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**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 under §240.14a-12

SYROS PHARMACEUTICALS, INC.

(Name of Registrant as Specified In Its Charter)

(Name of Person(s) Filing Proxy Statement, if other than the Registrant)

Payment of Filing Fee (Check the appropriate box):

- No fee required.
- Fee computed on table below per Exchange Act Rules 14a-6(i)(1) and 0-11.
(1) Title of each class of securities to which transaction applies:

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

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

(4) Proposed maximum aggregate value of transaction:

(5) Total fee paid:

 Fee paid previously with preliminary materials.

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

(1) Amount Previously Paid:

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

(3) Filing Party:

(4) Date Filed:



SYROS PHARMACEUTICALS, INC.

**620 Memorial Drive, Suite 300
Cambridge, Massachusetts 02139
(617) 744-1340**

**NOTICE OF 2018 ANNUAL MEETING OF STOCKHOLDERS
To Be Held on June 14, 2018**

Dear Stockholders:

You are cordially invited to attend the 2018 annual meeting of stockholders of Syros Pharmaceuticals, Inc. to be held on Thursday, June 14, 2018 at 1:00 p.m., Eastern Daylight Time, at our corporate offices located at 620 Memorial Drive, Suite 300, Cambridge, Massachusetts 02139. At the annual meeting, stockholders will consider and vote on the following matters:

1. The election of four Class II directors, Srinivas Akkaraju, M.D., Ph.D., Vicki L. Sato, Ph.D., Phillip A. Sharp, Ph.D. and Richard A. Young, Ph.D., nominated by our board of directors, each to serve for a three-year term expiring at the 2021 annual meeting of stockholders and until his or 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, 2018; and
3. The transaction of any other business that may properly come before the annual meeting or any adjournment or postponement thereof.

Stockholders of record at the close of business on April 20, 2018 will be entitled to notice of and to vote at the annual meeting or any adjournment or postponement thereof. This Notice, the accompanying proxy statement and a form of proxy card are being mailed beginning on or about April 26, 2018 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 in person. However, whether or not you plan to attend the annual meeting in person, 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 Simonian".

Nancy Simonian
President and Chief Executive Officer

Cambridge, Massachusetts
April 26, 2018

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Important Notice Regarding Internet Availability of Proxy Materials: The attached proxy statement and our 2017 annual report to stockholders, which includes our Annual Report on Form 10-K for the fiscal year ended December 31, 2017, are available at www.envisionreports.com/SYRS. These documents are also available to any stockholder who wishes to receive a paper copy by calling (866) 641-4276, by emailing investorvote@computershare.com with "Proxy Materials Syros Pharmaceuticals, Inc." in the subject line, or by submitting a request over the Internet at www.envisionreports.com/SYRS.

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**620 Memorial Drive, Suite 300
Cambridge, Massachusetts 02139
(617) 744-1340**

**PROXY STATEMENT
2018 ANNUAL MEETING OF STOCKHOLDERS
To Be Held on June 14, 2018**

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 Thursday, June 14, 2018 at 1:00 p.m., Eastern Daylight Time, at our corporate offices located at 620 Memorial Drive, Suite 300, Cambridge, Massachusetts 02139, and at any adjournment thereof. 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 the means by which you actually 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, 2017 available to stockholders for the first time on or about April 26, 2018.

A copy of our Annual Report on Form 10-K for the fiscal year ended December 31, 2017, 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., 620 Memorial Drive, Suite 300, Cambridge, Massachusetts 02139 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, 2017 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 2018 annual meeting of stockholders to be held at our corporate offices located at 620 Memorial Drive, Suite 300, Cambridge, Massachusetts 02139 on Thursday, June 14, 2018 at 1:00 p.m., Eastern Daylight Time. As a holder of common stock, you are invited to attend the annual meeting 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.

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 2017 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 four Class II directors, Srinivas Akkaraju, M.D., Ph.D., Vicki L. Sato, Ph.D., Phillip A. Sharp, Ph.D. and Richard A. Young, Ph.D., nominated by our board of directors, each to serve for a three-year term expiring at the 2021 annual meeting of stockholders or until his or 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, 2018 (Proposal 2); and
3. The transaction of any other business that may properly come before the annual meeting or any adjournment or postponement thereof.

Q. 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 20, 2018, the record date for our annual meeting. There were 32,481,830 shares of our common stock outstanding and entitled to vote at the annual meeting as of the record date.

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.

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 meeting in person or by proxy as follows:

1. **Over the Internet:** 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

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or your Internet vote cannot be completed, and you will receive an error message. You must submit your Internet proxy before 11:59 p.m., Eastern Daylight Time, on June 13, 2018, the day before the annual meeting, for your proxy to be valid and your vote to count.

2. **By Telephone:** To vote by telephone, please call (800) 652-VOTE (8683), and follow the instructions provided on the proxy card. If you vote by telephone, you do not need to complete and mail your proxy card or vote your proxy over the Internet. You must specify how you want your shares voted and confirm your vote at the end of the call or your telephone vote cannot be completed. You must submit your telephonic proxy before 11:59 p.m., Eastern Daylight Time, on June 13, 2018, the day before the annual meeting, for your proxy to be valid and your vote to count.
3. **By Mail:** To vote by mail, you must mark, sign and date the proxy card and then mail the proxy card in accordance with the instructions on the proxy card. If you vote by mail, you do not need to vote your proxy over the Internet or by telephone. Computershare Trust Company, N.A. must receive the proxy card not later than June 13, 2018, 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 particular matter, they will be voted in accordance with the recommendations of our board of directors.
4. **In Person at the Meeting:** If you attend the annual meeting, you may deliver your completed proxy card in person or you may vote by completing a ballot, which we will provide to you at the meeting.

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. In order to vote your shares, you will need to follow the instructions that your broker provides you. Many brokers solicit voting instructions over the Internet or by telephone.

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

However, under applicable stock exchange rules that regulate voting by registered brokerage firms, the election of our nominees to serve as Class II directors (Proposal 1) is not considered to be a discretionary item. Accordingly, if you do not give your broker voting instructions on Proposal 1, your broker may not vote your shares with respect to this matter and your shares will be counted as "broker non-votes" with respect to the proposal. A "broker non-vote" occurs when shares held by a broker are not voted with respect to a particular 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. You may not vote shares held in street name in person at the meeting, however, unless you obtain a legal proxy, executed in your favor, from the holder of record (i.e., your broker). A legal proxy is *not* the form of proxy included with this proxy statement.

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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. 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 annual meeting and vote in person as instructed above. Attending the annual meeting will not alone revoke your Internet vote, telephone vote or proxy card submitted by mail, as the case may be.
4. Give our corporate secretary written notice before or at the meeting that you want to revoke your proxy.

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 in person at the annual meeting if you obtain a legal proxy as described in the answer above.

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 in person 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 in person at the meeting. Further, for purposes of establishing a quorum, we will count as present shares that a stockholder holds even if the stockholder votes to abstain or only votes on one of the proposals. In addition, we will count as present shares held in "street name" by brokers who indicate on their proxies that they do not have authority to vote those shares. If a quorum is not present, we expect to adjourn the annual meeting until we obtain a quorum.

