
**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

Spero Therapeutics, 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:



675 Massachusetts Avenue, 14th Floor
Cambridge, Massachusetts 02139

September 30, 2020

To Our Stockholders:

You are cordially invited to attend the 2020 annual meeting of stockholders of Spero Therapeutics, Inc. to be held at 10:00 a.m. Eastern Time on Tuesday, October 27, 2020. As a result of public health and travel guidance due to COVID-19, this year's annual meeting will be conducted solely via live audio webcast on the Internet. You will be able to attend the annual meeting, vote and submit your questions during the annual meeting by visiting www.meetingcenter.io/266420432. The password for the meeting is SPRO2020. You will not be able to attend the annual meeting in person.

Details regarding the meeting, the business to be conducted at the meeting, and information about Spero Therapeutics, Inc. that you should consider when you vote your shares are described in this proxy statement.

At the annual meeting, three people will be elected to our board of directors. In addition, we will ask stockholders to ratify the selection of PricewaterhouseCoopers LLP as our independent registered public accounting firm for our fiscal year ending December 31, 2020. The board of directors recommends the approval of each of the proposals. Such other business will be transacted as may properly come before the annual meeting.

We hope you will be able to attend the annual meeting. Whether you plan to attend the annual meeting or not, it is important that you cast your vote either in person or by proxy. You may vote over the Internet as well as by telephone or by mail. When you have finished reading the proxy statement, you are urged to vote in accordance with the instructions set forth in this proxy statement. We encourage you to vote by proxy so that your shares will be represented and voted at the meeting, whether or not you can attend.

Thank you for your continued support of Spero Therapeutics, Inc. We look forward to seeing you at the annual meeting.

Sincerely,

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

Ankit Mahadevia, M.D.
President and Chief Executive Officer

SPERO THERAPEUTICS, INC.
675 Massachusetts Avenue, 14th Floor
Cambridge, Massachusetts 02139

September 30, 2020

NOTICE OF 2020 ANNUAL MEETING OF STOCKHOLDERS

TIME: 10:00 a.m. Eastern Time

DATE: Tuesday, October 27, 2020

ACCESS: www.meetingcenter.io/266420432

This year's annual meeting will be a virtual meeting via live audio webcast on the Internet. You will be able to attend the annual meeting, vote and submit your questions during the meeting by visiting www.meetingcenter.io/266420432 with the password SPRO2020 and entering the 15-digit control number included in the proxy card that you receive. For further information about the virtual annual meeting, please see the Questions and Answers about the Annual Meeting beginning on page 2.

PURPOSES:

1. To elect three directors to serve three-year terms expiring in 2023;
2. To ratify the appointment of PricewaterhouseCoopers LLP as the Company's independent registered public accounting firm for the fiscal year ending December 31, 2020; and
3. To transact such other business that is properly presented at the annual meeting and any adjournments or postponements thereof.

WHO MAY VOTE:

You may vote if you were the record owner of Spero Therapeutics, Inc. common stock at the close of business on September 15, 2020.

A list of stockholders of record will be available at the annual meeting, and during the 10 days prior to the annual meeting at our principal executive offices located at 675 Massachusetts Avenue, 14th Floor, Cambridge, Massachusetts 02139.

All stockholders are cordially invited to attend the annual meeting. **Whether you plan to attend the annual meeting or not, we urge you to vote and submit your proxy by the Internet, telephone or mail by following the instructions as described in this proxy statement in order to ensure the presence of a quorum.** You may change or revoke your proxy at any time before it is voted at the meeting.

BY ORDER OF THE BOARD OF DIRECTORS



Ankit Mahadevia, M.D.
President and Chief Executive Officer

TABLE OF CONTENTS

IMPORTANT INFORMATION ABOUT THE ANNUAL MEETING AND VOTING	2
SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT	8
MANAGEMENT AND CORPORATE GOVERNANCE MATTERS	12
EXECUTIVE OFFICER AND DIRECTOR COMPENSATION	21
EQUITY COMPENSATION PLANS AND OTHER BENEFIT PLANS	30
REPORT OF AUDIT COMMITTEE	33
CERTAIN RELATIONSHIPS AND RELATED PERSON TRANSACTIONS	34
ELECTION OF DIRECTORS	36
INDEPENDENT PUBLIC ACCOUNTANTS	37
CODE OF CONDUCT AND ETHICS	39
OTHER MATTERS	39
STOCKHOLDER PROPOSALS AND NOMINATIONS FOR DIRECTOR	39

SPERO THERAPEUTICS, INC.
675 Massachusetts Avenue, 14th Floor
Cambridge, Massachusetts 02139

PROXY STATEMENT FOR SPERO THERAPEUTICS, INC.
2020 ANNUAL MEETING OF STOCKHOLDERS TO BE HELD ON OCTOBER 27, 2020

This proxy statement, along with the accompanying Notice of 2020 Annual Meeting of Stockholders, contains information about the 2020 annual meeting of stockholders of Spero Therapeutics, Inc. (“Annual Meeting”), including any adjournments or postponements of the Annual Meeting. We are holding the Annual Meeting at 10:00 a.m. Eastern Time on Tuesday, October 27, 2020. As a result of public health and travel guidance due to COVID-19, this year’s annual meeting will be conducted solely via live audio webcast on the Internet. You will be able to attend the annual meeting, vote and submit your questions during the annual meeting by visiting www.meetingcenter.io/266420432. You will not be able to attend the annual meeting in person.

In this proxy statement, we refer to Spero Therapeutics, Inc. as “Spero,” “the Company,” “we” and “us.”

This proxy statement relates to the solicitation of proxies by our board of directors (“Board of Directors”) for use at the Annual Meeting.

On or about September 30, 2020, we intend to begin sending this proxy statement, the attached Notice of Annual Meeting of Stockholders and the enclosed proxy card to all stockholders entitled to vote at the Annual Meeting.

Although not part of this proxy statement, we are also sending, along with this proxy statement, our Annual Report on Form 10-K for the fiscal year ended December 31, 2019, which includes our financial statements for the fiscal year ended December 31, 2019.

**IMPORTANT NOTICE REGARDING THE AVAILABILITY OF PROXY MATERIALS FOR THE
SHAREHOLDER MEETING TO BE HELD ON OCTOBER 27, 2020**

This proxy statement and our Annual Report on Form 10-K are available for viewing, printing and downloading at www.edocumentview.com/SPRO. To view these materials, please have your 15-digit control number available that appears on your proxy card. On this website, you can also elect to receive future distributions of our proxy statements and annual reports to stockholders by electronic delivery.

Additionally, you can find a copy of our Annual Report on Form 10-K, which includes our financial statements, for the fiscal year ended December 31, 2019 on the website of the Securities and Exchange Commission (the “SEC”), at www.sec.gov, or in the “SEC Filings” section of the “Investors & Media” section of our website at www.sperotherapeutics.com. You may also obtain a printed copy of our Annual Report on Form 10-K, including our financial statements, free of charge, from us by sending a written request to: Spero Therapeutics, Inc., Attn: Investor Relations, 675 Massachusetts Avenue, 14th Floor, Cambridge, Massachusetts 02139. Exhibits will be provided upon written request and payment of an appropriate processing fee.

