stockholder upon written or oral request to Syros Pharmaceuticals, Inc., 35 CambridgePark Drive, 4th Floor, Cambridge, Massachusetts 02140 or by calling (866) 641-4276, by emailing investorvote@computershare.com with "Proxy Materials Syros Pharmaceuticals, Inc." in the subject line, or by submitting a request over the Internet at www.envisionreports.com/SYRS. This proxy statement and our Annual Report on Form 10-K for the fiscal year ended December 31, 2021 are also available on the SEC's website at www.sec.gov.

IMPORTANT INFORMATION ABOUT THE ANNUAL MEETING AND VOTING

Q. Why did I receive these proxy materials?

A. Our board of directors has made these materials available to you on the Internet in connection with the solicitation of proxies for use at our 2022 annual meeting of stockholders to be held virtually at www.meetnow.global/M7TXWW9 on Wednesday, June 1, 2022 at 11:00 a.m., Eastern Daylight Time. As a holder of common stock, you are invited to attend the annual meeting online and are requested to vote on the items of business described in this proxy statement. This proxy statement includes information that we are required to provide to you under SEC rules and that is designed to assist you in voting your shares.

Table of Contents

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

- A. In accordance with SEC rules, we may furnish proxy materials, including this proxy statement and our 2021 annual report, to our stockholders by providing access to such documents on the Internet instead of mailing printed copies. If you would like to receive a paper copy of our proxy materials, you should follow the instructions for requesting such materials in the notice.

Q. What is the purpose of the annual meeting?

- A. At the annual meeting, stockholders will consider and vote on the following matters:
1. The election of three Class III directors, S. Gail Eckhardt, M.D., Marsha H. Fanucci, and Nancy A. Simonian, M.D., nominated by our board of directors, each to serve for a three-year term expiring at the 2025 annual meeting of stockholders or until her successor has been duly elected and qualified (Proposal 1);
 2. The ratification of the appointment of Ernst & Young LLP as our independent registered public accounting firm for the fiscal year ending December 31, 2022 (Proposal 2);
 3. The approval, on a non-binding advisory basis, of the compensation of our named executive officers (Proposal 3);
 4. The recommendation, on a non-binding advisory basis, of the frequency of future advisory votes on the compensation of our named executive officers (Proposal 4); and
 5. The transaction of any other business that may properly come before the annual meeting or any adjournment or postponement thereof.

Q. Why is the 2022 annual meeting a virtual, online meeting?

- A. Our 2022 annual meeting will be a virtual meeting of stockholders where stockholders will participate by accessing a website using the Internet. There will not be a physical meeting location. We believe that hosting a virtual meeting will facilitate stockholder attendance and participation at our 2022 annual meeting by enabling stockholders to safely participate remotely from any location around the world. We have designed the virtual annual meeting to provide the same rights and opportunities to participate as stockholders have at an in-person meeting, including the right to vote and ask questions through the virtual meeting platform.

Q. How do I attend the annual meeting virtually?

- A. The annual meeting will be a completely virtual meeting of stockholders, which will be conducted exclusively by webcast. No physical meeting will be held. You are entitled to participate in the annual meeting only if you were a stockholder of record as of the close of business on April 4, 2022, the record date for our annual meeting, or if you hold a valid legal proxy for the annual meeting.

You will be able to attend the annual meeting online and submit your questions during the meeting by visiting www.meetnow.global/M7TXWW9. You also will be able to vote your shares online by attending the annual meeting by webcast.

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

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

Table of Contents

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

Q. How do I register to attend the virtual annual meeting?

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

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

To register to attend the annual meeting online by webcast you must submit proof of your proxy power (legal proxy) reflecting your holdings of shares of our common stock along with your name and email address to Computershare. A legal proxy is *not* the form of proxy included with this proxy statement. Requests for registration must be labeled as “Legal Proxy” and be received no later than 5:00 p.m., Eastern Daylight Time, on Thursday, May 26, 2022.

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

Requests for registration should be directed to Computershare as follows:

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

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

Q. What if I have trouble accessing the annual meeting virtually?

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

Q. Who can vote at the annual meeting?

- A. To be entitled to vote, you must have been a stockholder of record at the close of business on April 4, 2021, the record date for our annual meeting. There were 62,082,997 shares of our common stock outstanding and entitled to vote at the annual meeting as of the record date. The list of our stockholders of record will be available, via link on the meeting page (www.meetnow.global/M7TXWW9), during the annual meeting. In addition, we will make available a list of stockholders of record as of the record date for inspection by stockholders for any purpose germane to the annual meeting during the ten days preceding the annual meeting. To access the stockholder list during this time, please send your request, and proof of ownership, to our corporate secretary at 35 CambridgePark Drive, 4th Floor, Cambridge MA 02140, attention: Corporate Secretary.

Q. How many votes do I have?

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

Table of Contents

Q. How do I vote?

- A. **If you are the “record holder” of your shares** meaning that your shares are registered in your name in the records of our transfer agent, Computershare Trust Company, N.A., you may vote your shares at the virtual meeting or by proxy as follows:
1. **Over the Internet prior to or during the annual meeting:**To vote over the Internet, please go to the following website: www.envisionreports.com/SYRS, and follow the instructions at that site for submitting your proxy electronically. If you vote over the Internet, you do not need to complete and mail your proxy card or vote your proxy by telephone. You must specify how you want your shares voted or your Internet vote cannot be completed, and you will receive an error message. You must submit your Internet proxy before the closing of the polls at the annual meeting on June 1, 2022 for your proxy to be valid and your vote to count.
 2. **By telephone prior to the annual meeting:**To vote by telephone, please call (800)652-VOTE (8683), and follow the instructions provided on the proxy card. If you vote by telephone, you do not need to complete and mail your proxy card or vote your proxy over the Internet. You must specify how you want your shares voted and confirm your vote at the end of the call or your telephone vote cannot be completed. You must submit your telephonic proxy before 11:59 p.m., Eastern Daylight Time, on May 31, 2022, the day before the annual meeting, for your proxy to be valid and your vote to count.
 3. **By mail prior to the annual meeting:**To vote by mail, you must mark, sign and date the proxy card and then mail the proxy card in accordance with the instructions on the proxy card. If you vote by mail, you do not need to vote your proxy over the Internet or by telephone. Computershare Trust Company, N.A. must receive the proxy card not later than May 31, 2022, the day before the annual meeting, for your proxy to be valid and your vote to count. If you return your proxy card but do not specify how you want your shares voted on any individual matter, your shares will be voted in accordance with the recommendations of our board of directors.
 4. **Virtually at the annual meeting:** You will also be able to vote your shares online by attending the annual meeting by webcast by visiting www.meetnow.global/M7TXWW9. To participate in the annual meeting, you will need to review the information included on your notice, on your proxy card or on the instructions that accompanied your proxy materials.

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

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

However, under applicable stock exchange rules that regulate voting by registered brokerage firms, the election of our nominees to serve as Class III directors (Proposal 1), the advisory vote on the compensation paid to our named executive officers (Proposal 3), and the advisory vote to determine the frequency of future advisory votes on the compensation paid to our named executive officers (Proposal 4) are not considered to be discretionary items. Accordingly, if you do not give your broker voting instructions on Proposal 1, Proposal 3 or Proposal 4, your broker may not vote your shares with respect to these matters and

Table of Contents

your shares will be counted as “broker non-votes” with respect to these proposals. A “broker non-vote” occurs when shares held by a broker are not voted with respect to a proposal because the broker does not have or did not exercise discretionary authority to vote on the matter and has not received voting instructions from its clients.

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

Q. Can I change my vote?

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

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

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

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

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

A. Proposal 1—Election of Class III Directors

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

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

The affirmative vote of the holders of shares of common stock representing a majority of the votes cast on the matter is required for the ratification of the appointment of Ernst & Young LLP as our independent registered public accounting firm for the year ended December 31, 2022.

[Table of Contents](#)

Although stockholder approval of our audit committee's appointment of Ernst & Young LLP as our independent registered public accounting firm for the year ended December 31, 2022 is not required, we believe that it is advisable to give stockholders an opportunity to ratify this appointment. If this proposal is not approved at the annual meeting, our audit committee will reconsider its appointment of Ernst & Young LLP as our independent registered public accounting firm for the year ended December 31, 2022.

Proposal 3—Advisory Vote on the Compensation Paid to Named Executive Officers

To approve Proposal 3, holders of a majority of the votes cast on the matter must vote FOR the proposal. Proposal 3 is non-binding. Because this vote is advisory and not binding on us or our board in any way, our board may decide that it is in our and our stockholders' best interests to compensate our named executive officers in an amount or manner that differs from that which is approved by our stockholders.

Proposal 4—Advisory Vote on the Frequency of Future Advisory Votes on the Compensation Paid to Named Executive Officers

The approval of one of the three frequency options under Proposal 4 requires a majority of the votes cast on the matter. With respect to this proposal, if none of the frequency options (one year, two years or three years) receive a majority vote, we will consider the frequency that receives the highest number of votes cast by stockholders to be the frequency that has been recommended by stockholders. Proposal 4 is non-binding. Because this vote is advisory and not binding on us or our board in any way, our board may decide that it is in our and our stockholders' best interests to hold an advisory vote on executive compensation more or less frequently than the alternative approved by our stockholders.

Shares that abstain from voting and "broker non-votes" with respect to a matter will not be counted as votes in favor of such matter and will also not be counted as shares voting on such matter. Accordingly, abstentions and "broker non-votes" will have no effect on the voting on Proposal 1, Proposal 2, Proposal 3 or Proposal 4 referenced above.

Q. Who will count the vote?

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

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

- A. Our board of directors recommends that you vote:

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

FOR the ratification of the appointment of Ernst & Young LLP as our independent registered public accounting firm for the fiscal year ending December 31, 2022;

FOR the approval, on an advisory (non-binding) basis, of the compensation of our named executive officers; and

FOR holding, on an advisory (non-binding) basis, an annual vote on the compensation of our named executive officers.

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

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

[Table of Contents](#)

Q. How do I submit a question at the annual meeting?

- A. You will be able to attend the annual meeting online and submit your questions during the meeting by visiting www.meetnow.global/M7TXWW9, as further described above under “How do I attend the virtual annual meeting?”. Questions pertinent to meeting matters will be answered during the meeting, subject to time constraints. The meeting is not to be used as a forum to present personal matters, or general economic, political or other views that are not directly related to our business and the matters properly before the meeting, and therefore questions on such matters will not be answered. All questions received from stockholders before or during the virtual annual meeting will be posted on our website at ir.syros.com as soon as practicable following the annual meeting.

Q. Where can I find the voting results?

- A. We plan to announce preliminary voting results at the annual meeting and will report final voting results in a Current Report on Form 8-K filed with the SEC within four business days following the date of our annual meeting.

Q. What are the costs of soliciting these proxies?

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

BOARD OF DIRECTORS AND CORPORATE GOVERNANCE

Election of Directors

Our board of directors is divided into three classes, with members of each class holding office for staggered three-year terms. There are currently three Class III directors (S. Gail Eckhardt, M.D., Marsha H. Fanucci and Nancy A. Simonian, M.D.) whose terms expire at this annual meeting of stockholders, three Class I directors (Mark J. Alles, Amir Nashat, Ph.D., and Peter Wirth) whose terms expire at the 2023 annual meeting of stockholders, and four Class II directors (Srinivas Akkaraju, M.D., Ph.D., Deborah Dunsire, M.D., Phillip A. Sharp, Ph.D., and Richard A. Young, Ph.D.) whose terms expire at the 2024 annual meeting of stockholders (in all cases subject to the election and qualification of their successors or to their earlier death, resignation or removal). We believe that our classified board structure:

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

Set forth below are the names of and certain information for each member of our board, including the nominees for election as Class III directors, as of March 31, 2022. The information presented includes each director’s and nominee’s principal occupation and business experience for the past five years, and the names of other public companies of which he or she has served as a director during the past five years. The information presented below regarding the specific experience, qualifications, attributes and skills of each director and nominee led our nominating and corporate governance committee and our board of directors to conclude that he or she should serve as a director. In addition, we believe that all of our directors and nominees possess the attributes or characteristics described in “Corporate Governance Matters—Director Nomination Process” that the nominating

Table of Contents

and corporate governance committee expects of each director. There are no family relationships among any of our directors, nominees for director, or executive officers.