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

A. Proposal 1—Election of Class II Directors

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

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

The affirmative vote of the holders of shares of common stock representing a majority of the votes cast on the matter is required for the ratification of the appointment of Ernst & Young LLP as our independent registered public accounting firm for the year ended December 31, 2018.

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

Q. Who will count the vote?

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

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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 four nominees to serve as Class II directors, each for a three-year term; and

FOR the ratification of the appointment of Ernst & Young LLP as our independent registered public accounting firm for the fiscal year ending December 31, 2018.

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 II directors and the ratification of the appointment of Ernst & Young LLP as our independent registered public accounting firm. If any other matters are properly presented at the annual meeting, the persons named in the accompanying proxy intend to vote, or otherwise act, in accordance with their judgment on the matter.

Q. 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.

Implications of Being an "Emerging Growth Company"

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, and may remain an emerging growth company for up to five years from the date of our initial public offering, or IPO. The JOBS Act contains provisions that, among other things, reduce certain reporting requirements for an "emerging growth company." For so long as we remain an emerging growth company, we are permitted and plan to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include reduced disclosure obligations regarding executive compensation. In addition, as an emerging growth company, we are not required to conduct votes seeking approval, on an advisory basis, of the compensation of our named executive officers or the frequency with which such votes must be conducted. We may take advantage of some or all these exemptions until such time as we are no longer an emerging growth company. We would cease to be an emerging growth company if we have more than \$1.07 billion in annual revenue, we have more than \$700 million in market value of our stock held by non-affiliates or we issue more than \$1 billion of non-convertible debt over a three-year period. We have taken advantage of certain reduced reporting obligations in this proxy statement. Accordingly, the information contained herein may be different than the information you receive from other public companies in which you hold stock.

BOARD OF DIRECTORS AND CORPORATE GOVERNANCE

Election of Directors

Our board of directors is divided into three classes, with members of each class holding office for staggered three-year terms. There are currently four Class II directors (Srinivas Akkaraju, M.D., Ph.D., Vicki L. Sato, Ph.D., Phillip A. Sharp, Ph.D. and Richard A. Young, Ph.D.) whose terms expire at this annual meeting of stockholders; three Class III directors (Marsha H. Fanucci, Sanj K. Patel and Nancy Simonian M.D.) whose terms expire at the 2019 annual meeting of stockholders; and three Class I directors (Amir Nashat, Ph.D., Robert T. Nelsen and Peter Wirth) whose terms expire at the 2020 annual meeting of stockholders (in all cases subject to the election and qualification of their successors or to their earlier death, resignation or removal).

Set forth below are the names of and certain information for each member of our board, including the nominees for election as Class II directors, as of March 31, 2018. The information presented includes each director's and nominee's principal occupation and business experience for the past five years, and the names of other public companies of which he or she has served as a director during the past five years. The information presented below regarding the specific experience, qualifications, attributes and skills of each director and nominee led our nominating and corporate governance committee and our board of directors to conclude that he or she should serve as a director. In addition, we believe that all of our directors and nominees possess the attributes or characteristics described in "Corporate Governance Matters—Director Nomination Process" that the nominating and corporate governance committee expects of each director. There are no family relationships among any of our directors, nominees for director, or executive officers.

Name	Age	Position(s)
<i>Class II Director Nominees</i>		
Srinivas Akkaraju, M.D., Ph.D.(1)(2)	50	Director
Vicki L. Sato, Ph.D.(1)(2)	69	Director
Phillip A. Sharp, Ph.D.(2)(3)	73	Director
Richard A. Young, Ph.D.(2)	64	Director
<i>Class I Directors</i>		
Amir Nashat, Ph.D.(1)(4)	45	Director
Robert T. Nelsen(3)	54	Director
Peter Wirth(3)	67	Chair of the Board of Directors
<i>Class III Directors</i>		
Marsha H. Fanucci(4)	64	Director
Sanj K. Patel(4)	48	Director
Nancy Simonian, M.D.	57	President and Chief Executive Officer, Director

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

Class II Director Nominees

Srinivas Akkaraju, M.D., Ph.D. has served on our board of directors since June 2017. Dr. Akkaraju is a founder and managing general partner of Samsara BioCapital, a venture capital firm, a position he has held since March 2017. From April 2013 to February 2016, Dr. Akkaraju served as a general

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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 Seattle Genetics, Inc., Intercept Pharmaceuticals, Inc., Versartis, Inc. and aTyr Pharma, Inc., publicly traded biotechnology companies. Previously, he served as a director of Barrier Therapeutics, Inc., Eyetech Pharmaceuticals, Inc., ZS Pharma Inc. and Synageva Biopharma Corp., all publicly traded biotechnology companies, and Amarin Corporation plc, a foreign 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.

Vicki L. Sato, Ph.D. has served on our board of directors since August 2013. She was a professor of management practice at Harvard Business School from September 2006 to July 2017 and was a professor in the Department of Molecular and Cell Biology at Harvard University from July 2005 until October 2015. Previously, she served as president of Vertex Pharmaceuticals, Inc., a publicly-traded biotechnology company, which she joined in 1992. Prior to becoming president of Vertex, she was the chief scientific officer and senior vice president of research and development. Prior to joining Vertex, Dr. Sato served as vice president of research at Biogen Inc., a publicly-traded biotechnology company. Dr. Sato is a member of the boards of directors of the following public companies: Bristol Myers Squibb Company, BorgWarner, Inc., and Denali Therapeutics, Inc. She previously served on the board of directors of PerkinElmer, Inc. Dr. Sato received her A.B. from Radcliffe College and her A.M. and Ph.D. degrees from Harvard University. She conducted her postdoctoral work at both the University of California Berkeley and Stanford Medical Center. We believe Dr. Sato is qualified to serve on our board of directors because of her experience as a senior executive and as a director of several life sciences companies, and because of her knowledge of our industry.

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 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 has served on the board of directors of Alnylam Pharmaceuticals, Inc., a biopharmaceutical company, since 2002. He earned his B.A. from Union College (Kentucky) in 1966 and a Ph.D. in chemistry from the University of Illinois, Champaign-Urbana in 1969. 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 the Massachusetts Institute of Technology 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 previously served as a director of Enzon Pharmaceuticals, Inc., a biopharmaceutical 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.

Class I Directors

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

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boards of directors of aTyr Pharma, Inc., Fate Therapeutics, Inc. and Selecta Biosciences, Inc., all biopharmaceutical companies. He previously served on the boards of directors of Bind Therapeutics, Inc. and Receptos, Inc., each a biopharmaceutical company. Dr. Nashat received a Ph.D. in chemical engineering from the Massachusetts Institute of Technology, 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.