IMPORTANT INFORMATION ABOUT THE ANNUAL MEETING AND VOTING

Why is the Company Soliciting My Proxy?

The Board of Directors of Spero Therapeutics, Inc. is soliciting your proxy to vote at the 2020 Annual Meeting of stockholders to be held on Tuesday, October 27, 2020 at 10:00 a.m. Eastern Time. As a result of public health and travel guidance due to COVID-19, this year's annual meeting and any adjournments of the meeting will be conducted solely via live audio webcast on the Internet. You will be able to attend the annual meeting, vote and submit your questions during the annual meeting by visiting www.meetingcenter.io/266420432. You will not be able to attend the annual meeting in person. The proxy statement along with the accompanying Notice of Annual Meeting of Stockholders summarizes the purposes of the meeting and the information you need to know to vote at the Annual Meeting.

We have made available to you on the Internet or have sent you this proxy statement, the Notice of Annual Meeting of Stockholders, the proxy card and a copy of our Annual Report on Form 10-K for the fiscal year ended December 31, 2019 because you owned shares of Spero Therapeutics, Inc. common stock on the record date. The Company intends to commence distribution of the proxy materials to stockholders on or about September 30, 2020.

Why Are you Holding a Virtual Annual Meeting?

Due to the public health impact of COVID-19 and to support the health and well-being of our stockholders, this year's Annual Meeting will be held in a virtual meeting format only. We have designed our virtual format to enhance, rather than constrain, stockholder access, participation and communication. For example, the virtual format allows stockholders to communicate with us in advance of, and during, the Annual Meeting so they can ask questions of our Board of Directors or management, as time permits.

How can I attend the Annual Meeting?

The Annual Meeting will be a completely virtual meeting of stockholders, which will be conducted exclusively by webcast. You are entitled to participate in the Annual Meeting only if you were a stockholder of the Company as of the close of business on the Record Date, or if you hold a valid proxy for the Annual Meeting. No physical meeting will be held.

You will be able to attend the Annual Meeting online and submit your questions during the meeting by visiting www.meetingcenter.io/266420432. You also will be able to vote your shares online by attending the Annual Meeting by webcast.

To participate in the Annual Meeting, you will need to review the information included on your proxy card or on the instructions that accompanied your proxy materials. The password for the meeting is SPRO2020.

If you hold your shares through an intermediary, such as a bank or broker, you must register in advance using the instructions below.

The online meeting will begin promptly at 10:00 a.m. Eastern Time. We encourage you to access the meeting prior to the start time leaving ample time for the check in. Please follow the registration instructions as outlined in this proxy statement.

How do I register to attend the Annual Meeting virtually on the Internet?

If you are a registered shareholder (i.e., you hold your shares through our transfer agent, Computershare), you do not need to register to attend the Annual Meeting virtually on the Internet. Please follow the instructions on the proxy card that you received.

[Table of Contents](#)

If you hold your shares through an intermediary, such as a bank or broker, you must register in advance to attend the Annual Meeting virtually on the Internet.

To register to attend the Annual Meeting online by webcast you must submit proof of your proxy power (legal proxy) reflecting your Spero holdings along with your name and email address to Computershare. Requests for registration must be labeled as “Legal Proxy” and be received no later than 5:00 p.m., Eastern Time, on October 22, 2020.

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

Requests for registration should be directed to us at the following:

By email:

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

By mail:

Computershare
Spero Legal Proxy
P.O. Box 43001
Providence, RI 02940-3001

What Happens if There Are Technical Difficulties during the Annual Meeting?

We will have technicians ready to assist you with any technical difficulties you may have accessing the virtual Annual Meeting, voting at the Annual Meeting or submitting questions at the Annual Meeting. If you encounter any difficulties accessing the virtual Annual Meeting during the check-in or meeting time, please call 877-373-6374 (toll free).

Who Can Vote?

Only stockholders who owned our common stock at the close of business on September 15, 2020 are entitled to vote at the Annual Meeting. On this record date, there were 25,970,105 shares of our common stock outstanding and entitled to vote. Our common stock is our only class of voting stock.

You do not need to attend the Annual Meeting to vote your shares. Shares represented by valid proxies, received in time for the Annual Meeting and not revoked prior to the Annual Meeting, will be voted at the Annual Meeting. For instructions on how to change or revoke your proxy, see “May I Change or Revoke My Proxy?” below.

How Many Votes Do I Have?

Each share of our common stock that you own entitles you to one vote.

How Do I Vote?

Whether you plan to attend the Annual Meeting or not, we urge you to vote by proxy. All shares represented by valid proxies that we receive through this solicitation, and that are not revoked, will be voted in accordance with your instructions on the proxy card or as instructed via Internet or telephone. You may specify whether your shares should be voted for or withheld for each nominee for director, and whether your shares should be voted for, against or abstain with respect to the ratification of PricewaterhouseCoopers LLP as the Company’s independent registered public accounting firm for the fiscal year ending December 31, 2020. If you properly submit a proxy without giving specific voting instructions, your

[Table of Contents](#)

shares will be voted in accordance with the Board of Directors' recommendations as noted below. Voting by proxy will not affect your right to attend the Annual Meeting. If your shares are registered directly in your name through our stock transfer agent, Computershare Trust Company, N.A., or you have stock certificates registered in your name, you may vote:

- **By Internet or by telephone.** Follow the instructions included in the Notice or, if you received printed materials, in the proxy card to vote by Internet or telephone.
- **By mail.** If you received a proxy card by mail, you can vote by mail by completing, signing, dating and returning the proxy card as instructed on the card. If you sign the proxy card but do not specify how you want your shares voted, they will be voted in accordance with the Board of Directors' recommendations as noted below.
- **At the meeting.** If you attend the meeting, you may vote by completing an electronic ballot, which will be available at the meeting.

If you are a registered shareholder (i.e., you hold your shares through our transfer agent, Computershare), you do not need to register to attend the Annual Meeting virtually on the Internet. Please follow the instructions on the proxy card that you received.

If you hold your shares through an intermediary, such as a bank or broker, you must register in advance to attend the Annual Meeting virtually on the Internet.

To register to attend the Annual Meeting online by webcast you must submit proof of your proxy power (legal proxy) reflecting your Spero holdings along with your name and email address to Computershare. Requests for registration must be labeled as "Legal Proxy" and be received no later than 5:00 p.m., Eastern Time, on October 22, 2020.

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

Requests for registration should be directed to us at the following:

By email:

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

By mail:

Computershare
Spero Legal Proxy
P.O. Box 43001
Providence, RI 02940-3001

Telephone and Internet voting facilities for stockholders of record will be available 24 hours a day until the Annual Meeting begins at 10:00 a.m. Eastern Time on Tuesday, October 27, 2020.

If your shares are held in "street name" (held in the name of a bank, broker or other holder of record), you will receive instructions from the holder of record. You must follow the instructions of the holder of record in order for your shares to be voted. Telephone and Internet voting also will be offered to stockholders owning shares through certain banks and brokers. If your shares are not registered in your own name and you plan to vote your shares in person at the Annual Meeting, you should contact your broker or agent to obtain a legal proxy or broker's proxy card in order to vote.