Name	Age	Position(s)
<i>Class III Director Nominees</i>		
S. Gail Eckhardt, M.D. (1)(2)	64	Director
Marsha H. Fanucci (3)	68	Director
Nancy A. Simonian, M.D.	61	President and Chief Executive Officer, Director
<i>Class I Directors</i>		
Mark J. Alles (3)	62	Director
Amir Nashat, Ph.D. (1)(3)	49	Director
Peter Wirth (4)	71	Chair of the Board of Directors
<i>Class II Directors</i>		
Srinivas Akkaraju, M.D., Ph.D. (1)(2)	54	Director
Deborah Dunsire, M.D. (2)(4)	59	Director
Phillip A. Sharp, Ph.D. (2)(4)	77	Director
Richard A. Young, Ph.D. (2)	68	Director

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

Class III Director Nominees

S. Gail Eckhardt, M.D. has been a member of our board of directors since September 2020. Dr. Eckhardt is a tenured Professor, inaugural Director of the Livestrong Cancer Institutes, Chair of the Department of Oncology, and Associate Dean of Cancer Programs at the University of Texas at Austin's Dell Medical School, or UT Austin. She has been a faculty member at the institution since January of 2017. Prior to joining UT Austin, Dr. Eckhardt was at the University of Colorado School of Medicine from 1999 to January 2017, where she had numerous roles and responsibilities, including Division Head of Medical Oncology, Associate Director for Translational Research at the University of Colorado Comprehensive Cancer Center and Director of the Phase I Program and Fellowship. Dr. Eckhardt served on the Board of Directors of NuGenerex Immuno-Oncology, Inc., a public biotechnology company, from March 2020 to May 2021, and has served on the Board of Directors of OncoTex Inc., a private biotechnology company, since January 2022. She has also served on numerous committees and study sections, including the ASCO Molecular Oncology Task Force, the ASCO Board of Directors, the FDA Oncology Drugs Advisory Committee, and the National Cancer Institute (NCI) Cancer Centers Study Section. She is a member of the NCI Investigational Drug Steering Committee and serves on several external advisory boards of NCI-designated cancer centers, was a lead mentor in ASCO's Leadership Development Program and currently is a member of the Board of Directors of the Association of American Cancer Institutes. Dr. Eckhardt earned her B.S. degree in chemistry from Stephen F. Austin State University and her M.D. from the University of Texas Medical Branch in Galveston. She conducted her internship and residency in Internal Medicine at the University of Virginia Medical School, followed by a post-doctoral research fellowship in Experimental and Molecular Medicine at Scripps Research Institute in La Jolla, California, and a fellowship in Medical Oncology at the University of California San Diego. We believe that Dr. Eckhardt is qualified for service on our board of directors due to her expertise in the preclinical and early clinical development of novel agents and her extensive drug development experience.

Marsha H. Fanucci has been a member of our board of directors since October 2015. Since 2009, Ms. Fanucci has been an independent consultant. From 2004 to 2009, she served as senior vice president and chief financial officer of Millennium Pharmaceuticals, Inc., a biopharmaceutical company, or Millennium, that was subsequently acquired by Takeda Pharmaceuticals Company, a publicly traded biopharmaceutical company,

Table of Contents

or Takeda. She previously served in various other roles at Millennium, including as vice president, finance and corporate strategy and vice president, corporate development. Ms. Fanucci is a member of the boards of directors of Alnylam Pharmaceuticals, Inc., Cycleron Therapeutics, Inc. and Forma Therapeutics Holdings, Inc., each a publicly traded biopharmaceutical company. She previously served as a director of Momenta Pharmaceuticals, Inc. and Ironwood Pharmaceuticals, Inc., each a publicly traded biopharmaceutical company. Ms. Fanucci received her B.S. in pharmacy from West Virginia University and her M.B.A. from Northeastern University. We believe Ms. Fanucci is qualified to serve on our board of directors due to her expertise with public and financial accounting matters and her experience leading financial organizations in biotechnology companies.

Nancy A. Simonian, M.D. has been our chief executive officer since July 2012. From 2001 to October 2011, Dr. Simonian was employed by Takeda and at Millennium. prior to its acquisition by Takeda, most recently as chief medical officer and senior vice president of clinical, medical and regulatory affairs. From 1995 to 2001, Dr. Simonian served at Biogen, Inc., a publicly traded biotechnology company, most recently as vice president of clinical development. She is a member of the board of directors of Seattle Genetics, Inc., a publicly traded biopharmaceutical company, the Damon Runyon Cancer Research Foundation and the Biotechnology Industry Organization. She previously served as a member of the board of directors of Evelo Biosciences, Inc. from April 2018 to June 2021. Prior to joining the biopharmaceutical industry, Dr. Simonian was on the faculty of Massachusetts General Hospital and Harvard Medical School as an assistant professor of neurology. She received a B.A. in biology from Princeton University and an M.D. from the University of Pennsylvania School of Medicine. We believe Dr. Simonian is qualified to serve on our board because of her role as our chief executive officer, her experience in the biopharmaceutical industry and her other executive leadership and board of directors experience.

Class I Directors

Mark J. Alles has served on our board of directors since December 2019. Mr. Alles served as chief executive officer of Celgene Corporation, a global biopharmaceutical company, or Celgene, from March 2016 to June 2018 and as its chairman and chief executive officer from February 2018 until its acquisition by Bristol-Myers Squibb Company in November 2019. Prior to these roles, Mr. Alles served as Celgene's president and chief operating officer from August 2014 to February 2016 and as its chief commercial officer and executive vice president, hematology & oncology from December 2012 to July 2014. Mr. Alles first joined Celgene in April 2004 and served in a number of commercial management positions of increasing responsibility at the company. Before joining Celgene, he held senior commercial management roles at Aventis Pharmaceuticals Inc. (Rhône-Poulenc Rorer) from 1993 to 2004. He is currently chairman of the board of directors of Turning Point Therapeutics, Inc., a public oncology company, and also serves on the board of directors of Antengene Corporation Limited and BioMarin Pharmaceuticals, both public biopharmaceutical companies. He is also a member of the board of directors and consulting CEO for PIKSci, Inc., a private biotechnology company. Mr. Alles received B.S. degree from Lock Haven University of Pennsylvania and served as a Captain in the United States Marine Corps. We believe that Mr. Alles is qualified for service on our board of directors due to his extensive executive experience and his track record of building successful global oncology organizations and commercializing innovative therapies.

Amir Nashat, Ph.D. has served on our board of directors since January 2016. He is a managing partner at Polaris Partners, a venture capital firm, where he has worked since 2002. Dr. Nashat also serves on the advisory board of the Partners Healthcare Innovation Fund. Dr. Nashat serves on the board of directors of Scholar Rock, Inc., a biopharmaceutical company. He previously served on the boards of directors of aTyr Pharma, Inc., Bind Therapeutics, Inc., Fate Therapeutics, Inc., Receptos, Inc. and Selecta Biosciences, Inc., each a biopharmaceutical company. Dr. Nashat received a Ph.D. in chemical engineering from MIT, and an M.S. and B.S. in materials science and mechanical engineering from the University of California, Berkeley. We believe Dr. Nashat is qualified to serve on our board of directors because of his experience on the boards of directors of other publicly traded companies and his experience as an investor in biotechnology and life sciences companies.

Table of Contents

Peter Wirth has served as Chair of our board of directors since January 2017. Mr. Wirth currently serves as chair of Forma Therapeutics Holdings, Inc., a publicly traded biotechnology company, as a director and senior advisor to Zai Lab Limited, a publicly traded biopharmaceutical company based in Shanghai, China, and as a director at Kira Pharmaceuticals, Inc., and Centrexion Therapeutics Corp., each a privately held biotechnology company. Mr. Wirth was a senior executive at Genzyme Corporation, or Genzyme, from 1996 until after its acquisition by Sanofi-Aventis in 2011, most recently serving as executive vice president, legal and corporate development, chief risk officer and corporate secretary. During his time at Genzyme, Mr. Wirth had senior management responsibility for the company's legal function, corporate development function, molecular oncology division, polymer drug discovery and development division and enterprise risk management function. Mr. Wirth received his B.A. from the University of Wisconsin-Madison and his J.D. from Harvard Law School. We believe Mr. Wirth is qualified to serve on our board of directors due to his expertise in corporate governance and his experience in corporate strategy, product development and law in the biotechnology industry.

Class II Directors

Srinivas Akkaraju, M.D., Ph.D. has served on our board of directors since June 2017. Dr. Akkaraju is a founder and managing general partner of Samsara BioCapital, a venture capital firm, a position he has held since March 2017. From April 2013 to February 2016, Dr. Akkaraju served as a general partner of Sofinnova Ventures, a venture capital firm. From January 2009 to April 2013, Dr. Akkaraju served as managing director of New Leaf Venture Partners, a venture capital firm. Dr. Akkaraju received an M.D. and a Ph.D. in immunology from Stanford University and undergraduate degrees in biochemistry and computer science from Rice University. Dr. Akkaraju serves as a director of Intercept Pharmaceuticals, Inc., a publicly traded biotechnology company, and Jiya Acquisition Corp., a publicly traded special purpose acquisition company. Previously, he served as a director of Aravive, Inc., aTyr Pharma, Inc., Principia Biopharma Inc., Seattle Genetics, Inc., and ZS Pharma Inc., each a publicly traded biotechnology company. We believe that Dr. Akkaraju is qualified to serve on our board of directors because of his strong scientific background and extensive experience in private equity and venture capital investing.

Deborah Dunsire, M.D. has served on our board of directors since September 2021. Dr. Dunsire is President and Chief Executive Officer of H. Lundbeck A/S, a public biopharmaceutical company, a position she has held since September 2018. She previously served as President and Chief Executive Officer and a Director of Xtuit Pharmaceuticals, Inc., a private biopharmaceutical company, from January 2017 to March 2018. Prior to her position at Xtuit, she served as President and Chief Executive Officer and a Director of FORUM Pharmaceuticals Inc., a private pharmaceutical company, from July 2013 to May 2016. Prior to FORUM, Dr. Dunsire worked for Takeda Pharmaceutical Company Limited as a corporate officer from June 2010 to June 2011 and a Director from June 2011 to June 2013. She served as President, Chief Executive Officer and a Director of Millennium Pharmaceuticals, Inc. between 2005 and 2008, when it was acquired by Takeda, and then as President and Chief Executive Officer of Millennium: The Takeda Oncology Company after the acquisition between 2008 and 2013. Prior to Millennium, Dr. Dunsire held various roles of increasing responsibility at Novartis Pharma AG between 1988 and 2005. She currently serves as a Board member of Ultragenyx Pharmaceutical Inc, a public biopharmaceutical company. She obtained an MBBCh from the University of the Witwatersrand in South Africa. We believe that Dr. Dunsire is qualified to serve on the Board due to her extensive experience in the biotechnology and pharmaceutical sectors, including service as the chief executive officer of various pharmaceutical companies.