Robert T. Nelsen has served on our board of directors since our inception in November 2011 and was our lead independent director from December 2015 to January 2017. Mr. Nelsen was a co-founder of ARCH Venture Partners, a venture capital firm, and has served in various capacities for ARCH and affiliated entities since 1994. He is currently a managing director of ARCH Venture Corporation. Mr. Nelsen is a director of Denali Therapeutics, Inc., Juno Therapeutics, Inc. and Sienna Biopharmaceuticals, Inc., each a biopharmaceutical company. Mr. Nelsen previously served as a trustee of the Fred Hutchinson Cancer Research Institute, a trustee of the Institute for Systems Biology, and a director of the National Venture Capital Association. He has also served as a director of the following biopharmaceutical companies: Agios Pharmaceuticals, Inc., Bellerophon Therapeutics, Inc., Fate Therapeutics, Inc., Kythera Biopharmaceuticals, Inc., NeurogesX, Inc. and Sage Therapeutics, Inc. Mr. Nelsen received a B.S. with majors in biology and economics from the University of Puget Sound and an M.B.A. from the University of Chicago. We believe Mr. Nelsen is qualified to serve on our board of directors due to his extensive experience as an investor in, and director of, early stage biopharmaceutical and life sciences companies.

Peter Wirth has served as Chair of our board of directors since January 2017. Mr. Wirth currently serves as Chairman of FORMA Therapeutics Holdings LLC, a privately-held small molecule drug discovery company, Executive Chairman of ZappRx, Inc., a privately-held digital health company, and Senior Advisor to Zai Lab Limited, a publicly-held biopharmaceutical company based in Shanghai, China. From November 2011 to April 2014, Mr. Wirth served as President and director of Lysosomal Therapeutics, Inc., a privately-held biopharmaceutical company. Mr. Wirth was a senior executive at Genzyme Corporation 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 previously served as a director of Synageva BioPharma Corp., a biopharmaceutical company. Mr. Wirth was a 2012 Advanced Leadership Fellow at Harvard University. He 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 III Directors

Marsha H. Fanucci has been a member of our board of directors since October 2015. Since 2009, Ms. Fanucci has been an independent consultant. From 2004 through 2009, she served as senior vice president and chief financial officer of Millennium Pharmaceuticals, Inc., a biopharmaceutical company that was subsequently acquired by Takeda Pharmaceuticals Company, or Takeda. She previously served in various other roles at Millennium, including as vice president, finance and corporate strategy and vice president, corporate development. Ms. Fanucci is a member of the boards of directors of Alnylam Pharmaceuticals, Inc. and Ironwood Pharmaceuticals, Inc., each a publicly-traded biopharmaceutical company. She previously served as a director of Momenta Pharmaceuticals, Inc., a publicly-traded biopharmaceutical company. Ms. Fanucci received her B.S. in pharmacy from West Virginia University

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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.

Sanj K. Patel has served on our board of directors since May 2016. Mr. Patel is the founder, chief executive officer and chairman of Kiniksa Pharmaceuticals, Ltd., a privately-held biotechnology company. Before founding Kiniksa in June 2015, Mr. Patel was the president and chief executive officer and a director of Synageva BioPharma Corp. from June 2008 until its acquisition by Alexion, Inc. in June 2015. From 1999 to 2008, Mr. Patel worked at Genzyme Corporation, where most recently he was the head of U.S. sales, marketing and commercial operations for its lysosomal storage disorder franchise. Previously, Mr. Patel held several cross-functional senior leadership roles at Genzyme, including vice president, clinical research and head of the global clinical research operations council. Prior to Genzyme, Mr. Patel held roles in clinical research and commercial development with increasing levels of responsibility at Burroughs Wellcome, a private foundation; Hoechst Marion Roussel, a privately-held life sciences company; and Fujisawa Pharmaceutical Co. Ltd., a privately-held pharmaceutical company. Mr. Patel is a member of the board of directors of BioCryst Pharmaceuticals, Inc., a biotechnology company, and was previously a member of the board of directors of Intercept Pharmaceuticals, Inc., a biotechnology company. Mr. Patel obtained his B.Sc. with honors in biotechnology from the University of the South Bank, London. He completed his post graduate management and business degree, and doctorate level research program at Ealing College, London, and the Wellcome Foundation, respectively. We believe Mr. Patel is qualified to serve as a director based on his extensive healthcare industry leadership experience.

Nancy Simonian, M.D. has been our chief executive officer since July 2012. From 2001 to October 2011, Dr. Simonian was employed by Takeda Pharmaceuticals Company, a publicly-held biopharmaceutical company, and at Millennium Pharmaceuticals, Inc. 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-held biotechnology company, most recently as vice president of clinical development. She is a member of the boards of directors of Seattle Genetics, Inc., a biotechnology company, the Damon Runyon Cancer Research Foundation and the Biotechnology Industry Organization. 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.

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., 620 Memorial Drive, Suite 300, Cambridge, Massachusetts 02139, Attention: Chief Financial Officer.

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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. Our president and chief executive officer is responsible for setting the strategic direction for our company and the day-to-day leadership and performance of our company, while the chair of our board of directors presides over meetings of the board of directors, including executive sessions of the board of directors, and performs oversight responsibilities. We do not currently have a lead independent director because the chair of our board of directors is independent within the meaning of the Nasdaq Listing Rules. Our board of directors has standing audit, compensation and nominating and corporate governance committees that currently consist of, and are chaired by, independent directors. Our board of directors delegates substantial responsibilities to the committees, which then report their activities and actions back to the full board of directors. We believe that the independent committees of our board of directors and their chairpersons promote effective independent governance. We believe this structure represents an appropriate allocation of roles and responsibilities for our company at this time 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

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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 on account of a stock option granted to him in September 2016 in consideration for consulting services. Our board of directors also determined that Marsha H. Fanucci, Amir Nashat, Ph.D. and Sanj K. Patel, who currently comprise our audit committee, Robert T. Nelsen, Phillip A. Sharp, Ph.D. and Peter Wirth, who currently comprise our compensation committee and Srinivas Akkaraju, M.D., Ph.D., Amir Nashat, Ph.D., and Vicki L. Sato, 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 addition, our board of directors determined that Vicki L. Sato, Ph.D., who served on the compensation committee for part of 2017, at the time of such service, satisfied the applicable independence standards for such committee. In making such determinations, our board of directors considered the relationships that each such non-employee director has with our company and all other facts and circumstances our board of directors deemed relevant in determining independence, including the beneficial ownership of our capital stock by each non-employee director.

Board of Director Meetings and Attendance

Our board of directors held five meetings, and acted by written consent five times, during the year ended December 31, 2017, or fiscal 2017. During fiscal 2017, each of the directors then in office attended at least 75% of the aggregate number of board of director meetings and the number of meetings held by all committees of the board of directors on which such director then served. Our corporate governance guidelines provide that directors are expected to attend the annual meeting of stockholders. All but one member of our board of directors attended our 2017 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.

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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, 620 Memorial Drive, Suite 300, Cambridge, Massachusetts 02139.

Committees of the Board of Directors

We have established an audit committee, a compensation committee and a nominating and corporate governance committee. In March 2018, we established a research and development committee. Each of these committees operates under a charter that has been approved by our board of directors. A copy of each committee's charter can be found under the "Investors & Media—Governance" section of our website, which is located at www.syros.com.