How Does the Board of Directors Recommend That I Vote on the Proposals?

The Board of Directors recommends that you vote as follows:

- **“FOR”** the election of the nominees for director; and
- **“FOR”** the ratification of the selection of PricewaterhouseCoopers LLP as our independent registered public accounting firm for our fiscal year ending December 31, 2020.

If any other matter is presented at the Annual Meeting, your proxy provides that your shares will be voted by the proxy holder listed in the proxy in accordance with his best judgment. At the time this proxy statement was first made available, we knew of no matters that needed to be acted on at the Annual Meeting, other than those discussed in this proxy statement.

May I Change or Revoke My Proxy?

If you give us your proxy, you may change or revoke it at any time before the Annual Meeting. You may change or revoke your proxy in any one of the following ways:

- if you received a proxy card, by signing a new proxy card with a date later than your previously delivered proxy and submitting it as instructed above;
- by re-voting by Internet or by telephone as instructed above;
- by notifying the Company’s Secretary in writing before the Annual Meeting that you have revoked your proxy; or
- by attending the Annual Meeting and voting at the meeting. Attending the Annual Meeting will not in and of itself revoke a previously submitted proxy. You must specifically request at the Annual Meeting that it be revoked. Your most current vote, whether by telephone, Internet or proxy card is the one that will be counted.

What if I Receive More Than One Notice or Proxy Card?

You may receive more than one Notice or proxy card if you hold shares of our common stock in more than one account, which may be in registered form or held in street name. Please vote in the manner described above under “How Do I Vote?” for each account to ensure that all of your shares are voted.

Will My Shares be Voted if I Do Not Vote?

If your shares are registered in your name or if you have stock certificates, they will not be counted if you do not vote as described above under “How Do I Vote?” If your shares are held in street name and you do not provide voting instructions to the bank, broker or other nominee that holds your shares as described above, the bank, broker or other nominee that holds your shares has the authority to vote your unvoted shares only on certain of the proposals set forth in this proxy statement without receiving instructions from you. Therefore, we encourage you to provide voting instructions to your bank, broker or other nominee. This ensures your shares will be voted at the Annual Meeting and in the manner you desire. A “broker non-vote” will occur if your broker cannot vote your shares on a particular matter because it has not received instructions from you and does not have discretionary voting authority on that matter or because your broker chooses not to vote on a matter for which it does have discretionary voting authority.

What Vote is Required to Approve Each Proposal and How are Votes Counted?

Proposal 1: Elect Directors

The nominees for director who receive the most votes (also known as a “plurality” of the votes cast) will be elected. You may vote either FOR each of the nominees, WITHHOLD your vote from each of the nominees or WITHHOLD your vote from any of the nominees. Votes that are withheld will not be included in the vote tally for the election of the directors. Brokerage firms do not have authority to vote customers’ unvoted shares held by the firms in street name for the election of the directors. As a result, any shares not voted by a customer will be treated as a broker non-vote. Such broker non-votes will have no effect on the results of this vote.

Proposal 2: Ratify Selection of Independent Registered Public Accounting Firm

The affirmative vote of a majority in voting power of the shares of our common stock present or represented at the meeting and voting affirmatively or negatively for this proposal is required to ratify the selection of our independent registered public accounting firm. Abstentions will have no effect on the results of this vote. Brokerage firms have authority to vote customers’ unvoted shares held by the firms in street name on this proposal. If a broker does not exercise this authority, such broker non-votes will have no effect on the results of this vote. We are not required to obtain the approval of our stockholders to select our independent registered public accounting firm. However, if our stockholders do not ratify the selection of PricewaterhouseCoopers LLP as our independent registered public accounting firm for 2020, our Audit Committee of our Board of Directors will reconsider its selection.

Is Voting Confidential?

We will keep all the proxies, ballots and voting tabulations private. We only let our Inspectors of Election, Computershare Trust Company, N.A., examine these documents. Management will not know how you voted on a specific proposal unless it is necessary to meet legal requirements. We will, however, forward to management any written comments you make on the proxy card or otherwise provide.

Where Can I Find the Voting Results of the Annual Meeting?

The preliminary voting results will be announced at the Annual Meeting, and we will publish preliminary, or final results if available, in a Current Report on Form 8-K within four business days of the Annual Meeting. If final results are unavailable at the time we file the Form 8-K, then we will file an amended report on Form 8-K to disclose the final voting results within four business days after the final voting results are known.

What Are the Costs of Soliciting these Proxies?

We will pay all of the costs of soliciting these proxies. Our directors and employees may solicit proxies in person or by telephone, fax or email. We will pay these employees and directors no additional compensation for these services. We will ask banks, brokers and other institutions, nominees and fiduciaries to forward these proxy materials to their principals and to obtain authority to execute proxies. We will then reimburse them for their expenses.

What Constitutes a Quorum for the Annual Meeting?

The presence, in person or by proxy, of the holders of a majority of the voting power of all outstanding shares of our capital stock entitled to vote at the Annual Meeting is necessary to constitute a quorum at the Annual Meeting. Votes of stockholders of record who are present at the Annual Meeting in person or by proxy, abstentions, and broker non-votes are counted for purposes of determining whether a quorum exists.

Attending the Annual Meeting

The Annual Meeting will be held at 10:00 a.m. Eastern Time on Tuesday, October 27, 2020. This year, our Annual Meeting will be held in a virtual meeting format only. To attend the virtual Annual Meeting, go to www.meetingcenter.io/266420432 shortly before the meeting time, and follow the instructions for downloading the webcast. You need not attend the Annual Meeting in order to vote.

Householding of Annual Disclosure Documents

The SEC has adopted rules that permit companies and intermediaries such as brokers to satisfy delivery requirements for proxy statements and annual reports with respect to two or more stockholders sharing the same address by delivering a single proxy statement or annual report, as applicable, addressed to those stockholders. This process, which is commonly referred to as “householding,” potentially provides extra convenience for stockholders and cost savings for companies.

Spero has not instituted householding for stockholders of record. However, certain brokerage firms may have instituted householding for beneficial owners of shares of Spero’s common stock held through brokerage firms. If your household has multiple accounts holding shares of Spero’s common stock, you may have already received householding notification from your broker. Please contact your broker directly if you have any questions or require additional copies of this joint proxy statement/prospectus. The broker will arrange for delivery of a separate copy of this proxy statement promptly upon your request. Spero stockholders may decide at any time to revoke a decision to household, and thereby receive multiple copies.

Electronic Delivery of Company Stockholder Communications

Most stockholders can elect to view or receive copies of future proxy materials over the Internet instead of receiving paper copies in the mail.

You can choose this option and save the Company the cost of producing and mailing these documents by going to www.computershare.com and logging into the Investor Center to follow the instructions provided.

SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT

The following table sets forth certain information with respect to the beneficial ownership of our common stock as of September 1, 2020 for (a) the executive officers named in the Summary Compensation Table on page 21 of this proxy statement, (b) each of our directors and director nominees, (c) all of our current directors and executive officers as a group and (d) each stockholder known by us to own beneficially more than 5% of our common stock. Beneficial ownership is determined in accordance with the rules of the SEC and includes voting or investment power with respect to the securities. We deem shares of common stock that may be acquired by an individual or group within 60 days of September 1, 2020, including pursuant to the exercise of options, to be outstanding for the purpose of computing the percentage ownership of such individual or group, but not outstanding for the purpose of computing the percentage ownership of any other person shown in the table. Except as indicated in footnotes to this table, we believe that the stockholders named in this table have sole voting and investment power with respect to all shares of common stock shown to be beneficially owned by them based on information provided to us by these stockholders. Percentage of ownership is based on 21,183,748 shares of common stock outstanding on September 1, 2020.

<u>Name of Beneficial Owner</u>	<u>Number of Shares Beneficially Owned</u>	<u>Percent of Shares Beneficially Owned</u>
<i>Principal Stockholders</i>		
S.R. One, Limited (1)	1,819,478	8.59%
Entities affiliated with BVF Inc. (2)	2,028,405	9.99%
Atlas Venture Fund IX, L.P. (3)	1,376,968	6.50%
GV 2015, L.P. (4)	1,112,473	5.25%
Entities affiliated with Aquilo Capital Management, LLC (5)	1,154,356	5.45%
<i>Named Executive Officers and Directors</i>		
Ankit Mahadevia, M.D. (6)	721,919	3.41%
Cristina Larkin (7)	162,664*	
David Melnick, M.D. (8)	121,251*	
Milind Deshpande, Ph.D. (9)	72,664*	
Jean-François Formela, M.D. (10)	2,424,330	11.44%
Scott Jackson (11)	1,667*	
John C. Pottage, Jr., M.D. (12)	14,508*	
Cynthia Smith (13)	12,483*	
Frank E. Thomas (14)	38,967*	
Patrick Vink, M.D. (15)	42,734*	
All current executive officers and directors as a group (12 persons) (16)	3,693,169	17.43%

* Indicates beneficial ownership of less than 1%.

- (1) Consists of 1,819,478 shares of common stock owned by S.R. One, Limited, or S.R. One, an indirect wholly owned subsidiary of GlaxoSmithKline plc. The address for S.R. One is 161 Washington Street, Suite 500, Eight Tower Bridge, Conshohocken, Pennsylvania 19428. This information is based solely on a Schedule 13D/A filed by GlaxoSmithKline plc with the SEC on June 4, 2020, which reported ownership as of such date.
- (2) Includes (i) 1,217,924 shares of common stock held by Biotechnology Value Fund, L.P., or BVF, (ii) 664,230 shares of common stock held by Biotechnology Value Fund II, L.P., or BVF II, and (iii) 55,550

Table of Contents

shares of common stock held by Biotechnology Value Trading Fund OS LP, or Trading Fund OS. BVF I GP LLC, or BVF GP, as general partner of BVF, may be deemed to beneficially own 1,217,924 shares of common stock beneficially owned by BVF. BVF II GP LLC, or BVF II GP, as general partner of BVF II, may be deemed to beneficially own 664,230 shares of common stock beneficially owned by BVF II. BVF Partners OS Ltd, or Partners OS, as general partner of Trading Fund OS, may be deemed to beneficially own 55,550 shares of common stock beneficially owned by Trading Fund OS. BVF GP Holdings LLC, or BVF GPH, as the sole member of BVF GP and BVF II GP, may be deemed to beneficially own 1,882,154 shares of common stock beneficially owned in the aggregate by BVF GP and BVF II GP. BVF Partners L.P., or Partners, as investment manager of BVF, BVF II and Trading Fund OS, and the sole member of Partners OS, may be deemed to beneficially own the 2,028,405 shares of common stock beneficially owned in the aggregate by BVF, BVF II, Trading Fund OS, and certain managed accounts of Partners, or the Partners Managed Accounts, including 90,701 shares of common stock held in the Partners Managed Accounts. BVF Inc., as the general partner of Partners, may be deemed to beneficially own the 2,028,405 shares of common stock owned by Partners. Mark N. Lampert is a director and officer of BVF Inc., and may be deemed to beneficially own the 2,028,405 shares of common stock beneficially owned by BVF, Inc. Together, BVF, BVF II, BVF GP, BVF II GP, Trading Fund OS, BVF GPH, Partners OS, Partners, BVF Inc. and Mark N. Lampert (the “BVF Entities”) hold 1,720 shares of Series A Convertible Preferred Stock (“Series A Preferred”) convertible for an aggregate of 1,720,000 shares of common stock. The Series A Preferred may not be converted if, after such conversion, the BVF Entities would beneficially own more than 9.99% of the common stock then issued and outstanding (the “Series A Blocker”). As of December 31, 2019, the Series A Blocker limited the aggregate conversion of Series A Preferred by the BVF Entities to 1,183,000 of the 1,720,000 shares of common stock underlying the Series A Preferred. As a result of the Series A Blocker, included in the percentage of shares beneficially owned as of December 31, 2019 is the maximum number of shares of common stock issuable upon conversion of Series A Preferred as of December 31, 2019 up to the limit imposed by the Series A Blocker, and excluded are the remaining shares of common stock issuable upon conversion of Series A Preferred that are prevented from converting due to the Series A Blocker. Together, the BVF Entities also hold 1,000 shares of Series B Convertible Preferred Stock (the “Series B Preferred”) convertible for an aggregate of 1,000,000 shares of common stock. The Series B Preferred may not be converted if, after such conversion, the BVF Entities would beneficially own more than 9.99% of the common stock then issued and outstanding (the “Series B Blocker”). As of December 31, 2019, the Series B Blocker limited the aggregate conversion of Series B Preferred by the BVF Entities to 0 out of the 1,000,000 shares of common stock underlying the Series B Preferred. BVF GP disclaims beneficial ownership of the shares of common stock beneficially owned by BVF. BVF II GP disclaims beneficial ownership of the shares of common stock beneficially owned by BVF II. Partners OS disclaims beneficial ownership of the shares of common stock beneficially owned by Trading Fund OS. BVF GPH disclaims beneficial ownership of the shares of common stock beneficially owned by BVF GP and BVF II GP. Each of Partners, BVF Inc. and Mr. Lampert disclaims beneficial ownership of the shares of common stock beneficially owned by BVF, BVF II, Trading Fund OS, and the Partners Management Accounts. The address of the principal business and office of BVF Inc. and certain of its affiliates is 1 Sansome Street, 30th Floor, San Francisco, California, 94194. This information is based solely on a Schedule 13G/A filed with the SEC on February 18, 2020, which reported ownership as of December 31, 2019.

- (3) All shares are held directly by Atlas Venture Fund IX. Atlas Venture Associates IX, L.P., or AVA IX LP, is the general partner of Atlas Venture Fund IX, and Atlas Venture Associates IX, LLC, or AVA IX LLC, is the general partner of AVA IX LP. Peter Barrett, Bruce Booth, Jean-François Formela, M.D., Jeff Fagnan, and Ryan Moore are the members of AVA IX LLC and collectively make investment decisions on behalf of Atlas Venture Fund IX. Dr. Formela is also a member of our Board of Directors. Dr. Formela disclaims beneficial ownership of such shares of common stock, except to the extent of his pecuniary interest therein, if any. The address for Atlas Venture Fund IX, is 25 First Street, Suite 303, Cambridge, Massachusetts 02141. This information is based solely on a Schedule 13G/A filed by Atlas Venture Fund IX, L.P. with the SEC on February 4, 2020, which reported ownership as of December 31, 2019.