Phillip A. Sharp, Ph.D. has served on our board of directors since December 2012. Dr. Sharp has been an institute professor at the Massachusetts Institute of Technology, or MIT, since 1999. Much of Dr. Sharp's scientific work has been conducted at MIT's Center for Cancer Research (now the Koch Institute), which he joined in 1974 and directed from 1985 to 1991. He subsequently led the Department of Biology from 1991 to 1999 before assuming the directorship of the McGovern Institute from 2000 to 2004. Dr. Sharp is the winner of the 1993 Nobel Prize in Physiology or Medicine. Dr. Sharp is a member of the board of directors of Alnylam Pharmaceuticals, Inc. and Vir Biotechnology, Inc., each a publicly traded biopharmaceutical company. He earned

Table of Contents

his B.A. from Union College (Kentucky) and a Ph.D. in chemistry from the University of Illinois, Champaign-Urbana. He did his postdoctoral training at the California Institute of Technology. We believe Dr. Sharp is qualified to serve on our board of directors due to his scientific expertise and his experience as a director of a publicly traded company.

Richard A. Young, Ph.D. has served on our board of directors since our inception in November 2011. He is also one of our scientific co-founders and a member of our scientific advisory board. He has been a member of the Whitehead Institute and professor of Biology at MIT since 1984. In May 2012, he was elected into the National Academy of Sciences. Dr. Young has served as an advisor to Science magazine and the World Health Organization. Dr. Young currently serves on the board of directors of Omega Therapeutics, Inc., a public biotechnology company, and on the boards of directors of Camp4 Therapeutics, Inc. and Dewpoint Therapeutics, Inc., each a private biotechnology company. Dr. Young received his Ph.D. in molecular biophysics and biochemistry from Yale University. We believe Dr. Young is qualified to serve on our board of directors because of his scientific expertise and his role as one of our scientific co-founders.

Corporate Governance Matters

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

Corporate Governance Guidelines

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

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

Board Leadership Structure

Our corporate governance guidelines provide that the nominating and corporate governance committee shall periodically assess the board of directors’ leadership structure, including whether the offices of chief executive officer and chair of the board of directors should be separate. Our guidelines provide the board of directors with flexibility to determine whether the two roles should be combined or separated based upon our needs and the board of directors’ assessment of its leadership from time to time. We currently separate the roles of chief executive officer and chair of the board of directors. Dr. Simonian, as our president and chief executive officer, is responsible for setting the strategic direction for our company and for providing day-to-day leadership of our company, while Mr. Wirth, as chair of our board of directors, presides over meetings of the board of directors,

Table of Contents

including executive sessions of the board of directors, and performs oversight responsibilities. We do not currently have a lead independent director because the chair of our board of directors is independent within the meaning of the Nasdaq Listing Rules. Our board of directors has standing audit, compensation and nominating and corporate governance committees that currently consist of, and are chaired by, independent directors. Our board of directors delegates substantial responsibilities to the committees, which then report their activities and actions back to the full board of directors. We believe that the independent committees of our board of directors and their chairpersons promote effective independent governance. We believe this structure currently represents an appropriate allocation of roles and responsibilities for our company because it strikes an effective balance between management and independent leadership participation in our board of directors proceedings.

Board Determination of Independence

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

Our board of directors undertook a review of the composition of our board of directors and its committees and the independence of each director. Based upon information requested from and provided by each director concerning his or her background, employment and affiliations, including family relationships, our board of directors has determined that each of our directors other than Drs. Simonian and Young is an "independent director" as defined under Rule 5605(a)(2) of the Nasdaq Listing Rules. Dr. Simonian is not an independent director under Rule 5605(a)(2) because she is our president and chief executive officer, and Dr. Young is not an independent director because of consideration paid to him for consulting services. Our board of directors also determined that Mark J. Alles, Marsha H. Fanucci, and Amir Nashat, Ph.D., who currently comprise our audit committee, Deborah Dunsire, M.D., Phillip A. Sharp, Ph.D., and Peter Wirth, who currently comprise our compensation committee, and Srinivas Akkaraju, M.D., Ph.D., S. Gail Eckhardt, M.D., and Amir Nashat, Ph.D., who currently comprise our nominating and corporate governance committee, satisfy the independence standards for such committees established by the SEC and the Nasdaq Listing Rules, as applicable, including in the case of all members of the audit committee, the independence requirements contemplated by Rule 10A-3 under the Exchange Act and, in the case of all members of the compensation committee, the independence requirements contemplated by Rule 10C-1 under the Exchange Act. In making such determinations, our board of directors considered the relationships that each such non-employee director has with our company and all other facts and circumstances our board of directors deemed relevant in determining independence, including the beneficial ownership of our capital stock by each non-employee director.

[Table of Contents](#)

Board Diversity Matrix (as of March 31, 2022)

Board Size:				
Total Number of Directors	10			
	Female	Male	Non-binary	Did not Disclose Gender
Gender:				
Directors	4	6	0	0
Number of Directors who identify in Any of the Categories Below:				
African American or Black	0	0	0	0
Alaskan Native or Native American	0	0	0	0
Asian	0	2	0	0
Hispanic or Latinx	0	0	0	0
Native Hawaiian or Pacific Islander	0	0	0	0
White	4	4	0	0
Two or More Races or Ethnicities	0	0	0	0
Member of the LGBTQ+ Community	0	0	0	0
Did Not Disclose	0	0	0	0

Board of Director Meetings and Attendance

Our board of directors held seven meetings during the year ended December 31, 2021, or fiscal 2021. During fiscal 2021, each of the directors then in office attended at least 75% of the aggregate number of board of director meetings and the number of meetings held by all committees of the board of directors on which such director then served. Our corporate governance guidelines set out an expectation that directors attend the annual meeting of stockholders. Seven of the nine directors who were then serving on our board of directors attended our 2021 annual meeting of stockholders.

Communicating with the Independent Directors

Our board of directors will give appropriate attention to written communications that are submitted by stockholders and will respond if and as appropriate. The chair of the board of directors is primarily responsible for monitoring communications from stockholders and for providing copies or summaries to the other directors as he considers appropriate.

Communications are forwarded to all directors if they relate to important substantive matters and include suggestions or comments that the chair of the board considers to be important for the directors to know. In general, communications relating to corporate governance and corporate strategy are more likely to be forwarded than communications relating to ordinary business affairs, personal grievances and matters as to which we receive repetitive or duplicative communications.

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

Committees of the Board of Directors

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

Table of Contents

Audit Committee

Our audit committee's responsibilities include:

- appointing, approving the compensation of, and assessing the independence of our registered public accounting firm;
- overseeing the work of our independent registered public accounting firm, including through the receipt and consideration of reports from such firm;
- reviewing and discussing with management and our independent registered public accounting firm our annual and quarterly financial statements and related disclosures;
- monitoring our internal control over financial reporting, disclosure controls and procedures and code of business conduct and ethics;
- overseeing our internal audit function, if any;
- overseeing our risk assessment and risk management policies;
- establishing procedures for the receipt and retention of accounting related complaints and concerns;
- meeting independently with our internal auditing staff, if any, our independent registered public accounting firm and management;
- reviewing and approving or ratifying any related person transactions; and
- preparing the audit committee report required by SEC rules.

The current members of our audit committee are Mark J. Alles, Marsha H. Fanucci and Amir Nashat, Ph.D. Ms. Fanucci chairs the audit committee. Our board of directors has determined that Ms. Fanucci qualifies as an "audit committee financial expert" within the meaning of applicable SEC rules. The audit committee held five meetings during fiscal 2021.

Compensation Committee

Our compensation committee's responsibilities include:

- reviewing and approving, or making recommendations to our board with respect to, the compensation of our chief executive officer and other executive officers;
- overseeing the evaluation of our senior executives;
- overseeing and administering our cash and equity incentive plans;
- reviewing and making recommendations to our board of directors with respect to director compensation and management succession planning;
- reviewing and discussing annually with management our "Compensation Discussion and Analysis" disclosure if and to the extent such disclosure is then required by SEC rules; and
- preparing the compensation committee report if and to the extent then required by SEC rules.

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

The current members of our compensation committee are Deborah Dunsire, M.D., Phillip A. Sharp, Ph.D., and Peter Wirth. Mr. Wirth chairs the compensation committee. The compensation committee held seven meetings during fiscal 2021.

Table of Contents

Nominating and Corporate Governance Committee

Our nominating and corporate governance committee's responsibilities include:

- identifying individuals qualified to become members of our board of directors;
- recommending to our board the persons to be nominated for election as directors and to each of our board's committees;
- reviewing and making recommendations to our board of directors with respect to our board leadership structure and board committee structure;
- making recommendations to our board of directors with respect to accepting director resignations;
- developing and recommending to our board corporate governance principles; and
- overseeing an annual evaluation of our board.

The current members of our nominating and corporate governance committee are Srinivas Akkaraju, M.D., Ph.D., S. Gail Eckhardt, M.D., and Amir Nashat, Ph.D. Dr. Nashat chairs the nominating and corporate governance committee. The nominating and corporate governance committee held three meetings during fiscal 2021.

Research and Development Committee

Our research and development committee's responsibilities include:

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

The current members of our research and development committee are Srinivas Akkaraju, M.D., Ph.D., Deborah Dunsire, M.D., S. Gail Eckhardt, M.D., Phillip A. Sharp, Ph.D., and Richard A. Young, Ph.D. Dr. Young chairs the research and development committee. The research and development committee held three meetings during fiscal 2021.

Director Nomination Process

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

Criteria and Diversity

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

Table of Contents

The director biographies on pages 8 to 11 indicate each nominee’s experience, qualifications, attributes and skills that led our nominating and corporate governance committee and our board of directors to conclude he or she should continue to serve as a director. Our nominating and corporate governance committee and our board of directors believe that each of the nominees has the individual attributes and characteristics required of each of our directors, and the nominees as a group possess the skill sets and specific experience desired of our board of directors as a whole.

Our nominating and corporate governance committee does not have a policy (formal or informal) with respect to diversity, but believes that our board, taken as a whole, should embody a diverse set of skills, experiences and backgrounds. In this regard, the nominating and corporate governance committee also takes into consideration the diversity (for example, with respect to gender, race and national origin) of our board members. The nominating and corporate governance committee does not make any particular weighting of diversity or any other characteristic in evaluating nominees and directors.

Stockholder Nominations

Stockholders may recommend individuals to our nominating and corporate governance committee for consideration as potential director candidates by submitting their names, together with appropriate biographical information and background materials, a statement as to the number of shares of our common stock beneficially owned by the stockholder making the recommendation, and certain other information as set forth in our by-laws, to Syros Pharmaceuticals, Inc., Attention: Nominating and Corporate Governance Committee, 35 CambridgePark Drive, 4th Floor, Cambridge, Massachusetts 02140. If appropriate biographical and background material has been provided on or before the dates set forth in this proxy statement under the heading “Other Matters—Stockholder Proposals for our 2023 Annual Meeting,” the committee will evaluate stockholder-recommended candidates by following substantially the same process, and applying substantially the same criteria, as it follows for candidates submitted by others. If the board determines to nominate a stockholder-recommended candidate and recommends his or her election, then his or her name will be included in our proxy card for the next annual meeting.

Stockholders also have the right under our by-laws to directly nominate director candidates, without any action or recommendation on the part of the nominating and corporate governance committee or our board of directors, by following the procedures set forth under “Other Matters – Stockholder Proposals for our 2023 Annual Meeting.”

Oversight of Risk

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

Compensation Committee Interlocks and Insider Participation

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

Code of Business Conduct and Ethics

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

Policies and Procedures for Related Person Transactions

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

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

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

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

Table of Contents

- any other information regarding the related person transaction or the related person in the context of the proposed transaction that would be material to investors in light of the circumstances of the particular transaction.

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

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

Related Person Transactions

In addition to the compensation arrangements with directors and executive officers described elsewhere in this proxy statement, since January 1, 2020, we have engaged in the following transactions in which the amount involved exceeded the lesser of \$120,000 or 1% of the average of our total assets at year-end for the last two completed fiscal years, and any of our executive officers, directors, director nominees or 5% stockholders, or their immediate family members, or any person who was in any of those categories at the time of such transaction, had a direct or indirect material interest. We believe that all of these transactions were on terms comparable to terms that could have been obtained from unrelated third parties.