Audit Committee

Our audit committee's responsibilities include:

- appointing, approving the compensation of, and assessing the independence of our registered public accounting firm;
- overseeing the work of our independent registered public accounting firm, including through the receipt and consideration of reports from such firm;
- reviewing and discussing with management and our independent registered public accounting firm our annual and quarterly financial statements and related disclosures;
- 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 Marsha H. Fanucci, Amir Nashat, Ph.D. and Sanj K. Patel. 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 four meetings, and acted by written consent once, during fiscal 2017.

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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.

The current members of our compensation committee are Phillip A. Sharp, Ph.D., Robert T. Nelsen and Peter Wirth. Mr. Wirth chairs the compensation committee. Vicki L. Sato, Ph.D. served on this committee during January 2017. The compensation committee held four meetings, and acted by written consent three times, during fiscal 2017.

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., Amir Nashat, Ph.D., and Vicki L. Sato, Ph.D. Dr. Nashat chairs the nominating and corporate governance committee. The nominating and corporate governance committee held four meetings, and acted by written consent once, during fiscal 2017.

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 particular candidate for inclusion in our board of directors' slate of recommended director nominees, including candidates

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recommended by stockholders, the nominating and corporate governance committee of our board of directors applies the criteria set forth in our corporate governance guidelines. These criteria include the candidate's integrity, business acumen, knowledge of our business and industry, the ability to act in the interests of all stockholders, and lack of conflicts of interest.

The director biographies on pages 6 to 9 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, 620 Memorial Drive, Suite 300, Cambridge, Massachusetts 02139. Assuming that 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 2019 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 2019 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 and legal and compliance risks; our compensation committee oversees risk management activities relating to our compensation policies and practices and management succession planning; and our nominating and corporate

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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 \$120,000, 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;

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- whether the transaction was undertaken in the ordinary course of our business;
- whether the terms of the transaction are no less favorable to us than the terms that could have been reached with an unrelated third party;
- the purpose of, and the potential benefits to us of, the transaction; and
- any other information regarding the related person transaction or the related person in the context of the proposed transaction that would be material to investors in light of the circumstances of the particular transaction.

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

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

Related Person Transactions

In addition to the compensation arrangements with directors and executive officers described elsewhere in this proxy statement, since January 1, 2017, we have engaged in the following transactions in which the amount involved exceeded \$120,000 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 April 2017, we completed a private placement of 2,592,591 shares of our common stock at a price of \$13.50 per share, for an aggregate purchase price of \$35.0 million. Srinivas Akkaraju, M.D., Ph.D., who joined our board of directors in June 2017, is one of the managers of Samsara BioCapital GP, LLC, which is the general partner of Samsara BioCapital, L.P., a venture capital firm which purchased 740,740 shares in this private placement at an aggregate purchase price of \$10.0 million.

Consulting Agreement with Dr. Young

Richard A. Young, one of our directors, earned \$125,000 during fiscal 2017 pursuant to the terms of a consulting agreement he entered with our company that is unrelated to his service as a member of our board of directors.

Investors' Rights Agreement

We are a party to an amended and restated investors' rights agreement, dated as of October 9, 2014, with the purchasers of preferred stock prior to our IPO, including ARCH Venture Fund VII, L.P., entities affiliated with FMR LLC, entities affiliated with Flagship Ventures, entities affiliated with Polaris, Nancy Simonian, M.D. and Phillip A. Sharp, Ph.D., and Stéphane Bancel, a former director of our company. The investors' rights agreement provides these holders the right to demand that we file a registration statement or request that their shares be covered by a registration statement that we are otherwise filing.

EXECUTIVE AND DIRECTOR COMPENSATION

Executive Officers

Certain information regarding our executive officers who are not also directors, as of March 31, 2018, is set forth below.

Name	Age	Position(s)
Joseph J. Ferra, Jr.	42	Chief Financial Officer
Eric R. Olson, Ph.D.	60	Chief Scientific Officer
Gerald E. Quirk, Esq.	50	Chief Legal & Administrative Officer
David A. Roth, M.D.	55	Chief Medical Officer
Jeremy P. Springhorn, Ph.D.	56	Chief Business Officer

Joseph J. Ferra, Jr. has served as our chief financial officer since March 2018. Mr. Ferra joined us from JMP Securities LLC, where he served as Managing Director from March 2014 to March 2018 and Co-Head of Healthcare Investment Banking from March 2017 to March 2018. Previously, he was employed by UBS Investment Bank from September 2009 to March 2014 serving, most recently, as Executive Director of Global Healthcare Investment Banking. Mr. Ferra received a B.S. in chemistry with distinction from Purdue University and an M.B.A. from The Stephen M. Ross School of Business at the University of Michigan.

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

Gerald E. Quirk, Esq. has served as our chief legal officer from September 2016 to June 2017 and as our chief legal and administrative officer since June 2017. He previously served as executive vice president, business operations and general counsel of Tokai Pharmaceuticals, Inc., a biotechnology company, from May 2015 to August 2016. Prior to that, Mr. Quirk was a partner and co-chair of the life sciences practice at Choate, Hall & Stewart LLP, a Boston law firm, from August 2012 until May 2015. Mr. Quirk previously served as vice president, corporate affairs and general counsel at Infinity Pharmaceuticals, Inc. from August 2006 until August 2012, and prior to that held legal and business development positions of increasing responsibility at Genzyme Corporation. Mr. Quirk holds a B.A. in political science from Swarthmore College, an Ed.M. in educational administration from Harvard University, and a J.D. from Northeastern University.

David A. Roth, M.D. has been our chief medical officer since December 2015. Previously, Dr. Roth was employed by Infinity Pharmaceuticals, Inc., a pharmaceutical company, 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 Inc., a pharmaceutical company, from 2009 to August 2013. Prior to joining the pharmaceutical industry, Dr. Roth's experience included over 10 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 the Massachusetts Institute of Technology and his M.D. from Harvard Medical School in the Harvard MIT Division of Health Sciences and Technology, where he remains on the affiliated faculty.

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Jeremy P. Springhorn, Ph.D. has served as our chief business officer since November 2017. Prior to joining us, Dr. Springhorn served as a partner in corporate development at Flagship Pioneering, a venture capital firm, from March 2015 to June 2017. Prior to that, he served in a number of progressively-responsible positions in research and corporate development at Alexion Pharmaceuticals, Inc. from 1992 to March 2015, most recently as Vice President, Corporate Development. Dr. Springhorn has served on the board of directors of uniQure NV since September 2017. Dr. Springhorn holds a B.A. in chemistry and biochemistry from Colby College and a Ph.D. in biochemistry and molecular biology from the Louisiana State University Medical Center.

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 2017, our named executive officers are Nancy Simonian, M.D., our President and Chief Executive Officer, David A. Roth, M.D., our Chief Medical Officer, Jeremy P. Springhorn, Ph.D., our Chief Business Officer, and Kyle D. Kuvalanka, our former Chief Operating Officer, whose employment with us ended in September 2017. In addition, this section provides qualitative information regarding the manner and context in which compensation is awarded to and earned by our named executive officers and is intended to place in perspective the data presented in the following tables and the corresponding narrative.