Table of Contents

- (4) GV 2015 GP, L.L.C., the general partner of GV 2015, L.P., Alphabet Holdings LLC, the sole member of GV 2015 GP, L.L.C., Google LLC, the sole member of Alphabet Holdings LLC, XXVI Holdings Inc., the managing member of Google LLC, and Alphabet Inc., the sole stockholder of XXVI Holdings Inc., may be deemed to have sole power to vote or dispose of the shares held by GV 2015, L.P. The address for GV 2015, L.P., GV 2015 GP, L.L.C., Alphabet Holdings LLC, Google LLC, XXVI Holdings Inc. and Alphabet Inc. is 1600 Amphitheatre Parkway, Mountain View, California 94043. This information is based solely on a Schedule 13G filed by GV 2015, L.P. with the SEC on February 14, 2018, which reported ownership as of December 31, 2017.
- (5) Aquilo Capital Management, LLC is an investment advisor that serves as the general partner and investment manager to each of Aquilo Capital, L.P. and Aquilo Capital II, L.P., (collectively, the “Aquilo Funds”), and may be deemed to be the beneficial owner of all shares of common stock held by the Aquilo Funds. Mr. Marc Schneidman, as Managing Member of Aquilo Capital Management, LLC, with the power to exercise investment and voting discretion, may be deemed to be the beneficial owner of all shares of common stock held by the Aquilo Funds. Each of the Aquilo Funds and Mr. Schneidman expressly disclaims beneficial ownership over any of the shares of common stock held by the Aquilo Funds. The address for Aquilo Capital, L.P. and Aquilo Capital II, L.P. is One Letterman Drive, Suite D4900, Building D, The Presidio, San Francisco, California 94129. This information is based solely on a Schedule 13G/A filed by Aquilo Capital, L.P. with the SEC on February 14, 2020, which reported ownership as of such date.
- (6) Consists of (i) 65,817 shares of common stock held by Mahadevia-Mehta Family Trust, of which Dr. Mahadevia is the trustee, and (ii) 656,102 shares of common stock underlying options that are exercisable as of September 1, 2020 or will become exercisable within 60 days after such date held by Dr. Mahadevia.
- (7) Consists of (i) 1,500 shares of common stock and (ii) 161,164 shares of common stock underlying options that are exercisable as of September 1, 2020 or will become exercisable within 60 days after such date held by Ms. Larkin.
- (8) Consists of 121,251 shares of common stock underlying options that are exercisable as of September 1, 2020 or will become exercisable within 60 days after such date held by Dr. Melnick.
- (9) Consists of (i) 16,454 shares of common stock and (ii) 56,210 shares of common stock underlying options that are exercisable as of September 1, 2020 or will become exercisable within 60 days after such date held by Dr. Deshpande.
- (10) See footnote 3. Also includes 1,031,160 shares held directly by Atlas Venture Fund X, LLC, or Atlas Fund X. Atlas Venture Associates X, L.P., or AVA X LP, is the general partner of Atlas Venture Fund X, and Atlas Venture Associates X, LLC, or AVA X LLC, is the general partner of AVA X LP. Peter Barrett, Bruce Booth, Jean-François Formela, M.D., David Gragzel and Jason Rhodes are the members of AVA X LLC and collectively make investment decisions on behalf of Atlas Venture Fund X. Dr. Formela is also a member of our Board of Directors. Dr. Formela disclaims beneficial ownership of such shares, except to the extent of his pecuniary interest therein, if any. This information is based solely on a Schedule 13D filed by Atlas Venture Fund X, L.P. with the SEC on March 14, 2018, which reported ownership as of December 31, 2017. Also includes 16,202 shares of common stock underlying options that are exercisable as of September 1, 2020 or will become exercisable within 60 days after such date held by Dr. Formela.
- (11) Consists of 1,667 shares of common stock underlying options that are exercisable as of September 1, 2020 or will become exercisable within 60 days after such date held by Mr. Jackson.
- (12) Consists of 14,508 shares of common stock underlying options that are exercisable as of September 1, 2020 or will become exercisable within 60 days after such date held by Dr. Pottage.

[Table of Contents](#)

- (13) Consists of 12,483 shares of common stock underlying options that are exercisable as of September 1, 2020 or will become exercisable within 60 days after such date held by Ms. Smith.
- (14) Consists of 38,967 shares of common stock underlying options that are exercisable as of September 1, 2020 or will become exercisable within 60 days after such date held by Mr. Thomas.
- (15) Consists of 42,734 shares of common stock underlying options that are exercisable as of September 1, 2020 or will become exercisable within 60 days after such date held by Dr. Vink.
- (16) See notes 3 and 6 through 15 above; also includes Stephen DiPalma and Timothy Keutzer, who are executive officers but not named executive officers.

MANAGEMENT AND CORPORATE GOVERNANCE MATTERS

The Board of Directors

Our amended and restated By-Laws provide that our business is to be managed by or under the direction of our Board of Directors. Our Board of Directors is divided into three classes for purposes of election. One class is elected at each annual meeting of stockholders to serve for a three-year term. Our Board of Directors currently consists of eight members, classified into three classes as follows:

- (1) Milind Deshpande, Ph.D., Jean-François Formela, M.D. and Ankit Mahadevia, M.D. constitute our Class III directors with a term ending at the upcoming 2020 Annual Meeting;
- (2) Cynthia Smith, John C. Pottage, Jr., M.D. and Scott Jackson constitute our Class I directors with a term ending at the 2021 annual meeting; and
- (3) Patrick Vink, M.D. and Frank E. Thomas constitute our Class II directors with a term ending at the 2022 annual meeting.

On March 31, 2020, our Board of Directors accepted the recommendation of the Nominating and Corporate Governance Committee and voted to nominate Milind Deshpande, Ph.D., Jean-François Formela, M.D. and Ankit Mahadevia, M.D. for election at the Annual Meeting for a term of three years to serve until the 2023 annual meeting of stockholders, and until their respective successors have been elected and qualified or subject to their earlier death, resignation or removal. Set forth below are the names of the persons nominated as directors and directors whose terms do not expire this year, their ages, their offices in the Company, if any, their principal occupations or employment for at least the past five years, the length of their tenure as directors and the names of other public companies in which such persons hold or have held directorships during the past five years. Additionally, information about the specific experience, qualifications, attributes or skills that led to our Board of Directors' conclusion at the time of filing of this proxy statement that each person listed below should serve as a director is set forth below:

<u>Name</u>	<u>Age</u>	<u>Position with the Company</u>
Milind Deshpande, Ph.D.	64	Chairman of the Board of Directors
Jean-François Formela, M.D.	64	Director
Scott Jackson	55	Director
Ankit Mahadevia, M.D.	39	Chief Executive Officer, President and Director
John C. Pottage, Jr., M.D.	67	Director
Cynthia Smith	51	Director
Frank E. Thomas	50	Director
Patrick Vink, M.D.	57	Director

Our Board of Directors has reviewed the materiality of any relationship that each of our directors has with Spero Therapeutics, Inc., either directly or indirectly. Based upon this review, our Board of Directors has determined that the following members of the Board of Directors are "independent directors" as defined by The Nasdaq Stock Market: Milind Deshpande, Ph.D., Jean-François Formela, M.D., Scott Jackson, John C. Pottage, Jr., M.D., Cynthia Smith, Frank E. Thomas, and Patrick Vink, M.D.