Private Placement

In December 2020, we completed a private placement of 10,312,500 shares of our common stock and, in lieu of common stock, pre-funded warrants to purchase an aggregate of 1,000,000 shares of common stock, and, in each case, accompanying warrants to purchase an aggregate of up to 2,828,125 additional shares of common stock (or pre-funded warrants to purchase common stock in lieu thereof) at a price of \$8.00 per share and accompanying warrant (or \$7.99 per pre-funded warrant and accompanying warrant). Samsara BioCapital, L.P., a venture capital firm, purchased 625,000 shares of our common stock and accompanying warrants to purchase 156,250 shares of our common stock (or pre-funded warrants to purchase common stock in lieu thereof) in this private placement at an aggregate purchase price of \$5.0 million. Srinivas Akkaraju, M.D., Ph.D. is one of the managers of Samsara BioCapital GP, LLC, which is the general partner of Samsara BioCapital, L.P.

Consulting Agreement with Dr. Young

Richard A. Young, Ph.D., earned \$115,000 during each of fiscal 2021 and fiscal 2020 pursuant to the terms of a consulting agreement he entered with our company that is unrelated to his service as a member of our board of directors.

Investors' Rights Agreement

Prior to its expiration in June 2021, we were a party to an amended and restated investors' rights agreement, dated as of October 9, 2014, with the purchasers of preferred stock prior to our IPO, including ARCH Venture Fund VII, L.P., entities affiliated with FMR LLC, entities affiliated with Flagship Ventures, entities affiliated with Polaris Partners (of which Amir Nashat is a managing partner), Nancy A. Simonian, M.D., and Phillip A. Sharp, Ph.D. The investors' rights agreement provided these holders the right to demand that we file a registration statement or request that their shares be covered by a registration statement that we are otherwise filing.

Restrictions on the Hedging or Pledging of Our Securities

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

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

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

Corporate Sustainability

Our mission is to build a sustainable company that provides long-term value for all our stakeholders. We support those environmental, social and governance (ESG) initiatives that may benefit the patients we aspire to serve, in a manner that aligns with our organizational culture, core values, and applicable regulatory requirements. Our board of directors provides oversight over these ESG initiatives by reference to those standards of the Sustainability Accounting Standards Boards relevant to our business as currently conducted. During fiscal 2021, the specific activities reviewed by our board of directors included:

- vendor oversight and auditing;
- clinical trial and data integrity;
- drug safety;
- supply chain management;
- business ethics; and
- employee matters such as diversity, equity and inclusion, compensation practices, and workplace safety.

We are committed to fostering an environment where all employees, regardless of race, sex, sexual orientation, gender identity, religion, ethnicity, national origin, physical disability, or age, are empowered to achieve their full potential. The unique talents, backgrounds and perspectives of each employee strengthens our coordinated expression, making our company stronger and helping us to achieve our mission of developing medicines to transform patients’ lives. Our Diversity, Equity & Inclusion (DEI) committee is an employee-led group that implements a variety of grassroots initiatives including, among other things, transparent pay equity analyses, a DEI speaker series, and a company-wide allyship program. We are proud of the fact that women currently comprise roughly half of our functional leaders and 40% of the members of our board of directors, and we remain committed to continuing greater equity in the workplace and expanding the representation of historically underrepresented individuals, recognizing that a diverse set of voices is vital to our success.

EXECUTIVE AND DIRECTOR COMPENSATION

Executive Officers

Certain information regarding our executive officers as of March 31, 2022 is set forth below.

Name	Age	Position(s)
Nancy A. Simonian, M.D. ⁽¹⁾	61	President & Chief Executive Officer
Conley Chee	52	Chief Commercial Officer
Jason Haas	54	Chief Financial Officer
Eric R. Olson, Ph.D.	64	Chief Scientific Officer
David A. Roth, M.D.	59	Chief Medical Officer
Kristin Stephens	49	Chief Development Officer

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

Conley Chee has been our chief commercial officer since September 2021. He previously served as global head of portfolio management, global pipeline strategy and precision medicine at Novartis Oncology, or Novartis, a global pharmaceutical company from October 2018 to February 2021. In this role, Mr. Chee had strategic responsibility for shaping Novartis' overall pipeline, including driving commercial planning for the company's early-stage portfolio and diagnostics strategy for oncology. Earlier in his career at Novartis, Mr. Chee served as vice president – global head oncology lung franchise from 2015 to October 2018, as well as in multiple U.S. sales and marketing leadership roles. Prior to joining Novartis, Mr. Chee spent five years in roles of increasing responsibility at Pfizer, Inc., a global pharmaceutical company, ultimately serving as team leader of international business development. He holds a B.Sc. Pharm from the University of Alberta and an M.B.A. from the Richard Ivey School of Business at the University of Western Ontario and completed his residency in Clinical Pharmacy at the University of British Columbia.

Jason Haas has been our chief financial officer since October 2021. He previously served asco-head of Americas, healthcare investment banking at Barclays from June 2016 to October 2021. Previously, he served as head of Americas, healthcare investment banking at Deutsche Bank from 2012 to June 2016. Prior to his role at Deutsche Bank, he was a managing director on the healthcare investment banking team at Goldman Sachs & Co. Mr. Haas holds a B.A. in International Relations and Economics from Colgate University and an M.B.A. in Finance from Columbia Business School.

Eric R. Olson, Ph.D. has been our chief scientific officer since April 2013. He previously served as research vice president for respiratory diseases at Vertex Pharmaceuticals, Inc., a biotechnology company, from 2001 to May 2013. Dr. Olson has also held positions as the director of antibacterials and molecular sciences departments at Warner-Lambert Co. as well as a research scientist focused on gene expression systems with The Upjohn Company, both of which were acquired by Pfizer Inc., a pharmaceutical company, or Pfizer. Dr. Olson serves on the boards of the Cystic Fibrosis Foundation and the National Brain Tumor Society. Dr. Olson received a B.S. in microbiology and immunology from the University of Minnesota and a Ph.D. in microbiology and immunology from the University of Michigan.

David A. Roth, M.D. has been our chief medical officer since December 2015. Previously, Dr. Roth was employed by Infinity from September 2013 until September 2015, serving most recently as its executive vice president and chief medical officer and previously as its senior vice president of clinical development and medical affairs. Prior to joining Infinity, Dr. Roth was the vice president, early development in the oncology business unit of Pfizer from 2009 to August 2013. Prior to joining the pharmaceutical industry, Dr. Roth's experience included over ten years in research and clinical practice as an academic hematologist, and he served on the full-time faculty at Harvard Medical School and Beth Israel Deaconess Medical Center in Boston. Dr. Roth received his B.S. from MIT and his M.D. from Harvard Medical School in the Harvard MIT Division of Health Sciences and Technology.

Table of Contents

Kristin Stephens has been our chief development officer since June 2020. She previously as our senior vice president of product development from August 2018 to June 2020, vice president of development operations from March 2018 to August 2018, and vice president of clinical operations from October 2015 to March 2018. Prior to Syros, Ms. Stephens spent nearly ten years at Millennium and Takeda in a variety of roles with escalating responsibilities, serving most recently as vice president of global clinical operations. Earlier in her career, Ms. Stephens worked at Quintiles Strategic Research Services, Clinical Assistance Programs and Eastern Cooperative Oncology Group. Ms. Stephens earned her B.A. in mathematics and psychology at William Smith College.

Executive Compensation

This section discusses the material elements of our executive compensation policies for our “named executive officers” and the most important factors relevant to an analysis of these policies. For 2021, our named executive officers are Nancy A. Simonian, M.D., our President and Chief Executive Officer, Jason Haas, our Chief Financial Officer, and David Roth, our Chief Medical Officer. In addition, this section provides qualitative information regarding the manner and context in which compensation is awarded to and earned by our named executive officers and is intended to place in perspective the data presented in the following tables and the corresponding narrative.

Summary Compensation Table

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

Name and Position of Named Executive Officers	Year	Salary (\$)	Option Awards (\$)(1)	Non-Equity Incentive Plan Comp-ensation (\$)(2)	All Other Comp-ensation (\$)(3)	Total (\$)
Nancy A. Simonian, M.D. (4)	2021	615,923	2,163,749	322,905	576	3,103,153
<i>President & Chief Executive Officer</i>	2020	597,692	1,503,457	429,000	360	2,530,509
Jason Haas (5)	2021	91,385	2,361,150	42,460	144	2,495,139
<i>Chief Financial Officer</i>	2020	—	—	—	—	—
David A. Roth, M.D.	2021	482,385	944,646	185,158	576	1,612,765
<i>Chief Medical Officer</i>	2020	468,269	480,697	244,400	360	1,193,726

- (1) The amounts reported in the “Option Awards” column reflects the aggregate grant date fair value of stock-based compensation awarded during the year computed in accordance with the provisions of Financial Accounting Standards Board Accounting Standard Codification, or ASC, Topic 718. This calculation does not give effect to any estimate of forfeitures related to service-based vesting but assumes that the named executive officer will perform the requisite service for the award to vest in full. See Note 12 to our financial statements included in our Annual Report on Form 10-K regarding assumptions underlying the valuation of equity awards.
- (2) The amounts reported in the “Non-Equity Incentive Plan Compensation” column reflect awards to our named executive officers under our performance-based cash incentive program. See “Cash Incentives” for a description of that program. Annual cash bonus awards earned during the year is typically paid in the following year.
- (3) The amounts reported in the “All Other Compensation” column reflect, for each named executive officer, the cost to us of life insurance premiums paid for the named executive officer.
- (4) Dr. Simonian also serves as a member of our board of directors but does not receive any additional compensation for her service as a director.
- (5) Mr. Haas commenced employment with us on October 12, 2021. Amounts shown for 2021 represent compensation earned by Mr. Haas during that partial year of employment.

Narrative Disclosure to Summary Compensation Table

We review compensation for our executive officers annually. The material terms of the elements of our executive compensation program for 2021 are described below.

Our compensation committee sets base salaries and bonuses and grants equity incentive awards to our executive officers. In setting base salaries and bonuses and granting equity incentive awards, our compensation committee considers compensation for comparable positions in the market, the historical compensation levels of our executives, individual and corporate performance as compared to our expectations and objectives, our desire to motivate our employees to achieve short- and long-term results that are in the best interests of our stockholders, and a long-term commitment to our company. As part of this process, Dr. Simonian, as our president and chief executive officer, prepares performance evaluations for the other executive officers and recommends annual salary increases, annual stock option awards and cash bonuses to the compensation committee. The compensation committee conducts a performance evaluation of Dr. Simonian. The compensation committee consults with the board of directors as to the achievement of corporate objectives that drive contingent compensation awards.

During its annual compensation review, our compensation committee also consults with external advisors. In fiscal 2021, the compensation committee engaged Compensia Inc. as its independent compensation consultant to provide comparative data on executive compensation practices in our industry and assess our executives' compensation relative to comparable companies.

Base Salary

We use base salaries to recognize the experience, skills, knowledge and responsibilities required of all our employees, including our named executive officers. None of our named executive officers is currently party to an employment agreement or other agreement or arrangement that provides for automatic or scheduled increases in base salary.

In February 2020, the compensation committee set Dr. Simonian's annualized base salary to \$600,000 effective February 10, 2020. In February 2021, the compensation committee increased Dr. Simonian's annualized base salary to \$618,000 effective February 22, 2021. In February 2022, the compensation committee increased Dr. Simonian's annualized base salary to \$640,000 effective February 21, 2022.

Mr. Haas commenced employment with us in October 2021. In 2021, we paid him a base salary of \$91,385 for his partial year of employment based on an annualized base salary of \$440,000. In February 2022, the compensation committee of our board of directors increased Mr. Haas's annualized base salary to \$470,000 effective February 21, 2022.