Summary Compensation Table

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

Name and Position of Current Named Executive Officers	Year	Salary (\$)	Option Awards \$(1)	Non-Equity Incentive Plan Compensation \$(S)	All Other Compensation \$(2)	Total \$(S)
Nancy Simonian, M.D.(3) President & Chief Executive Officer	2017	525,000	1,390,127	308,000	270	2,223,397
David A. Roth, M.D. Chief Medical Officer	2016	473,260	1,248,816	212,500	270	1,934,846
Jeremy P. Springhorn, Ph.D. (4) Chief Business Officer	2017	53,250	1,750,956	—	34	1,804,240
Name and Position of Named Executive Officer No Longer Employed by Us						
Kyle D. Kuvalanka(5) Former Chief Operating Officer	2017	283,705	619,600	—	300,255	1,203,560
	2016	380,000	—	115,045	270	495,315

- (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 Financial Accounting Standards Board Accounting Standard Codification, or ASC, Topic 718. Unlike the calculations contained in our consolidated financial statements, 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 10 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 "All Other Compensation" column reflect, for each named executive officer, the cost to us of life insurance premiums paid for the named executive officer. In the case of Mr. Kuvalanka, amounts in this column for 2017 also include \$292,744 in accrued severance

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payments and \$7,308 in accrued vacation associated with his separation from our company in September 2017.

- (3) 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.
- (4) Dr. Springhorn commenced employment with us on November 13, 2017. Amounts shown for 2017 represent compensation earned by Dr. Springhorn during that partial year of employment.
- (5) Mr. Kuvalanka's employment with us ended on September 22, 2017. Except as described in footnote (2) to this table, amounts shown for 2017 represent compensation earned by Mr. Kuvalanka 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 2017 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 2017, 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 January 2016, Dr. Simonian's base salary was set at \$455,000 and in September 2016, her annual base salary was increased to \$500,000 retroactive to the closing of our IPO in July 2016. Dr. Simonian's base salary increased to \$516,000 effective February 16, 2017. In September 2017, our board of directors increased Dr. Simonian's annual base salary to \$560,000 effective October 1, 2017.

The annualized base salaries for Dr. Roth and Mr. Kuvalanka for 2016 were \$380,000. Base salaries for Dr. Roth and Mr. Kuvalanka were increased to \$392,000 effective February 16, 2017. In September 2017, our board of directors increased Dr. Roth's annual base salary to \$430,000 effective October 1, 2017. Mr. Kuvalanka's employment with us ended in September 2017 and we paid him a base salary of \$283,705 for his partial year of employment. Under the terms of his offer letter, Mr. Kuvalanka became entitled to severance payments totaling \$292,744 upon his separation from our company, of which \$105,538 was paid in fiscal 2017.

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Dr. Springhorn commenced employment with us in November 2017. In 2017, we paid him a base salary of \$53,250 for his partial year of employment, and his annualized base salary is \$390,000.

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 50% of her annual base salary in 2016. In September 2017, our board of directors increased Dr. Simonian's bonus target to 55% of her annual base salary for fiscal 2017. Our other named executive officers are eligible for a performance-based cash bonus of a percentage of such named executive officer's base salary, 90% of which is tied to achievement of corporate goals as determined by the compensation committee, and 10% of which is tied to the achievement of individual goals as recommended by Dr. Simonian and approved by the compensation committee. The bonus target for our other named executive officers was 35% of such officers' annual base salary in 2016. In September 2017, our board of directors increased the bonus target for Dr. Roth to 40% of his annual base salary for fiscal 2017. The bonus target for Dr. Springhorn was set at 40% of his annual base salary upon commencement of his employment.

In February 2017, we made cash bonus awards of \$212,500 to Dr. Simonian, and \$115,045 to each of Dr. Roth and Mr. Kuvalanka, based on the compensation committee's assessment of achievement of corporate and individual goals during 2016. In March 2018, we made cash bonus awards of \$308,000 to Dr. Simonian and \$172,000 to Dr. Roth based on the compensation committee's assessment of achievement of corporate and individual goals during fiscal 2017. Dr. Springhorn was not eligible to receive a cash bonus award for fiscal 2017 performance based on his employment start date.

Equity Incentives

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

In February 2017, Dr. Simonian was granted an option to purchase 175,000 shares of our common stock. This option vested as to 25% of the shares on February 10, 2018, with the remaining shares vesting in equal monthly installments thereafter through February 28, 2021. In March 2016, Dr. Simonian was granted an option to purchase 93,333 shares of common stock, which option vested as to 25% of the shares on March 31, 2017, with the remaining shares vesting in equal monthly installments thereafter through March 31, 2020. In September 2016, Dr. Simonian was granted an option to purchase an additional 75,000 shares of common stock, which option vested as to 25% of the shares on September 16, 2017, with the remaining shares vesting in equal monthly installments thereafter through September 16, 2020.

In February 2017, Dr. Roth was granted an option to purchase 63,500 shares of our common stock. This option vested as to 25% of the shares on February 10, 2018, with the remaining shares vesting in

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equal monthly installments thereafter through February 28, 2021. Dr. Roth was not granted any stock options during 2016.

In November 2017, Dr. Springhorn was granted two options to purchase 150,000 and up to 50,000 shares of common stock, respectively. The first grant will vest as to 25% of the shares on November 13, 2018, with the remaining shares vesting in equal monthly installments thereafter through November 13, 2021. Dr. Springhorn's second grant vests upon the achievement of performance-based criteria, with 67% of the shares vesting upon execution by us of a collaboration agreement subject to certain limitations, and 33% of the shares vesting upon the earlier of clinical proof-of-concept for a company drug candidate other than SY-1425 or initiation of the first pivotal trial of a company drug candidate, in each case as determined by our board of directors, and in any event will vest in full on November 13, 2023.

In February 2017, Mr. Kuvalanka was granted an option to purchase 78,000 shares of our common stock. This option terminated in September 2017, prior to the vesting of any of the underlying shares, when Mr. Kuvalanka's employment with us ended. Mr. Kuvalanka was not granted any stock options during 2016.

Outstanding Equity Awards at Fiscal Year End 2017

The following table sets forth information regarding outstanding equity awards, which consist entirely of stock options, held by our named executive officers as of December 31, 2017.