Milind Deshpande, Ph.D. has served on our Board of Directors since January 2014 and currently serves as chairman of our Board of Directors. Dr. Deshpande is the President and Chief Executive Officer at Nayan Therapeutics since February 2019, and President and Chief Executive Officer of Avilar Therapeutics since January 2020. He is also a Venture Partner at RA Capital, where he has served since October 2018. Dr. Deshpande joined Achillion Pharmaceuticals, Inc. in September 2001 as Vice President of Chemistry, was named Head of Drug Discovery in April 2002, Senior Vice President of Drug Discovery in December 2002,

[Table of Contents](#)

Senior Vice President and Chief Scientific Officer in December 2004 and Executive Vice President of Research and Chief Scientific Officer in June 2007. He was promoted to President of Research and Development in October 2010. In May 2013, Dr. Deshpande was appointed President and Chief Executive Officer of Achillion and joined its board of directors on which he served until May 2018. Prior to joining Achillion, Dr. Deshpande was Associate Director of Lead Discovery and Early Discovery Chemistry at the Pharmaceutical Research Institute at Bristol-Myers Squibb Co. from 1991 to 2001, where he managed the identification of new clinical candidates to treat infectious and neurological diseases. From 1988 to 1991, he held a faculty position at Boston University Medical School. Dr. Deshpande received his Ph.D. in Organic Chemistry from Ohio University, following his undergraduate education in India. We believe that Dr. Deshpande is qualified to serve on our Board of Directors due to his extensive experience in the life sciences industry.

Jean-François Formela, M.D. has served on our Board of Directors since March 2013. Dr. Formela is currently a partner at Atlas Venture and focuses on novel drug discovery approaches and therapeutics. He joined Atlas Venture in 1993 to build the U.S. life sciences franchise. He is a director and co-founder of IFM Therapeutics, Intellia Therapeutics (Nasdaq: NTLA), Korro Bio, Triplet Therapeutics and Translate Bio (Nasdaq: TBIO). Jean-François also serves on the boards of F-star and Ikena Oncology. His prior investments include Adnexus, ArQule (Nasdaq: ARQL), Arteaus Therapeutics (acquired by Eli Lilly), CoStim Pharmaceuticals (acquired by Novartis), deCODE (Nasdaq: DCGN), Exelixis (Nasdaq: EXEL) and NxStage (Nasdaq: NXTM). Dr. Formela is a member of the Partners Healthcare Innovation Advisory Board and a former trustee of the Boston Institute of Contemporary Art. He received his M.D. from Paris University School of Medicine and his M.B.A. from Columbia University. We believe Dr. Formela's experience in the life sciences industry, as well as his practice of medicine, provides him with the qualifications and skills to serve as a director of our Company.

Scott Jackson has served on our Board of Directors since April 2020. Mr. Jackson served as Chief Executive Officer and as a member of the board of directors of Celator Pharmaceuticals, Inc. from April 2008 until July 2016, when the company was acquired by Jazz Pharmaceuticals plc. Mr. Jackson has more than thirty years of corporate leadership experience in the pharmaceutical and biotechnology industry and has held positions of increasing responsibility in sales, marketing and commercial development at Eli Lilly & Company, SmithKline Beecham plc, ImClone Systems Incorporated, Centocor Inc., a division of Johnson & Johnson, Eximias Pharmaceutical Corporation and YM BioSciences Inc. Mr. Jackson presently serves on the boards of MacroGenics, Inc. and GlycoMimetics, Inc. Mr. Jackson holds a B.S. in pharmacy from the Philadelphia College of Pharmacy and Science and an M.B.A. from the University of Notre Dame. We believe that Mr. Jackson's extensive executive leadership experience in the pharmaceutical industry and his experience as a member of the board of directors of other publicly traded biotechnology companies, as well as his broad life sciences industry knowledge qualifies him to serve on our Board of Directors.

Ankit Mahadevia, M.D. has served as our Chief Executive Officer and President since March 2015 and has been a member of our Board of Directors since September 2013. He was formerly a Venture Partner in the life sciences group at Atlas Venture, located in Cambridge, Massachusetts. In that capacity he supported the formation of eight companies focused on novel drug discovery platforms and therapeutic products, including Nimbus Therapeutics, Arteaus Therapeutics (acquired by Lilly), and Translate Bio (Nasdaq: TBIO). He led three of these companies as acting CEO, including Synlogic (Nasdaq: SYBX). Prior to joining Atlas Venture in 2008, Dr. Mahadevia worked on product and business development with the founding team at Arcion Therapeutics, Inc. He has also held positions in business development both at Genentech, Inc. and at Vanda Pharmaceuticals Inc. Previously, he worked in the health care groups of McKinsey & Company and Monitor Group. Dr. Mahadevia began his career in health care policy, with roles in the U.S. Senate Health, Education, Labor, and Pensions committees, the U.S. Government Accountability Office and the Mexican Institute of Social Security. He has spoken widely on entrepreneurship, including at Harvard University, Columbia University, Northwestern University, and the Berkeley Forum. Dr. Mahadevia has also been active in the policy of life science innovation, including service on the Advisory Council at the NIH National Center for Advancing Translational Sciences. Dr. Mahadevia holds an M.D. from the Johns Hopkins School of Medicine, an M.B.A. from the Wharton School at the University of Pennsylvania and a B.A. in Economics and Biology from Northwestern University. We

[Table of Contents](#)

believe that Dr. Mahadevia is qualified to serve on our Board of Directors due to his experience serving as our Chief Executive Officer and President and his extensive experience in the life sciences industry.

John C. Pottage, Jr., M.D. has served on our Board of Directors since September 2018. Dr. Pottage served as Senior Vice President and Chief Scientific and Medical Officer of ViiV Healthcare from November 2009 to October 2019. From September 2008 to November 2009, Dr. Pottage served as Senior Vice President, Head of Infectious Disease Medicine Development Center and, from June 2007 to September 2008, as the Vice President, Global Clinical Development of Antivirals, at GlaxoSmithKline. Prior to joining GlaxoSmithKline, Dr. Pottage served as Chief Medical Officer and Senior Vice President of Drug Development of Achillion Pharmaceuticals from May 2002 to May 2007. From July 1998 to May 2002, Dr. Pottage served as Medical Director of Vertex Pharmaceuticals. We believe that Dr. Pottage's extensive industry and executive experience, his broad experience within the biopharmaceutical sector and his knowledge of the life sciences industry qualifies him to serve on our Board of Directors.