In February 2020, the compensation committee set Dr. Roth's annualized base salary to \$470,000 effective February 10, 2020. In February 2021, the compensation committee increased Dr. Roth's annualized base salary to \$484,000 effective February 22, 2021. In February 2022, the compensation committee of our board of directors increased Dr. Roth's annualized base salary to \$500,000 effective February 21, 2022.

Cash Incentives

We have established a framework under which the compensation committee would, in its discretion, award annual performance-based cash bonuses to our executive officers for up to a specific percentage of his or her salary as a vehicle to reward achievement of value driving milestones and recognize individual performance. Dr. Simonian was eligible for a performance-based cash bonus of a percentage of her annual base salary, subject to achievement of corporate goals as determined by the compensation committee. Her bonus target was 55% of her annual base salary in the year ended December 31, 2020, or fiscal 2020, and fiscal 2021. Our other named executive officers are eligible for a performance-based cash bonus of a percentage of such named executive

Table of Contents

officer's base salary, 90% of which is tied to achievement of corporate goals as determined by the compensation committee, and 10% of which is tied to the achievement of individual goals as recommended by Dr. Simonian and approved by the compensation committee. The bonus target for our other named executive officers was 40% of the applicable officer's annual base salary for both fiscal 2020 and fiscal 2021.

In February 2021, we made cash bonus awards of \$429,000 to Dr. Simonian and \$244,400 to Dr. Roth based on the compensation committee's assessment of achievement of corporate and individual goals during fiscal 2020, and in February 2022, we made cash bonus awards of \$322,905 to Dr. Simonian, \$42,460 to Mr. Haas and \$185,158 to Dr. Roth based on the compensation committee's assessment of achievement of corporate and individual goals during fiscal year 2021.

Equity Incentives

Although we do not have a formal policy with respect to the grant of equity incentive awards to our executive officers, or any formal share ownership policy or guidelines applicable to them, we believe that equity awards are very effective in supporting executive recruitment, motivation, and retention in a highly competitive marketplace for experienced talent, provide our executive officers with a strong link to our long-term performance, create an ownership culture, and help to align the interests of our executive officers and our stockholders. In addition, we believe that equity awards with a time-based vesting condition promote executive retention because this feature incentivizes our executive officers to remain in our employment during the award's vesting period. Accordingly, the compensation committee periodically reviews the equity incentive compensation holdings of our named executive officers and from time to time may grant equity incentive awards to them in the form of stock options and/or restricted stock unit awards. The compensation committee carefully manages our share utilization and the dilutive effect of the equity incentive awards that it grants in order to ensure the long-term sustainability of our equity incentive plan. As a result of the ongoing volatility in the equity markets for development-stage companies in our industry and the imperative to continue to motivate and retain our executive officers through the completion of the potential value-creating clinical milestones in the future, we expect that the number of shares subject to the equity incentive awards granted by the compensation committee during 2022 will increase.

In February 2020, Dr. Simonian was granted an option to purchase 294,000 shares of our common stock and Dr. Roth was granted an option to purchase 94,000 shares of our common stock. These options vested as to 25% of the shares on February 28, 2021, with the remaining shares vesting in equal monthly installments thereafter through February 29, 2024, subject to the applicable officer's continued service through the applicable vesting date.

In February 2021, Dr. Simonian was granted an option to purchase 304,000 shares of our common stock and Dr. Roth was granted an option to purchase 119,000 shares of our common stock. These options vested as to 25% of the shares on February 28, 2022, with the remaining shares vesting in equal monthly installments thereafter through February 28, 2025, subject to the applicable officer's continued service through the applicable vesting date.

In October 2021, Mr. Haas was granted an option to purchase 750,000 shares of our common stock in connection with his appointment as our Chief Financial Officer as an inducement material to Mr. Haas' acceptance of employment with the company in accordance with Nasdaq Listing Rule 5635(c)(4). This option vests as to 25% of the shares subject to the option on October 12, 2022, with the remaining shares vesting in equal monthly installments thereafter through October 12, 2025, subject to Mr. Haas's continued service through each applicable vesting date. The size of this equity award was driven largely by the value of new-hire equity incentive awards granted to chief financial officers at comparable companies as well as the compensation committee's desire to make Mr. Haas whole of the value of the deferred compensation he would be forfeiting upon leaving his prior employer.

Outstanding Equity Awards at Fiscal Year End 2021

The following table sets forth information regarding outstanding equity awards held by our named executive officers as of December 31, 2021.

Current Named Executive Officers	Option Awards				Stock Awards	
	Number of Securities Underlying Unexercised Options Exercisable (#)	Number of Securities Underlying Unexercised Options Unexercisable (#)	Option Exercise Price (\$/share)	Option Expiration Date	Number of Shares or Units of Stock That Have Not Vested (#)	Market Value of Shares or Units of Stock That Have Not Vested (\$)(1)
Nancy A. Simonian, M.D.	37,666(2)	—	3.04	2/4/2025	188,000(8)	612,880
	34,838(2)	—	3.04	6/8/2025		
	21,524(2)	—	3.04	6/8/2025		
	79,165(2)	—	8.51	3/30/2026		
	75,000(2)	—	12.17	9/15/2026		
	175,000(2)	—(2)	10.90	2/9/2027		
	268,134(3)	11,878(3)	10.09	2/15/2028		
	201,872(4)	83,128(4)	6.71	2/11/2029		
	134,748(5)	159,252(5)	7.54	2/12/2030		
	—(6)	304,000(6)	11.41	2/16/2031		
Jason Haas	—(7)	750,000(7)	4.54	10/11/2031		
David A. Roth, M.D.	223,661(2)	—	9.08	12/22/2025	87,000(8)	283,620
	63,500(2)	—	10.90	2/9/2027		
	71,873(3)	3,127(3)	10.09	2/15/2028		
	53,123(4)	21,877(4)	6.71	2/11/2029		
	43,082(5)	50,918(5)	7.54	2/12/3030		
	—(6)	119,000(6)	11.41	2/16/2031		

- (1) Calculated based on the closing price per share of our common stock on December 31, 2021, which was \$3.26.
- (2) This option is fully vested.
- (3) This option was granted on February 16, 2018 and vested as to 25% of the shares on February 16, 2019 with the remaining shares vesting in equal monthly installments thereafter through February 28, 2022, subject to continued service.
- (4) This option was granted on February 12, 2019 and vested as to 25% of the shares on February 11, 2020 with the remaining shares vesting in equal monthly installments thereafter through February 28, 2023, subject to continued service.
- (5) This option was granted on February 13, 2020 and vested as to 25% of the shares on February 12, 2021 with the remaining shares vesting in equal monthly installments thereafter through February 29, 2024, subject to continued service.
- (6) This option was granted on February 17, 2021 and vested as to 25% of the shares on February 17, 2022 with the remaining shares vesting in equal monthly installments thereafter through February 28, 2025, subject to continued service.
- (7) This option was granted on October 12, 2021 and vests as to 25% of the shares on October 12, 2022 with the remaining shares vesting in equal monthly installments thereafter through October 12, 2025, subject to continued service.
- (8) This restricted stock unit award vested in full on March 31, 2022.

Employment Agreements; Potential Payments upon Termination or Change in Control

We have entered into written offer letters with each of our named executive officers. These offer letters set forth the terms of the named executive officer's compensation, including his or her initial base salary, severance and annual cash bonus opportunity. In addition, the offer letters provide that the named executive officers are eligible to participate in company-sponsored benefit programs that are available generally to all of our employees. In connection with the commencement of their employment with us, our named executive officers executed our standard invention and non-disclosure agreement and non-competition and non-solicitation agreement.

Change in Control

The offer letter with Dr. Simonian provides that if her employment is terminated by us without cause, or by her with good reason, as such terms are defined in her offer letter, she will receive monthly severance payments equal to her then-current monthly salary rate for 12 months and payment of an incentive bonus pro-rated for the portion of the then-current calendar year during which she was employed by us, subject to certain conditions, including the execution of a release of all claims against the Company. In addition, in the event of a change in control of our company, as defined in the offer letter, all unvested stock options then held by Dr. Simonian will vest in full 12 months after the change in control, or earlier if her employment is terminated by us without cause or by her for good reason in contemplation of, pursuant to or following a change in control, referred to as the CIC Equity Vesting.

The offer letter with each of our other named executive officers provides that if his employment is terminated by us without cause, or by him with good reason, as such terms are defined in his offer letter, he will receive monthly severance payments equal to his then-current monthly rate of salary for nine months, subject to certain conditions, including the execution of a release of all claims against the Company. Our other named executive officers are also eligible for the CIC Equity Vesting.

Other Agreements

We have also entered into employee confidentiality, inventions, non-solicitation, and non-competition agreements with each of our named executive officers. Under the employee confidentiality, inventions, non-solicitation, and non-competition agreements, each named executive officer has agreed (1) not to compete with us during his or her employment and for a period of one year after the termination or cessation of his or her employment for any reason, (2) not to solicit our employees during his or her employment and for a period of one year after the termination or cessation of his or her employment for any reason, (3) to protect our confidential and proprietary information and (4) to assign to us related intellectual property developed during the course of his or her employment.

401(k) Retirement Plan

We maintain a 401(k) retirement plan that is intended to be a tax-qualified defined contribution plan under Section 401(k) of the Internal Revenue Code. In general, all of our employees are eligible to participate, beginning on the first day of the month following commencement of their employment. The 401(k) plan includes a salary deferral arrangement pursuant to which participants may elect to reduce their current compensation by up to the statutorily prescribed limit, equal to \$19,500 in each of 2020 and 2021, and have the amount of the reduction contributed to the 401(k) plan. Participants over the age of 50 are entitled to an additional catch-up contribution up to the statutorily prescribed limit, equal to \$6,500 in each of 2020 and 2021. We make matching contributions at a rate of 100% of each employee's contribution up to a maximum matching contribution of 2% of the employee's compensation and 50% of each employee's contribution in excess of 2% up to a maximum of 6% of the employee's compensation.

Indemnification

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

Tax Deductibility

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

Director Compensation

We pay our non-employee directors a cash retainer for service on the board of directors and for service on each committee on which the director is a member pursuant to a director compensation program that was initially adopted by our board of directors effective upon completion of our initial public offering in July 2016. The chair of each committee and the chair of the board of directors receive higher retainers for such service. In December 2019, our board of directors amended the director compensation program to increase the cash retainer for our non-employee directors by \$5,000, the retainer for members of the Nominating and Corporate Governance Committee by \$500, and the retainer for the chair of the Nominating and Corporate Governance Committee by \$1,000. These fees are payable in arrears in four equal quarterly installments on the last day of each quarter, subject to proration for any portion of such quarter that the director is not serving on our board of directors, on such committee or in such position. Effective January 1, 2020, the fees paid to non-employee directors for service on the board of directors and for service on each committee of the board of directors on which the director is a member are as follows:

	Base	Incremental Chair	Incremental Non-Chair
Board of Directors	\$40,000	\$ 30,000	
Audit Committee		\$ 15,000	\$ 7,500
Compensation Committee		\$ 10,000	\$ 5,000
Research and Development Committee		\$ 10,000	\$ 5,000
Nominating and Corporate Governance Committee		\$ 8,000	\$ 4,000

In addition, under this director compensation program, we will grant to new non-employee directors upon their initial election to the board, an initial option to purchase 35,000 shares of our common stock, with an exercise price equivalent to fair market value of a share of common stock at the time of grant, which option will vest as to 16.66% of the shares on the six month anniversary of the date of grant and as to the remainder of the shares in equal monthly installments thereafter until the third anniversary of the date of grant, subject to continued service, with full acceleration upon a change in control of our company. The option will have a term of ten years.

Immediately following each annual meeting of our stockholders, we will grant to each non-employee director who has served on our board of directors for at least six months an option to purchase 17,500 shares of our common stock, with an exercise price equivalent to fair market value of a share of common stock at the time of grant, which option will vest as to 50% of the shares on the six-month anniversary of the date of grant and as to the remainder of the shares in equal monthly installments thereafter until the first anniversary of the date of grant, subject to continued service, with full acceleration upon a change in control of our company. The option will have a term of ten years.