Current Named Executive Officers	Number of Securities Underlying Unexercised Options Exercisable (#)		Number of Securities Underlying Unexercised Options Unexercisable (#)		Option Exercise Price (\$/share)	Option Expiration Date
	Options Exercisable (#)	Options Unexercisable (#)	Options Exercisable (#)	Options Unexercisable (#)		
Nancy Simonian, M.D.	23,455	—	—	75,050(1)	1.01	5/21/2023
	—	8,333(2)	3,751(2)	3,751(2)	1.01	5/21/2023
	41,795(3)	29,300(3)	29,300(3)	3,04	10/21/2024	
	26,904(4)	16,144(4)	16,144(4)	3.04	2/4/2025	
	21,523(5)	21,524(5)	21,524(5)	3.04	6/8/2025	
	40,831(6)	52,502(6)	52,502(6)	8.51	3/30/2026	
	23,436(7)	51,564(7)	51,564(7)	12.17	9/15/2026	
	—	175,000(8)	175,000(8)	10.90	2/9/2027	
David A. Roth, M.D.	86,023(9)	86,024(9)	86,024(9)	9.08	12/22/2025	
	—	51,614(10)	51,614(10)	9.08	12/22/2025	
	—	63,500(8)	63,500(8)	10.90	2/9/2027	
Jeremy P. Springhorn, Ph.D.	—	150,000(11)	150,000(11)	11.65	11/12/2027	
	—	50,000(12)	50,000(12)	11.65	11/12/2027	
Named Executive Officer No Longer Employed by Us						
Kyle D. Kuvalanka	—	—	—	—	—	—

- (1) This option was granted on May 22, 2013 and vests upon the achievement of performance-based criteria, and in any event will vest in full on July 2, 2018, subject to continued service.
- (2) This option was granted on October 22, 2014 and vested as to 25% of the shares on September 29, 2015 with the remaining shares vesting in equal monthly installments thereafter through September 29, 2018, subject to continued service.

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- (3) This option was granted on February 5, 2015 and vested as to 25% of the shares on February 5, 2016 with the remaining shares vesting in equal monthly installments thereafter through February 5, 2019, subject to continued service.
- (4) This option was granted on June 9, 2015 and vested as to 25% of the shares on June 9, 2016 with the remaining shares vesting in equal monthly installments thereafter through June 9, 2019, subject to continued service.
- (5) This option was granted on June 9, 2015 and vests upon the achievement of performance-based criteria, and in any event will vest in full on June 9, 2021, subject to continued service.
- (6) This option was granted on March 31, 2016 and vested as to 25% of the shares on March 31, 2017 with the remaining shares vesting in equal monthly installments thereafter through March 31, 2020, subject to continued service.
- (7) This option was granted on September 16, 2016 and vested as to 25% of the shares on September 16, 2017 with the remaining shares vesting in equal monthly installments thereafter through September 16, 2020, subject to continued service.
- (8) This option was granted on February 10, 2017 and vested as to 25% of the shares on February 10, 2018 with the remaining shares vesting in equal monthly installments thereafter through February 28, 2021, subject to continued service.
- (9) This option was granted on December 23, 2015 and vested as to 25% of the shares on December 7, 2016 with the remaining shares vesting in equal monthly installments thereafter through December 7, 2019, subject to continued service.
- (10) This option was granted on December 23, 2015 and vests upon the achievement of performance-based criteria, and in any event will vest in full on December 7, 2021, subject to continued service.
- (11) This option was granted on November 13, 2017 and vests as to 25% of the shares on November 13, 2018 with the remaining shares vesting in equal monthly installments thereafter through November 13, 2021, subject to continued service.
- (12) This option was granted on November 13, 2017 and vests upon the achievement of performance-based criteria, and in any event will vest in full on November 13, 2023, subject to continued service.

Employment and Change in Control Arrangements

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

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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 of his or her employment, (2) not to solicit our employees during his or her employment and for a period of one year after the termination of his or her employment, (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 \$18,000 in 2017 and \$18,500 in 2018, 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 \$6,000 in 2017 and 2018. We make matching contributions at a rate of 100% of each employee's contribution up to a maximum matching contribution of 1% of the employee's compensation and 50% of each employee's contribution in excess of 1% 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 Considerations

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 to each of the company's chief executive officer and the three most highly compensated executive officers (other than the chief executive officer and chief financial officer). Pursuant to tax legislation signed into law on December 22, 2017 (referred to in this paragraph as the Tax Act), for taxable years beginning after December 31, 2017, the Section 162(m) deduction limitation is expanded so that it also applies to compensation in excess of \$1 million paid to a public company's chief financial officer. 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 Act 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 to each of the executives described

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above (other than certain grandfathered compensation or compensation paid pursuant to certain equity awards granted before or during a transition period following our IPO) will not be deductible by us.

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. The chair of each committee and the chair of the board of directors receive higher retainers for such service. These fees are payable in arrears in four equal quarterly installments on the last day of each quarter, subject to proration for any portion of such quarter that the director is not serving on our board of directors, on such committee or in such position. 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	\$ 35,000	\$ 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	\$ 7,000	\$ 3,500	

In addition, under this director compensation program, we granted the directors who were in office at the time of the closing of our IPO, and will grant to new non-employee directors upon their initial election to the board, an initial option to purchase 22,000 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 monthly 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 director who has served on our board of directors for at least six months an option to purchase 11,000 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 50% of the shares on the six-month anniversary of the date of grant and as to the remainder of the shares monthly 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.

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.

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The following table sets forth information regarding compensation earned by our non-employee directors during fiscal 2017.

Name	Fees Earned or Paid in Cash (\$)	Option Awards (\$)(1)	Total (\$)
Srinivas Akkaraju, M.D., Ph.D.	21,685	238,680	260,365
Marsha H. Fanucci	50,000	116,709	166,709
Amir Nashat, Ph.D.	47,971	116,709	164,680
Robert T. Nelsen	40,000	116,709	156,709
Sanj K. Patel	42,500	116,709	158,579
Vicki L. Sato, Ph.D.	40,436	116,709	157,145
Phillip A. Sharp, Ph.D.	42,184	116,709	158,893
Peter Wirth	67,114	170,890	238,004
Richard A. Young, Ph.D.(2)	35,000	116,709	151,709

- (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. Unlike the calculations contained in our consolidated financial statements, 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 10 to our financial statements included in our Annual Report on Form 10-K regarding assumptions underlying the valuation of equity awards.
- (2) Dr. Young also earned \$125,000 during fiscal 2017 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.

As of December 31, 2017, 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.	22,000
Marsha H. Fanucci	47,666
Amir Nashat, Ph.D.	33,000
Robert T. Nelsen	33,000
Sanj K. Patel	47,666
Vicki L. Sato, Ph.D.	58,095
Phillip A. Sharp, Ph.D.	75,857
Peter Wirth	22,000
Richard A. Young, Ph.D.	108,000

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;

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

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

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

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

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

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

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

SECURITIES AUTHORIZED FOR ISSUANCE UNDER EQUITY COMPENSATION PLANS

The following table contains information about our equity compensation plans as of December 31, 2017. As of December 31, 2017, we had three equity compensation plans, each of which was approved by our stockholders: our 2012 Plan, our 2016 Plan and our 2016 Employee Stock Purchase Plan, or 2016 ESPP.