Cynthia Smith has served on our Board of Directors since March 2019. Ms. Smith was Chief Commercial Officer of ZS Pharma, from June 2013 to December 2016. ZS Pharma became a subsidiary of AstraZeneca after its acquisition in December 2015. Prior to joining ZS Pharma, Ms. Smith was Vice President, Market Access & Commercial Development at Affymax, Inc., a biotechnology company focused on the development and commercialization of novel renal therapies, including a new anemia drug for chronic kidney disease patients. Ms. Smith was employed at Affymax from October 2008 to March 2013. Prior to Affymax, Ms. Smith was Executive Director of Healthcare System and Medicare Strategy at Merck. During her tenure at Merck from June 2000 to October 2008, she also held various leadership positions in corporate strategy, public policy, and external affairs, including global crisis management for the Vioxx recall. Before joining the pharmaceutical industry, she served in the White House Office of Management and Budget (OMB) in the Clinton Administration. Ms. Smith earned an MBA from the Wharton School of the University of Pennsylvania, an MS in public policy from the Eagleton Institute of Politics at Rutgers University, and a BA from the University of North Carolina at Chapel Hill. Ms. Smith also serves on the boards of directors of Dicerna Pharmaceuticals and Akebia Therapeutics. We believe that Ms. Smith's extensive management experience in the healthcare industry and her experience as a member of the board of directors of other publicly traded biotechnology companies, as well as her broad life sciences industry knowledge, qualifies her to serve on our Board of Directors.

Frank E. Thomas has served on our Board of Directors since July 2017. Mr. Thomas is currently President and Chief Operating Officer of Orchard Therapeutics, a development-stage biotechnology company based in the United Kingdom, where he served as Chief Financial Officer and Chief Business Officer from January 2018 to December 2019. Prior to Orchard, Mr. Thomas served as the President and Chief Operating Officer of AMAG Pharmaceuticals, Inc., a publicly traded commercial-stage pharmaceutical company, from April 2015 to April 2017, as AMAG's Executive Vice President and Chief Operating Officer from May 2012 through April 2015 and as Executive Vice President, Chief Financial Officer and Treasurer from August 2011 through May 2012. Prior to AMAG, he served as Senior Vice President, Chief Operating Officer and Chief Financial Officer for Molecular Biometrics, Inc., a commercial-stage medical diagnostics company, from October 2008 to July 2011. Prior to Molecular Biometrics, Mr. Thomas spent four years at Critical Therapeutics, Inc., a public biopharmaceutical company, from April 2004 to March 2008, where he was promoted to President in June 2006 and Chief Executive Officer in December 2006 from the position of Senior Vice President and Chief Financial Officer. He also served on the board of directors of Critical Therapeutics from 2006 to 2008. Prior to 2004, Mr. Thomas served as the Chief Financial Officer and Vice President of Finance and Investor Relations at Esperion Therapeutics, Inc., a public biopharmaceutical company. Mr. Thomas was a member of the board of directors of the Massachusetts Biotechnology Council from 2007 to 2015 and currently serves as a member of the board of directors of Zafgen, Inc., a public biopharmaceutical company, which he joined in June 2014. Mr. Thomas holds a B.B.A. from the University of Michigan, Ann Arbor. We believe that Mr. Thomas' extensive commercial and operational management experience at biopharmaceutical companies and with financial matters qualifies him to serve on our Board of Directors.

Patrick Vink, M.D. has served on our Board of Directors since September 2015. Dr. Vink has been an advisor to the pharmaceutical industry since 2015 and non-executive board member of several companies. Previously, Dr. Vink was employed at Cubist Pharmaceuticals, Inc. Most recently, he served as Executive Vice-President and Chief Operating Officer, overseeing all worldwide commercial and technical operations as well as global alliance management and managing the company's profit and loss. He joined Cubist in 2012 as Senior Vice-president and Head of all International Business Operations. In this role, he was responsible for the all business activities in International markets outside USA. Prior to joining Cubist, Dr. Vink served as Senior Vice President, Global Head of Hospital Business and Global Head of Biologics for Mylan Inc. In this role, Dr. Vink managed the global hospital business of the company. He joined Mylan in 2008 and established a number of global functions for the company in Switzerland. Before joining Mylan, Dr. Vink held several leadership positions across the industry, including Head of Global Business Franchise Biopharmaceuticals for Novartis Sandoz; Vice President International Business for Biogen, Inc.; and Head of Worldwide Marketing, Cardiovascular and Thrombosis for Sanofi-Synthelabo SA. Dr. Vink served as a member of the Executive Committee of the European Federation of Pharmaceutical Industries and Associations (EFPIA) between 2013 and 2015. Dr. Vink graduated as a medical doctor from the University of Leiden, Netherlands in 1988 and obtained his M.B.A. in 1992 from the University of Rochester. Dr. Vink serves on the boards of directors of Santhera Pharmaceuticals AG, Amryt Pharma PLC., and is Chairman of the board of directors of Targovax Oy, Acacia Pharma and two privately held companies. We believe that Dr. Vink is qualified to serve on our Board of Directors because of his extensive operational business experience, significant knowledge of the activities of our company, and diverse background serving on the board of directors of various public and private life science companies.

Committees of the Board of Directors and Meetings

Meeting Attendance. During the fiscal year ended December 31, 2019, there were four meetings of our Board of Directors, and the various committees of the Board of Directors met a total of nine times. No director attended fewer than 75% of the total number of meetings of the Board of Directors and of committees of the Board of Directors on which such director served during fiscal 2019. The Board of Directors has adopted a policy under which each member of the Board of Directors makes every effort to but is not required to attend each annual meeting of our stockholders.

Audit Committee. Our Audit Committee met four times during the fiscal year ended December 31, 2019. This committee currently has four members, Frank E. Thomas (Chairman), Scott Jackson, John C. Pottage, Jr., M.D., and Patrick Vink, M.D. During the period of January 1, 2019 through May 14, 2020, our Audit Committee was comprised of Mr. Thomas (Chairman), Dr. Pottage and Dr. Vink. On May 15, 2020, Mr. Jackson joined as a member of our Audit Committee. Our Audit Committee's role and responsibilities are set forth in the Audit Committee's written charter and include the authority to retain and terminate the services of our independent registered public accounting firm. In addition, the Audit Committee reviews annual financial statements, considers matters relating to accounting policy and internal controls and reviews the scope of annual audits. All members of the Audit Committee satisfy the current independence standards promulgated by the SEC and by The Nasdaq Stock Market, as such standards apply specifically to members of audit committees. The Board of Directors has determined that Mr. Thomas is an "audit committee financial expert," as the SEC has defined that term in Item 407 of Regulation S-K. Please also see the report of the Audit Committee set forth elsewhere in this proxy statement.

A copy of the Audit Committee's written charter is publicly available on our website at www.sperotherapeutics.com.

Compensation Committee. Our Compensation Committee met four times during the fiscal year ended December 31, 2019. This committee currently has four members, Patrick Vink, M.D. (Chairman), Jean-François Formela, M.D., Milind Deshpande, Ph.D., and Cynthia Smith. Our Compensation Committee's role and responsibilities are set forth in the Compensation Committee's written charter and include reviewing, approving

[Table of Contents](#)

and making recommendations regarding our compensation policies, practices and procedures to ensure that legal and fiduciary responsibilities of the Board of Directors are carried out and that such policies, practices and procedures contribute to our success. Our Compensation Committee also administers the Spero Therapeutics, Inc. 2017 Stock Incentive Plan, as amended, or the 2017 Plan and our 2019 Inducement Equity Incentive Plan, as amended. The Compensation Committee is responsible for the determination of the compensation of our chief executive officer, and shall conduct its decision making process with respect to that issue without the chief executive officer present. All members of the Compensation Committee qualify as independent under the definition promulgated by The Nasdaq Stock Market.