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

Table of Contents

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

The following table sets forth information regarding compensation earned by our non-employee directors during fiscal 2021.

Name	Fees Earned or Paid in Cash (\$)	Option Awards (\$)(1)	All Other Compensation (\$)	Total (\$)
Srinivas Akkaraju, M.D., Ph.D.	49,000	73,294	—	122,294
Mark J. Alles	47,500	73,294	—	120,794
Deborah Dunsire, M.D. (2)	15,353	125,829	—	141,182
S. Gail Eckhardt, M.D.	46,228	73,294	—	119,522
Marsha H. Fanucci	55,000	73,294	—	128,294
Amir Nashat, Ph.D.	55,500	73,294	—	128,794
Phillip A. Sharp, Ph.D.	50,000	73,294	—	123,294
Peter Wirth	80,000	73,294	—	153,294
Richard A. Young, Ph.D.	50,000	73,294	115,000(3)	238,294

- (1) The amounts reported in the “Option Awards” column reflect the aggregate grant date fair value of stock-based compensation awarded during the year computed in accordance with the provisions of ASC Topic 718. This calculation does not give effect to any estimate of forfeitures related to service-based vesting but assumes that the applicable director will perform the requisite service for the award to vest in full. See Note 12 to our financial statements included in our Annual Report on Form 10-K regarding assumptions underlying the valuation of equity awards.
- (2) Dr. Dunsire was appointed to our board of directors in September 2021.
- (3) Represents consideration paid during fiscal 2021 pursuant to the terms of a consulting agreement Dr. Young entered with our company that is unrelated to his service on our board of directors.

As of December 31, 2021, our non-employee directors held the following stock options, all of which were granted under our 2012 Equity Incentive Plan, as amended, or 2012 Plan, and our 2016 Stock Incentive Plan, or 2016 Plan:

Name	Option Awards
Srinivas Akkaraju, M.D., Ph.D.	79,000
Mark J. Alles	70,000
Deborah Dunsire, M.D.	35,000
S. Gail Eckhardt, M.D.	52,500
Marsha H. Fanucci	104,666
Amir Nashat, Ph.D.	90,000
Phillip A. Sharp, Ph.D.	132,857
Peter Wirth	79,000
Richard A. Young, Ph.D.	165,000

Limitation of Liability and Indemnification

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

- any breach of the director’s duty of loyalty to us or our stockholders;
- any act or omission not in good faith or that involves intentional misconduct or a knowing violation of law;

Table of Contents

- any unlawful payments related to dividends or unlawful stock repurchases, redemptions or other distributions; or
- any transaction from which the director derived an improper personal benefit.

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

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

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

The indemnification provisions contained in our certificate of incorporation are not exclusive. In addition, we have entered into indemnification agreements with each of our directors and executive officers. Each of these indemnification agreements provides, among other things, that we will indemnify such director or executive officer to the fullest extent permitted by law for claims arising in his or her capacity as a director or executive officer, as applicable, provided that he or she acted in good faith and in a manner that he or she reasonably believed to be in, or not opposed to, our best interests and, with respect to any criminal proceeding, had no reasonable cause to believe that his or her conduct was unlawful. Each of these indemnification agreements provides that in the event that we do not assume the defense of a claim against a director or executive officer, as applicable, we are required to advance his or her expenses in connection with his or her defense, provided that he or she undertakes to repay all amounts advanced if it is ultimately determined that he or she is not entitled to be indemnified by us.

We believe that these provisions and agreements are necessary to attract and retain qualified persons as directors and executive officers. Insofar as indemnification for liabilities arising under the Securities Act of 1933, as amended, or the Securities Act, may be permitted to directors, officers or persons controlling our company pursuant to the foregoing provisions, we understand that in the opinion of the SEC such indemnification is against public policy as expressed in the Securities Act and is therefore unenforceable.

In addition, we maintain standard policies of insurance under which coverage is provided to our directors and officers against losses arising from claims made by reason of breach of duty or other wrongful act, and to us with respect to payments which may be made by us to such directors and officers pursuant to the above indemnification provisions or otherwise as a matter of law.

SECURITIES AUTHORIZED FOR ISSUANCE UNDER EQUITY COMPENSATION PLANS

The following table contains information about our equity compensation plans as of December 31, 2021. As of December 31, 2021, we had three equity compensation plans, each of which was approved by our stockholders: our 2012 Plan, our 2016 Plan and our 2016 Employee Stock Purchase Plan, or 2016 ESPP.

Equity Compensation Plan Information

Plan Category	Number of securities to be issued upon exercise of outstanding options, warrants and rights (a)	Weighted average exercise price of outstanding options, warrants and rights (b)	Number of securities remaining available for future issuance under equity compensation plans (excluding securities reflected in column (a)) (c)
Equity compensation plans approved by security holders	8,197,055 ⁽¹⁾	\$ 6.57	4,475,271 ⁽²⁾
Equity compensation plans not approved by security holders	1,147,700 ⁽³⁾	\$ 4.48	—
Total	9,344,755	\$ 6.31	4,475,271⁽⁴⁾

- (1) Consists of (i) 711,338 shares to be issued upon exercise of outstanding options under our 2012 Plan as of December 31, 2021 (ii) 4,798,230 shares to be issued upon exercise of outstanding options under our 2016 Plan, and (iii) 2,687,487 shares to be issued upon vesting of outstanding restricted stock units under our 2016 Plan as of December 31, 2021.
- (2) Consists of (i) 2,238,206 shares that remained available for future issuance under our 2016 Plan as of December 31, 2021, and (ii) 2,237,065 shares that remained available for future issuance under our 2016 ESPP as of December 31, 2021. No shares remained available for future issuance under the 2012 Plan as of December 31, 2021.
- (3) Consists of (i) 37,700 shares to be issued upon exercise of anon-statutory stock option granted by our board of directors to the Branta Group, LLC on December 5, 2012 in consideration for consulting services, which was fully vested upon grant with an exercise price equal to the fair market value of such shares as determined by our board of directors on the date of the grant, (ii) 360,000 shares to be issued upon exercise of an option award granted to Conley Chee on September 27, 2021, as an inducement material to Mr. Chee's acceptance of employment with the company in accordance with Nasdaq Listing Rule 5635(c)(4), with an exercise price equal to the closing price of our common stock on the date of the grant, that vests over four years with 25% of the shares underlying the option vesting on September 27, 2022, and 1/48th of the original number of shares vesting monthly thereafter, and (iii) 750,000 shares to be issued upon exercise of an option award granted to Jason Haas on October 12, 2021, as an inducement material to Mr. Haas' acceptance of employment with the company in accordance with Nasdaq Listing Rule 5635(c)(4), with an exercise price equal to the closing price of our common stock on the date of the grant, that vests over four years with 25% of the shares underlying the option vesting on October 12, 2022, and 1/48th of the original number of shares vesting monthly thereafter. These options were granted outside of any of our equity incentive plans.
- (4) Our 2016 Plan has an evergreen provision that allows for an annual increase in the number of shares available for issuance under the 2016 Plan to be added on the first day of each fiscal year through the 2025 fiscal year, equal to the least of 1,600,000 shares of our common stock, 4% of the number of shares of our common stock outstanding on the first day of the applicable fiscal year and an amount determined by our board of directors. On January 1, 2022, 1,600,000 additional shares were reserved for issuance under the 2016 Plan pursuant to this provision. Our 2016 ESPP has an evergreen provision that allows for an annual increase in the number of shares available for issuance under the 2016 ESPP to be added on the first day of each fiscal year through the 2025 fiscal year, in an amount equal to the least of 1,173,333 shares of our common stock, 1% of the total number of shares of our common stock outstanding on the first day of the applicable fiscal year and an amount determined by our board of directors. On January 1, 2022, 620,241 additional shares were reserved for issuance under the 2016 ESPP pursuant to this provision.

REPORT OF THE AUDIT COMMITTEE OF THE BOARD OF DIRECTORS

Our audit committee has reviewed our audited consolidated financial statements for the fiscal year ended December 31, 2021 and discussed them with our management and our independent registered public accounting firm, Ernst & Young LLP.

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

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

Based on the review and discussions referred to above, our audit committee recommended to our board of directors that the audited consolidated financial statements be included in our Annual Report on Form 10-K for the year ended December 31, 2021.

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

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

MATTERS TO BE VOTED ON

Proposal 1: Election of Directors

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

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

- Class I is comprised of Mark J. Alles, Amir Nashat, Ph.D., and Peter Wirth, each with a term ending at the 2023 annual meeting of stockholders;
- Class II is comprised of Srinivas Akkaraju, M.D., Ph.D., Deborah Dunsire, M.D., Phillip A. Sharp, Ph.D., and Richard A. Young, Ph.D., each with a term ending at the 2024 annual meeting of stockholders; and
- Class III is comprised of S. Gail Eckhardt, M.D., Marsha H. Fanucci and Nancy A. Simonian, M.D., each with a term ending at the 2022 annual meeting of stockholders.

At each annual meeting of stockholders, directors are elected for a full term of three years to succeed those directors whose terms are expiring. Our board of directors, on the recommendation of our nominating and corporate governance committee, has set the number of directors at ten and nominated S. Gail Eckhardt, M.D., Marsha H. Fanucci and Nancy A. Simonian, M.D., for re-election as Class III directors, each with a term ending at the 2025 annual meeting of stockholders.

Unless otherwise instructed in the proxy or unless authority to vote is withheld, all executed proxies will be voted "FOR" the election of each of the Class III director nominees identified above to a three-year term ending at the 2025 annual meeting of stockholders, each such nominee to hold office until her successor has been duly elected and qualified. Each of the nominees has indicated a willingness to continue to serve as director, if elected. If any nominee should be unable to serve, discretionary authority is reserved for the named proxy holders to vote for a substitute, or to reduce the number of directors to be elected, or both. We do not expect that any of the nominees will be unable to serve if elected.

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

OUR BOARD OF DIRECTORS RECOMMENDS THAT STOCKHOLDERS VOTE "*FOR*" THE ELECTION OF S. GAIL ECKHARDT, M.D., MARSHA H. FANUCCI AND NANCY A. SIMONIAN, M.D., TO SERVE AS CLASS III DIRECTORS.

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

Our audit committee has appointed the firm of Ernst & Young LLP, or E&Y, an independent registered public accounting firm, as independent auditors for the fiscal year ending December 31, 2022. Although stockholder approval of our audit committee's appointment of E&Y is not required by law, our board of directors believes that it is advisable to give stockholders an opportunity to ratify this appointment. If this proposal is not approved at the annual meeting, our audit committee will reconsider its appointment of E&Y. E&Y has no direct or indirect material financial interest in our company or our subsidiaries. Representatives of E&Y are expected to attend the virtual annual meeting and will have the opportunity to make a statement, if they desire to do so, and will be available to respond to appropriate questions from our stockholders.

Table of Contents

Audit Fees and Services

E&Y was our independent registered public accounting firm for the years ended December 31, 2021 and December 31, 2020. The following table summarizes the fees of E&Y billed to us for each of the last two fiscal years. All such services and fees were pre-approved by our audit committee in accordance with the “Pre-Approval Policies and Procedures” described below.

<u>Fee Category</u>	<u>2021</u>	<u>2020</u>
Audit Fees (1)	\$ 590,640	\$ 599,910
Audit-Related Fees	—	—
Tax Fees (2)	34,495	50,040
All Other Fees (3)	2,000	1,790
Total Fees	\$ 627,135	\$ 705,987

- (1) “Audit Fees” consist of fees for the audit of our annual financial statements, the review of the interim financial statements included in our quarterly reports on Form 10-Q, our follow-on public offering completed in January 2021, and other professional services provided in connection with regulatory filings or engagements.
- (2) “Tax Fees” consist of fees for professional services, including tax consulting and compliance performed by E&Y.
- (3) “All Other Fees” consist of database subscription fees paid to E&Y.