Equity Compensation Plan Information

<u>Plan Category</u>	<u>Number of securities to be issued upon exercise of outstanding options, warrants and rights</u> <u>(a)</u>	<u>Weighted average exercise price of outstanding options, warrants and rights(1)</u> <u>(b)</u>	<u>Number of securities remaining available for future issuance under equity compensation plans (excluding securities reflected in column (a))</u> <u>(c)</u>
Equity compensation plans approved by security holders	2,808,968(2)\$	9.25	3,701,016(3)
Equity compensation plans not approved by security holders	37,700(4)\$	0.04	—
Total	2,846,668 \$	9.25	3,701,016(5)

- (1) Consists of the weighted average exercise price of the 2,846,668 stock options outstanding on December 31, 2017.
- (2) Consists of (i) 1,105,512 shares to be issued upon exercise of outstanding options under our 2012 Plan as of December 31, 2017 and (ii) 1,703,456 shares to be issued upon exercise of outstanding options under our 2016 Plan as of December 31, 2017.
- (3) Consists of (i) 2,880,493 shares that remained available for future issuance under our 2016 Plan as of December 31, 2017, and (ii) 820,523 shares that remained available for future issuance under our 2016 ESPP as of December 31, 2017. No shares remained available for future issuance under the 2012 Plan as of December 31, 2017.
- (4) Consists entirely of a non-statutory stock option granted by our board of directors to the Branta Group, LLC on December 5, 2012 in consideration for consulting services. This option, which is fully vested, was granted outside of any of our equity incentive plans.
- (5) 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, 2018, 1,056,935 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, 2018, 264,233 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, 2017 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 statement on Auditing Standards No. 1301, as adopted by the Public Company Accounting Oversight Board.

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, 2017.

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

Marsha H. Fanucci, Chair
Amir Nashat, Ph.D.
Sanj K. Patel

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 ten members, divided into three classes as follows:

- Class I is comprised of Amir Nashat, Ph.D., Robert T. Nelsen, and Peter Wirth, each with a term ending at the 2020 annual meeting of stockholders;
- Class II is comprised of Srinivas Akkaraju, M.D., Ph.D., Vicki L. Sato, Ph.D., Phillip A. Sharp, Ph.D., and Richard A. Young, Ph.D., each with a term ending at the 2018 annual meeting of stockholders; and
- Class III is comprised of Marsha H. Fanucci, Sanj K. Patel, and Nancy Simonian, M.D., each with a term ending at the 2019 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 Srinivas Akkaraju, M.D., Ph.D., Vicki L. Sato, Ph.D., Phillip A. Sharp, Ph.D., and Richard A. Young, Ph.D. for re-election as Class II directors, each with a term ending at the 2021 annual meeting of stockholders.

Unless otherwise instructed in the proxy or unless authority to vote is withheld, all executed proxies will be voted "FOR" the election of each of the Class II director nominees identified above to a three-year term ending at the 2021 annual meeting of stockholders, each such nominee to hold office until his or her successor has been duly elected and qualified. Each of the nominees has indicated a willingness to continue to serve as director, if elected. In the event that 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 in person or represented by proxy at the annual meeting and entitled to vote is required to elect each nominee as a director.

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

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

Our audit committee has appointed the firm of Ernst & Young LLP, or Ernst & Young, an independent registered public accounting firm, as independent auditors for the fiscal year ending December 31, 2018. Although stockholder approval of our audit committee's appointment of Ernst & Young 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 Ernst & Young. Ernst & Young has no direct or indirect material financial interest in our company or our subsidiaries. Representatives of Ernst & Young are expected to be present at the 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.

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Audit Fees and Services

Ernst & Young was our independent registered public accounting firm for the years ended December 31, 2017 and December 31, 2016. The following table summarizes the fees of Ernst & Young 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.

Fee Category	2017	2016
Audit Fees(1)	\$ 540,470	\$ 475,141
Audit-Related Fees	—	—
Tax Fees(2)	88,260	11,300
All Other Fees(3)	1,995	1,995
Total Fees	\$ 630,725	\$ 488,436

- (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 IPO that was completed in July 2016 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 Ernst & Young.
- (3) "All Other Fees" consist of database subscription fees paid to Ernst & Young.

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

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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, 2018.

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, 2018 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 32,236,427 shares of our common stock outstanding as of March 31, 2018. In addition, shares of common stock subject to options or other rights currently exercisable, or exercisable within 60 days of March 31, 2018, 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

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beneficial owner is c/o Syros Pharmaceuticals, Inc., 620 Memorial Drive, Suite 300, Cambridge Massachusetts 02139.

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					
ARCH Venture Fund VII, L.P.	4,637,137	—	—	4,637,137(1)	14.4%
Entities affiliated with FMR LLC	4,572,737	—	—	4,572,737(2)	14.2%
Entities affiliated with Flagship Ventures	3,204,437	—	—	3,204,437(3)	9.9%
Named Executive Officers and Directors					
Nancy Simonian, M.D.	530,700(4)	296,077	826,777	826,777	2.5%
David A. Roth, Ph.D.	—	132,092	132,092	132,092	*
Jeremy P. Springhorn, Ph.D.	—	6,667	6,667	6,667	*
Kyle D. Kuvalanka	—	—	—	—	—
Srinivas Akkaraju, M.D., Ph.D.	850,514(5)	6,720	857,234	857,234	2.7%
Marsha H. Fanucci	—	30,554	30,554	30,554	*
Amir Nashat, Ph.D.	1,586,653(6)	21,389	1,608,042	1,608,042	5.0%
Robert T. Nelsen	4,637,137(7)	21,389	4,658,526	4,658,526	14.4%
Sanj K. Patel	—	28,110	28,110	28,110	*
Vicki L. Sato, Ph.D.	—	43,886	43,886	43,886	*
Phillip A. Sharp, Ph.D.	266,666(8)	61,648	328,214	328,214	*
Peter Wirth	—	9,776	9,776	9,776	*
Richard A. Young, Ph.D.	420,101(9)	21,389	441,490	441,490	1.4%
All Current Executive Officers and Directors as a Group (15 persons)	8,291,771	932,540	9,224,311	9,224,311	27.8%

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

- (1) ARCH Venture Partners VII, L.P., or the GPLP, as the sole general partner of ARCH Venture Fund VII, L.P., or ARCH VII, may be deemed to beneficially own the shares held of record by ARCH VII. The GPLP disclaims beneficial ownership of all shares held of record by ARCH VII in which the GPLP does not have an actual pecuniary interest. ARCH Venture Partners VII, LLC, or the GPLLC, as the sole general partner of the GPLP, may be deemed to beneficially own the shares held of record by ARCH VII. The GPLLC disclaims beneficial ownership of all shares held of record by ARCH VII in which it does not have an actual pecuniary interest. Keith Crandell, Clinton Bybee and Robert T. Nelsen are the managing directors of the GPLLC, and may be deemed to share voting and dispositive power over the shares held of record by ARCH VII. Mr. Nelsen is a director of Syros. The managing directors disclaim beneficial ownership of all shares held of record by ARCH VII in which they do not have an actual pecuniary interest. ARCH Venture Fund VII, L.P. has an address at 8755 West Higgins Avenue, Suite 1025, Chicago, Illinois 60631. For information regarding ARCH VII, we have relied, without independent investigation, on the Schedule 13G/A filed by ARCH VII with the SEC on February 2, 2018.
- (2) FMR LLC ("FMR") and Abigail P. Johnson, a director, the chairman and the chief executive officer of FMR, each report beneficially owning and having sole dispositive power over 3,944,465 of the shares listed herein. Fidelity Growth Company Fund reports sole voting power over 1,665,189 of the shares listed herein. FMR reports sole voting power over 700,787 of the shares listed herein. Members of the Johnson family including Ms. Johnson, are the predominant owners,

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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 group 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, which power resides with the funds' boards of trustees. FMR has an address at 245 Summer Street, Boston, Massachusetts 02210. For information regarding FMR, we have relied, without independent investigation, on the Schedule 13G/A filed by FMR with the SEC on February 13, 2018. We also sold 628,272 shares of our common stock to Fidelity Management Trust Company ("FMTC") as part of a public offering completed in February 2018. The shares listed in this table as being beneficially owned by entities affiliated with FMR LLC include the shares sold to FMTC in the public offering.