Pre-Approval Policies and Procedures

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

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

OUR BOARD OF DIRECTORS RECOMMENDS THAT STOCKHOLDERS VOTE “*FOR*” THE RATIFICATION OF THE APPOINTMENT OF ERNST & YOUNG LLP AS OUR INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM FOR THE FISCAL YEAR ENDING DECEMBER 31, 2022.

Proposal 3: Advisory Vote on Executive Compensation

We are providing our stockholders the opportunity to vote to approve, on an advisory, non-binding basis, the compensation of our named executive officers as disclosed in this proxy statement in accordance with the SEC’s rules. This proposal, which is commonly referred to as “say-on-pay,” is required by the Dodd-Frank Wall Street Reform, or the Dodd-Frank Act, and Consumer Protection Act of 2010, which added Section 14A to the Securities Exchange Act of 1934, or the Exchange Act. Section 14A of the Exchange Act also requires that stockholders have the opportunity to cast an advisory vote with respect to whether future advisory votes on the compensation paid to our named executive officers will be held every one, two or three years, which is the subject of Proposal 4. Our executive compensation program is designed to reward value creation for stockholders and to attract, motivate, and retain our executive officers, who are critical to our success. Under this program, our named executive officers are rewarded for the achievement of our short- and long-term strategic and financial goals, which we believe serves to enhance short- and long-term value creation for our stockholders. The program contains elements of cash and equity-based compensation and are designed to align the interests of our executives with those of our stockholders and paying for performance.

The section of this proxy statement titled “Executive and Director Compensation” beginning on page 20 including “Narrative Disclosure to Summary Compensation Table,” describes in detail our executive compensation program and the decisions made by our compensation committee. Our executive compensation program rewards value creation for stockholders and progress towards achieving our mission and that promotes company performance. At the same time, we believe our program does not encourage excessive risk-taking by management. While we do not have a formal or informal policy for allocating between long-term and short-term compensation, between cash and non-cash compensation or among different forms of non-cash compensation, we generally strive to provide our named executive officers with a mix of short-term and long-term performance-based incentives to encourage consistently strong performance, and our board of directors believes that this link between compensation and the achievement of our near- and long-term business goals has helped drive our performance over time.

Our board of directors is asking stockholders to approve a non-binding advisory vote on the following resolution:

RESOLVED, that the compensation paid to the Company’s named executive officers, as disclosed pursuant to the compensation disclosure rules of the Securities and Exchange Commission, including the compensation tables and any related material disclosed in this proxy statement, is hereby approved.

As an advisory vote, this proposal is not binding. Neither the outcome of this advisory vote nor of the advisory vote included in Proposal 4 overrules any decision by the company or the board of directors (or any committee thereof), creates or implies any change to the fiduciary duties of the company or the board of directors (or any committee thereof), or creates or implies any additional fiduciary duties for the company or the board of directors (or any committee thereof). However, our compensation committee and board of directors value the opinions expressed by our stockholders in their vote on this proposal and intend to consider carefully the outcome of the vote when making future compensation decisions for named executive officers.

OUR BOARD OF DIRECTORS RECOMMENDS THAT STOCKHOLDERS VOTE TO APPROVE THE COMPENSATION OF OUR NAMED EXECUTIVE OFFICERS BY VOTING “*FOR*” THIS PROPOSAL.

Proposal 4: Advisory Vote on the Frequency of Future Executive Compensation Advisory Votes

In Proposal 3, we are providing our stockholders the opportunity to vote to approve, on an advisory, non-binding basis, the compensation of our named executive officers. In this Proposal 4, we are asking our stockholders to cast a non-binding advisory vote regarding the frequency of future executive compensation advisory votes. Stockholders may vote for a frequency of every one, two, or three years, or may abstain.

Our board of directors intends to consider carefully the outcome of this vote in making a determination about the frequency of future executive compensation advisory votes. However, because this vote is advisory and non-binding, the board of directors may decide that it is in the best interests of our stockholders and the company to hold the advisory vote to approve executive compensation more or less frequently, but no less frequently than once every three years, as required by the Dodd-Frank Act. In the future, we will propose an advisory vote on the frequency of the executive compensation advisory vote at least once every six calendar years as required by the Dodd-Frank Act.

After careful consideration, the board of directors believes that an executive compensation advisory vote should be held every year, and therefore our board of directors recommends that you vote for a frequency of every ONE YEAR for future executive compensation advisory votes.

The board of directors believes that an annual executive compensation advisory vote will facilitate more direct stockholder input about executive compensation. An annual executive compensation advisory vote is consistent with our policy of reviewing our compensation program annually, as well as seeking frequent input from our stockholders on corporate governance and executive compensation matters. We believe an annual vote would be the best governance practice for our company at this time.

OUR BOARD OF DIRECTORS RECOMMENDS THAT STOCKHOLDERS VOTE IN FAVOR OF AN ANNUAL ADVISORY VOTE ON EXECUTIVE COMPENSATION.

STOCK OWNERSHIP AND REPORTING

Security Ownership of Certain Beneficial Owners and Management

Unless otherwise provided below, the following table sets forth information regarding beneficial ownership of our common stock as of March 31, 2022 by:

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

Beneficial ownership is determined in accordance with the rules and regulations of the SEC and includes voting or investment power with respect to our common stock. Percentage of beneficial ownership is based on 62,806,096 shares of our common stock outstanding as of April 8, 2022. In addition, shares of common stock subject to options or other rights currently exercisable, or exercisable within 60 days of April 8, 2022, are deemed outstanding and beneficially owned for the purpose of computing the percentage beneficially owned by (i) the individual holding such options, warrants or other rights (but not any other individual) and (ii) the directors and executive officers as a group. Except as otherwise noted, the persons and entities in this table have sole voting and investing power with respect to all of the shares of our common stock beneficially owned by them, subject to community property laws, where applicable. Except as otherwise set forth below, the address of the beneficial owner is c/o Syros Pharmaceuticals, Inc., 35 CambridgePark Drive, 4th Floor, Cambridge Massachusetts 02140.

Name of Beneficial Owner	Shares of Common Stock Beneficially Owned	+	Common Stock Underlying Options and Other Rights Acquirable Within 60 Days	=	Total Beneficial Ownership	
					Shares Beneficially Owned	Percentage of Shares Beneficially Owned
5% Stockholders						
Entities affiliated with FMR LLC	9,332,797		—		9,332,797(1)	14.86%
Entities affiliated with Bain Capital Life Sciences, L.P.	5,504,661(2)		854,998(3)		6,359,659	9.99%
BlackRock, Inc.	4,232,268		—		4,232,268(4)	6.74%
Ally Bridge MedAlpha Master Fund L.P.	3,539,895(5)		390,625(6)		3,930,520	6.22%
Entities affiliated with Invus Public Equities, L.P.	3,500,000		—		3,500,000(7)	5.57%
Named Executive Officers and Directors						
Nancy Simonian, M.D.	911,606(8)		1,195,137		2,106,743	3.29%
Jason Haas	—		—		—	*
David A. Roth, M.D.	87,000		513,157		600,157	*
Srinivas Akkaraju, M.D., Ph.D.	1,899,616(9)		212,000(10)		2,111,616	3.35%
Mark J. Alles	10,000		63,193		73,193	*
Deborah Dunsire, M.D.	—		7,775		7,775	*
S. Gail Eckhardt, M.D.	—		37,915		37,915	*
Marsha H. Fanucci	—		104,666		104,666	*
Amir Nashat, Ph.D.	1,586,653(11)		90,000		1,676,653	2.67%
Phillip A. Sharp, Ph.D.	266,666(12)		132,857		399,523	*
Peter Wirth	—		79,000		79,000	*
Richard A. Young, Ph.D.	321,711		90,000		411,711	*
All Current Executive Officers and Directors as a Group (15 persons)						
	5,215,252		3,234,054		8,449,306	12.79%

Table of Contents

- * Represents beneficial ownership of less than 1% of our outstanding stock.
- (1) FMR LLC (“FMR”) and Abigail P. Johnson, a director, the chair and the chief executive officer of FMR, each report beneficially owning and having sole dispositive power over 9,332,797 of the shares listed herein. FMR reports sole voting power over 2,575,255 of the shares listed herein. Members of the Johnson family including Ms. Johnson, are the predominant owners, directly or through trusts, of Series B voting common shares of FMR, representing 49% of the voting power of FMR. The Johnson family group and all other Series B shareholders have entered into a shareholders’ voting agreement under which all Series B voting common shares will be voted in accordance with the majority vote of Series B voting common shares. Accordingly, through their ownership of voting common shares and the execution of the shareholders’ voting agreement, members of the Johnson family may be deemed under the Investment Company Act of 1940 (the “1940 Act”) to form a controlling group with respect to FMR. Neither FMR nor Ms. Johnson has the sole power to vote or direct the voting of the shares owned directly by the various investment companies registered under the 1940 Act advised by Fidelity Management & Research Company LLC, a wholly owned subsidiary of FMR (“FMR Co. LLC”), which power resides with the funds’ boards of trustees. FMR Co. LLC carries out the voting of the shares under written guidelines established by the funds’ boards of trustees. FMR has an address at 245 Summer Street, Boston, MA 02210. For information regarding FMR, we have relied, without independent investigation, on the Schedule 13G/A filed by FMR with the SEC on February 9, 2022.
 - (2) Bain Capital Life Sciences Fund II, L.P. (“BCLS II”) reports holding shared voting and dispositive power over 4,907,011 shares, and BCIP Life Sciences Associates, LP (“BCIPLS” and, together with BCLS II, the “Bain Capital Life Science Entities”) reports holding shared voting and dispositive power over 597,650 shares. Bain Capital Life Sciences Investors, LLC (“BCLSI”) is the ultimate general partner of BCLS II and governs the investment strategy and decision-making process with respect to investments held by BCIPLS. As a result, BCLSI may be deemed to share voting and dispositive power with respect to the shares of common stock held by the Bain Capital Life Sciences Entities. The address of the Bain Capital Life Sciences Entities is c/o Bain Capital Life Sciences, LP, 200 Clarendon Street, Boston, MA 02116. For information regarding the Bain Capital Life Science Entities, we have relied, without independent investigation, on the Schedule 13G/A filed by the Bain Capital Life Science Entities with the SEC on February 14, 2022.
 - (3) BCLS II owns warrants to purchase 1,114,286 shares of common stock (opre-funded warrants in lieu thereof) and pre-funded warrants to purchase 891,429 shares of common stock, and BCIPLS owns warrants to purchase 135,714 shares of common stock (or pre-funded warrants in lieu thereof) and pre-funded warrants to purchase 108,571 shares of common stock. The Bain Capital Life Science Entities are prohibited from exercising such warrants and pre-funded warrants, if, as a result of such exercise, the Bain Capital Life Science Entities would beneficially own more than 9.99% of the total number of shares of common stock then issued and outstanding immediately after giving effect to the exercise. For information regarding the Bain Capital Life Science Entities, we have relied, without independent investigation, on the Schedule 13G/A filed by the Bain Capital Life Science Entities with the SEC on February 14, 2022.
 - (4) BlackRock, Inc. (“BlackRock”) reports holding sole voting power as to 4,193,840 of the shares and sole dispositive power over all of the shares listed herein. BlackRock has an address at 55 East 52nd Street, New York, NY 10055. For information regarding BlackRock, we have relied, without independent investigation, on the Schedule 13G/A filed by BlackRock with the SEC on February 3, 2022.
 - (5) Ally Bridge MedAlpha Master Fund L.P. (“Ally Bridge”) reports holding shared voting and dispositive power with respect to all of the shares listed herein. Mr. Fan Yu is the sole shareholder of ABG Management Ltd., which is the sole member of Ally Bridge Group (NY) LLC, which manages Ally Bridge’s investments. As such, each of the foregoing entities and Mr. Fan Yu may be deemed to share beneficial ownership of the shares held of record by Ally Bridge. Each of them disclaims any such beneficial ownership. The address of Ally Bridge is c/o Ally Bridge Group (NY) LLC, 430 Park Avenue, 12th Floor, New York, NY 10022. For information regarding Ally Bridge, we have relied, without independent investigation, on the Schedule 13G/A filed by Ally Bridge with the SEC on February 11, 2022.
 - (6) Ally Bridge owns warrants to purchase 390,625 shares of common stock (opre-funded warrants in lieu thereof). For information regarding Ally Bridge, we have relied, without independent investigation, on the Schedule 13G/A filed by Ally Bridge with the SEC on February 11, 2022.

Table of Contents

- (7) Invus Public Equities, L.P. (“Invus Public Equities”) directly holds the 3,500,000 shares of common stock. Invus Public Equities Advisors, LLC (“Invus PE Advisors”), as the general partner of Invus Public Equities, controls Invus Public Equities and, accordingly, may be deemed to beneficially own the shares held by Invus Public Equities. The Geneva branch of Artal International S.C.A (“Artal International”), as the managing member of Invus PE Advisors, controls Invus PE Advisors, and, accordingly, may be deemed to beneficially own the shares that Invus PE Advisors may be deemed to beneficially own. Artal International Management S.A. (“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. (“Artal Group”), as the sole stockholder of Artal International Management, controls Artal International Management and, accordingly, may be deemed to beneficially own the shares that Artal International Management may be deemed to beneficially own. Westend S.A. (“Westend”), as the parent company of Artal Group, controls Artal Group and, accordingly, may be deemed to beneficially own the shares that Artal Group may be deemed to beneficially own. Stichting Administratiekantoor Westland (“Stichting”), as the majority stockholder of Westend, controls Westend and, accordingly, may be deemed to beneficially own the shares that Westend may be deemed to beneficially own. Mr. Amaury Wittouck (“Mr. Wittouck”), as the sole member of the board of the Stichting, controls the Stichting and, accordingly, may be deemed to beneficially own the shares that the Stichting may be deemed to beneficially own. The address for Invus Public Equities and Invus PE Advisors is 750 Lexington Avenue, 30th Floor, New York, NY 10022. The address for Artal International, Artal International Management, Artal Group, Westend and Mr. Wittouck is Valley Park, 44, Rue de la Vallée, L-2661, Luxembourg. The address for Stichting is Claude Debussylaan, 46, 1082 MD Amsterdam, The Netherlands. For information regarding Invus Public Equities, Invus PE Advisors, Artal International, Artal International Management, Artal Group, Westend, Stichting, and Mr. Wittouck, we have relied, without independent investigation, on the Schedule 13G filed by such parties with the SEC on February 11, 2022.
- (8) Consists of (i) 751,606 shares of common stock held by Dr. Simonian, (ii) 80,000 shares of common stock held of record by the Douglas and Nancy Cole Family Trust f/b/o Bennett H. Cole, and (iii) 80,000 shares of common stock held of record by the Douglas and Nancy Cole Family Trust f/b/o William B. Cole.
- (9) Consists of 1,899,616 shares owned by Samsara BioCapital, L.P. (“Samsara LP”). The general partner of Samsara LP is Samsara BioCapital GP, LLC (“Samsara LLC”). The managers of Samsara LLC are Srinivas Akkaraju and Michael Dybbs. These individuals may be deemed to have shared voting and investment power of the shares held by Samsara LP and may be deemed to beneficially own certain shares held by Samsara LP. Dr. Akkaraju disclaims beneficial ownership of these shares, except to the extent of his pecuniary interest therein.
- (10) Includes warrants to purchase 133,333 shares of common stock that are owned by Samsara LP and are currently exercisable. Dr. Akkaraju disclaims beneficial ownership of such warrants and the shares of common stock underlying them, except to the extent of his pecuniary interest therein.
- (11) Consists of 1,538,333 shares of common stock held by Polaris Partners VII, L.P. and 48,320 shares of common stock held by Polaris Entrepreneurs’ Fund VII, L.P. The general partner of Polaris Partners VII, L.P. and Polaris Entrepreneurs’ Fund VII, L.P. is Polaris Management Co. VII, L.L.C. (“Polaris Management”), and Polaris Management may be deemed to have sole voting and investment power over such shares. Polaris Management disclaims beneficial ownership of these shares, except to the extent of its pecuniary interest therein. Amir Nashat, a managing member of Polaris Management, may be deemed to have voting and investment power over such shares. The address of such stockholders is One Marina Park Drive, 10th Floor, Boston, MA 02210. For information regarding Polaris Partners VII, L.P. we have relied, without independent investigation, on the Schedule 13D/A filed by Polaris Management with the SEC on February 14, 2019.
- (12) Consists of (i) 146,666 shares of common stock held of record by Dr. Sharp, (ii) 40,000 shares of common stock held of record by Ann H. Sharp and Christine S. Carey, as Trustees of the Phillip A. Sharp 2008 Irrevocable Trust f/b/o Christine S. Carey, (iii) 40,000 shares of common stock held of record by Ann H. Sharp and Helena S. Gordon, as Trustees of the Phillip A. Sharp 2008 Irrevocable Trust f/b/o Helena H. Sharp, and (iv) 40,000 shares of common stock held of record by Ann H. Sharp and Sarah S. Brokaw, as Trustees of the Phillip A. Sharp 2008 Irrevocable Trust f/b/o Sara S. Brokaw.

OTHER MATTERS

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

Stockholder Proposals for our 2023 Annual Meeting

Stockholder Proposals Included in Proxy Statement

In order to be considered for inclusion in our proxy statement and proxy card relating to our 2023 annual meeting of stockholders, stockholder proposals must be received by us no later than December 22, 2022, which is 120 days prior to the first anniversary of the mailing date of this proxy, unless the date of the 2023 annual meeting of stockholders is changed by more than 30 days from the anniversary of our 2022 annual meeting, in which case, the deadline for such proposals will be a reasonable time before we begin to print and send our proxy materials. Upon receipt of any such proposal, we will determine whether or not to include such proposal in the proxy statement and proxy card in accordance with regulations governing the solicitation of proxies.

Stockholder Proposals Not Included in Proxy Statement

In addition, our by-laws establish an advance notice procedure for nominations for election to our board of directors and other matters that stockholders wish to present for action at an annual meeting other than those to be included in our proxy statement. In general, we must receive other proposals of stockholders (including director nominations) intended to be presented at the 2023 annual meeting of stockholders but not included in the proxy statement by March 3, 2023, but not before February 1, 2023, which is not less than 90 days nor more than 120 days prior to the anniversary date of the immediately preceding annual meeting. However, if the date of the annual meeting is more than 30 days before or more than 60 days after such anniversary date, notice must be received no earlier than the close of business 120 calendar days prior to such annual meeting and no later than the close of business on the later of 90 days prior to such annual meeting and 10 days following the day on which notice of the date of such annual meeting was mailed or public announcement of the date of such annual meeting was first made. If the stockholder fails to give notice by these dates, then the persons named as proxies in the proxies solicited by the board of directors for the 2023 annual meeting of stockholders may exercise discretionary voting power regarding any such proposal. Stockholders are advised to review our by-laws which also specify requirements as to the form and content of a stockholder's notice.

Any proposals, notices or information about proposed director candidates should be sent to Syros Pharmaceuticals, Inc., Attention: Nominating and Corporate Governance Committee, 35 CambridgePark Drive, 4th Floor, Cambridge, Massachusetts 02140.

Householding of Annual Meeting Materials

Some brokers and other nominee record holders may be "householding" our proxy materials. This means a single notice and, if applicable, the proxy materials, will be delivered to multiple stockholders sharing an address unless contrary instructions have been received. We will promptly deliver a separate copy of the notice and, if applicable, the proxy materials and our 2021 annual report to stockholders, which consists of our Annual Report on Form 10-K for the fiscal year ended December 31, 2021, to you if you write or call us at Syros Pharmaceuticals, Inc., 35 CambridgePark Drive, 4th Floor, Cambridge, Massachusetts 02140, Attention: Chief Financial Officer, telephone: (617) 744-1340. If you would like to receive separate copies of our proxy materials and annual reports in the future, or if you are receiving multiple copies and would like to receive only one copy for your household, you should contact your bank, broker, or other nominee record holder, or you may contact us at the above address and telephone number.



Your vote matters – here's how to vote!

You may vote online or by phone instead of mailing this card.

Online

Go to www.envisionreports.com/SYRS or scan the QR code – login details are located in the shaded bar below.



Phone

Call toll free 1-800-652-VOTE (8683) within the USA, US territories and Canada



Save paper, time and money!

Sign up for electronic delivery at www.envisionreports.com/SYRS

Using a black ink pen, mark your votes with an X as shown in this example. Please do not write outside the designated areas.



2022 Annual Meeting Proxy Card

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

A Proposals – The Board of Directors recommends a vote FOR all the nominees listed in Proposal 1, FOR Proposals 2 and 3 and for every 1 YEAR on Proposal 4.

1. Election of three Class III directors, each to serve for a three-year term expiring at the Company's 2025 annual meeting of stockholders and until her successor has been duly elected and qualified.

	For	Withhold		For	Withhold		For	Withhold
01 - S. Gail Eckhardt, M.D.	<input type="checkbox"/>	<input type="checkbox"/>	02 - Marsha H. Fanucci	<input type="checkbox"/>	<input type="checkbox"/>	03 - Nancy A. Simonian, M.D.	<input type="checkbox"/>	<input type="checkbox"/>

2. Ratification of the appointment of Ernst & Young LLP as the Company's independent registered public accounting firm for the fiscal year ending December 31, 2022.

For **Against** **Abstain**

3. Approval, on a non-binding advisory basis, of the compensation of the Company's named executive officers.

For **Against** **Abstain**

4. Recommendation, on a non-binding advisory basis, of the frequency of future advisory votes on the compensation of the Company's named executive officers.

1 Year **2 Years** **3 Years** **Abstain**

B Authorized Signatures – This section must be completed for your vote to count. Please date and sign below.

Please sign exactly as name(s) appears hereon. Joint owners should each sign. When signing as attorney, executor, administrator, corporate officer, trustee, guardian, or custodian, please give full title.

Date (mm/dd/yyyy) – Please print date below.

/ /

Signature 1 – Please keep signature within the box.

Signature 2 – Please keep signature within the box.



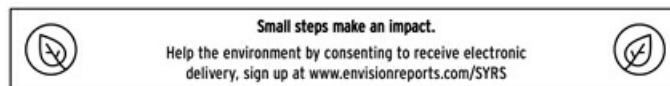
1 U P X



DLAWA

The 2022 Annual Meeting of Stockholders of Syros Pharmaceuticals, Inc. will be held on Wednesday, June 1, 2022, 11:00 a.m. local time, virtually via the internet at meetnow.global/M7TXWW9.

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



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

Proxy – Syros Pharmaceuticals, Inc.



Notice of 2022 Annual Meeting of Stockholders

Proxy Solicited by Board of Directors for Annual Meeting – Wednesday, June 1, 2022

Nancy A. Simonian, Jason Haas, or either of them (the "Proxies"), each with the power of substitution, are hereby authorized to represent and vote the shares of the undersigned, with all the powers which the undersigned would possess if personally present, at the Annual Meeting of Stockholders of Syros Pharmaceuticals, Inc. to be held virtually via the internet on June 1, 2022 or at any postponement or adjournment thereof.

Shares represented by this proxy will be voted by the stockholder. If no such directions are indicated, the Proxies will have authority to vote FOR each of the nominees listed in Proposal 1, FOR Proposal 2 and 3 and for every 1 YEAR on Proposal 4.

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

(Items to be voted appear on reverse side)

C Non-Voting Items

Change of Address – Please print new address below.

Comments – Please print your comments below.