- (3) Consists of 213,332 shares of common stock held by Flagship VentureLabs IV, LLC ("Flagship VentureLabs"), 2,378,663 shares of common stock held by Flagship Ventures Fund IV, L.P. ("Flagship Fund IV") and 612,442 shares of common stock held by Flagship Ventures Fund IV-Rx, L.P. ("Flagship Fund IV-Rx" and together with Flagship VentureLabs and Flagship IV, the "Flagship Funds"). Flagship Fund IV is a member of Flagship VentureLabs and also serves as its manager. The general partner of each of Flagship Fund IV and Flagship Fund IV-Rx is Flagship Ventures Fund IV General Partner LLC ("Flagship Fund IV GP"). Noubar B. Afeyan, Ph.D. and Edwin M. Kania, Jr. are the managers of Flagship Fund IV GP. Flagship Fund IV GP and each of these individuals may be deemed to share voting and investment power with respect to all shares held by the Flagship Funds. Each of the foregoing persons disclaims beneficial ownership of the shares except to the extent of any pecuniary interest therein. The address of such stockholder is 55 Cambridge Parkway, Suite 800E, Cambridge, Massachusetts 02142. For information regarding the Flagship Funds, we have relied, without independent investigation, on the Schedule 13D/A filed by the Flagship Funds with the SEC on August 21, 2017.
- (4) Consists of (i) 370,700 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.
- (5) Consists of 850,514 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.
- (6) Consists of 1,538,333 shares of common stock held by Polaris Partners VII, L.P. and 48,320 shares of common stock held by Polaris Entrepreneurs' Fund VII, L.P. The general partner of Polaris Partners VII, L.P. and Polaris Entrepreneurs' Fund VII, L.P. is Polaris Management Co. VII, L.L.C. ("Polaris Management"), and Polaris Management may be deemed to have sole voting and investment power over such shares. Polaris Management disclaims beneficial ownership of these shares, except to the extent of its pecuniary interest therein. Amir Nashat, a managing member of Polaris Management, may be deemed to have voting and investment power over such shares. The address of such stockholders is One Marina Park Drive, 10th Floor, Boston, Massachusetts 02210. For information regarding Polaris Partners VII, L.P. we

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have relied, without independent investigation, on the Schedule 13D filed by Polaris Management with the SEC on July 14, 2016.

- (7) See footnote 1.
- (8) 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.
- (9) Consists of (i) 315,101 shares of common stock held of record by Dr. Young and (ii) 105,000 shares of common stock held of record by the Richard Young 2017 Grantor Retained Annuity Trust.

Section 16(a) Beneficial Ownership Reporting Compliance

Section 16(a) of the Exchange Act requires our directors and officers and holders of more than 10% of our common stock to file with the SEC initial reports of ownership of our common stock and other equity securities on a Form 3 and reports of changes in such ownership on a Form 4 or Form 5. Directors and officers and holders of 10% of our common stock are required by SEC regulations to furnish us with copies of all Section 16(a) forms they file. To our knowledge, based solely on a review of our records and representations made by our directors and officers regarding their filing obligations, all Section 16(a) filing requirements were satisfied with respect to fiscal 2017.

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 2019 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 2019 annual meeting of stockholders, stockholder proposals must be received by us no later than December 27, 2018, which is 120 days prior to the first anniversary of the mailing date of this proxy, unless the date of the 2019 annual meeting of stockholders is changed by more than 30 days from the anniversary of our 2018 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 2019 annual meeting of stockholders but not included in the proxy statement by March 16, 2019, but not before February 14, 2019, 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 2019 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, 620 Memorial Drive, Suite 300, Cambridge, Massachusetts 02139.

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 2017 annual report to stockholders, which consists of our Annual Report on Form 10-K for the fiscal year ended December 31, 2017, to you if you write or call us at Syros Pharmaceuticals, Inc., 620 Memorial Drive, Cambridge, Massachusetts 02139, 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.



Admission Ticket

IMPORTANT ANNUAL MEETING INFORMATION

Electronic Voting Instructions

Available 24 hours a day, 7 days a week!

Instead of mailing your proxy, you may choose one of the voting methods outlined below to vote your proxy.

VALIDATION DETAILS ARE LOCATED BELOW IN THE TITLE BAR.

Proxies submitted by the Internet or telephone must be received by 11:59 p.m., Eastern Time, on June 13, 2018.

Vote by Internet

- Go to www.envisionreports.com/SYRS
- Or scan the QR code with your smartphone
- Follow the steps outlined on the secure website

Vote by telephone

- Call toll free 1-800-652-VOTE (8683) within the USA, US territories & Canada on a touch tone telephone
- Follow the instructions provided by the recorded message

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



Annual Meeting Proxy Card

▼ IF YOU HAVE NOT VOTED VIA THE INTERNET OR TELEPHONE, FOLD ALONG THE PERFORATION, 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 and FOR Proposal 2.

1. Election of Directors: For Withhold

01 – Srinivas Akkaraju,
M.D., Ph.D.

02 – Vicki L. Sato, Ph.D.

For Withhold

For Withhold

+

04 – Richard A. Young, Ph.D.

For Against Abstain

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, 2018.

B Non-Voting Items

Change of Address — Please print your new address below.

Comments — Please print your comments below.

Meeting Attendance

Mark the box to the right if you plan to attend the Annual Meeting.



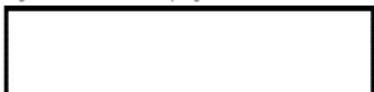
C Authorized Signatures — This section must be completed for your vote to be counted. — Date and Sign Below

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.



**2018 Annual Meeting Admission Ticket**

2018 Annual Meeting of
Syros Pharmaceuticals, Inc. Stockholders
Thursday, June 14, 2018, 1:00 p.m. Eastern Time
620 Memorial Drive, Suite 300
Cambridge, Massachusetts 02139

Upon arrival, please present this admission ticket
and photo identification at the registration desk.

▼ IF YOU HAVE NOT VOTED VIA THE INTERNET OR TELEPHONE, FOLD ALONG THE PERFORATION, DETACH AND RETURN THE BOTTOM PORTION IN THE ENCLOSED ENVELOPE. ▼



Proxy – Syros Pharmaceuticals, Inc.

Notice of 2018 Annual Meeting of Stockholders

620 Memorial Drive, Suite 300, Cambridge, MA 02139

Proxy Solicited by Board of Directors for Annual Meeting – June 14, 2018

Nancy A. Simonian, Gerald E. Quirk, or either of them, 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 on June 14, 2018 or at any postponement or adjournment thereof.

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

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

(Items to be voted appear on reverse side.)