The Compensation Committee initially engaged Pearl Meyer & Partners, LLC (“Pearl Meyer”) as an independent advisor to the Compensation Committee to provide executive compensation consulting services. Pearl Meyer was engaged by and reported solely to the Compensation Committee. The Compensation Committee has the sole authority to approve the terms of the engagement. Pearl Meyer did not provide any services to the Company other than executive compensation consulting services during the fiscal year ended December 31, 2019. In compliance with the SEC and the corporate governance rules of The Nasdaq Stock Market, Pearl Meyer provided the Compensation Committee with a letter addressing each of the six independence factors. Their responses affirm the independence of Pearl Meyer and the partners, consultants, and employees who service the Compensation Committee on executive compensation matters and governance issues. In July 2019, the Compensation Committee then retained Meridian Compensation Partners, LLC (“Meridian”) as an independent advisor to the Compensation Committee to provide executive compensation consulting services, with Meridian becoming the Company’s sole compensation consultant in September 2019. Meridian did not provide any services to the Company other than executive compensation consulting services during the fiscal year ended December 31, 2019. In compliance with the SEC and the corporate governance rules of The Nasdaq Stock Market, Meridian provided the Compensation Committee with a letter addressing each of the six independence factors. Their responses affirm the independence of Meridian and the partners, consultants, and employees who service the Compensation Committee on executive compensation matters and governance issues.

A copy of the Compensation Committee’s written charter is publicly available on our website at www.sperotherapeutics.com.

Nominating and Corporate Governance Committee. Our Nominating and Corporate Governance Committee (“Nominating Committee”) met once during the fiscal year ended December 31, 2019 and has three members, Milind Deshpande, Ph.D. (Chairman), Jean-François Formela, M.D., and Frank E. Thomas. Our Board of Directors has determined that all members of the Nominating Committee qualify as independent under the definition promulgated by The Nasdaq Stock Market. The Nominating Committee’s responsibilities are set forth in the Nominating Committee’s written charter and include:

- identifying and recommending candidates for membership on our Board of Directors;
- identifying and recommending candidates for membership on our Board of Directors;
- recommending directors to serve on board committees;
- reviewing and recommending our corporate governance guidelines and policies;
- reviewing proposed waivers of the code of conduct for directors and executive officers;
- evaluating, and overseeing the process of evaluating, the performance of our Board of Directors and individual directors; and
- assisting our Board of Directors on corporate governance matters.

[Table of Contents](#)

Generally, our Nominating Committee considers candidates recommended by stockholders as well as from other sources such as other directors or officers, third party search firms or other appropriate sources. Once identified, the Nominating Committee will evaluate a candidate's qualifications in accordance with the criteria set forth in our Corporate Governance Guidelines. Our Nominating Committee has not adopted a formal diversity policy in connection with the consideration of director nominations or the selection of nominees. However, the Nominating Committee will consider issues of diversity among its members in identifying and considering nominees for director, and strive where appropriate to achieve a diverse balance of backgrounds, perspectives, experience, age, gender, ethnicity and country of citizenship on the Board of Directors and its committees.

If a stockholder wishes to propose a candidate for consideration as a nominee for election to the Board of Directors, it must follow the procedures described in our amended and restated By-Laws and in "Stockholder Proposals and Nominations For Director" at the end of this proxy statement. Any such recommendation should be made in writing to the Nominating and Governance Committee, care of our Secretary at our principal office and should be accompanied by the following information concerning each recommending stockholder and the beneficial owner, if any, on whose behalf the nomination is made:

- all information relating to such person that would be required to be disclosed in a proxy statement;
- certain biographical and share ownership information about the stockholder and any other proponent, including a description of any derivative transactions in the Company's securities;
- a description of certain arrangements and understandings between the proposing stockholder and any beneficial owner and any other person in connection with such stockholder nomination; and
- a statement whether or not either such stockholder or beneficial owner intends to deliver a proxy statement and form of proxy to holders of voting shares sufficient to carry the proposal.

The recommendation must also be accompanied by the following information concerning the proposed nominee:

- certain biographical information concerning the proposed nominee;
- all information concerning the proposed nominee required to be disclosed in solicitations of proxies for election of directors;
- certain information about any other security holder of the Company who supports the proposed nominee;
- a description of all relationships between the proposed nominee and the recommending stockholder or any beneficial owner, including any agreements or understandings regarding the nomination; and
- additional disclosures relating to stockholder nominees for directors, including completed questionnaires and disclosures required by our amended and restated By-Laws.

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. The guidelines provide that:

- our Board of Directors' principal responsibility is to oversee the management of our Company;
- except as required by The Nasdaq Stock Market rules, a majority of the members of our Board of Directors must be independent directors;
- the independent directors meet in executive session at least twice a year;

[Table of Contents](#)

- directors have full and free access to management and, as necessary, independent advisors; and
- our nominating and corporate governance committee will oversee periodic self-evaluations of the Board of Directors to determine whether it and its committees are functioning effectively.

Copies of the Nominating Committee's written charter and our Corporate Governance Guidelines are publicly available on the Company's website at www.sperotherapeutics.com.

Compensation Committee Interlocks and Insider Participation. None of the members of our Compensation Committee has at any time during the prior three years been one of our officers or employees. None of our executive officers currently serves, or in the past fiscal year has served, as a member of our Board of Directors or Compensation Committee of any entity that has one or more executive officers serving on our Board of Directors or Compensation Committee. For a description of transactions between us and members of our Compensation Committee and affiliates of such members, see "Certain Relationships and Related Person Transactions."

Board Leadership Structure and Role in Risk Oversight

The Company's Board of Directors is currently chaired by Milind Deshpande, Ph.D. As a general policy, our Board of Directors believes that separation of the positions of chairman and chief executive officer reinforces the independence of our Board of Directors from management, creates an environment that encourages objective oversight of management's performance and enhances the effectiveness of our Board of Directors as a whole. As such, Dr. Mahadevia serves as our Chief Executive Officer while Dr. Deshpande serves as the chairman of our Board of Directors but is not an officer.

Our Board of Directors oversees the management of risks inherent in the operation of our business and the implementation of our business strategies. Our Board of Directors performs this oversight role by using several different levels of review. In connection with its reviews of the operations and corporate functions of our Company, our Board of Directors addresses the primary risks associated with those operations and corporate functions. In addition, our Board of Directors reviews the risks associated with the Company's business strategies periodically throughout the year as part of its consideration of undertaking any such business strategies.

Each of our board committees also oversees the management of the Company's risk that falls within the committee's areas of responsibility. In performing this function, each committee has full access to management, as well as the ability to engage advisors. Our Chief Executive Officer reports to the Audit Committee and is responsible for identifying, evaluating and implementing risk management controls and methodologies to address any identified risks. In connection with its risk management role, our Audit Committee meets privately with representatives from our independent registered public accounting firm and our Chief Executive Officer. The Audit Committee oversees the operation of our risk management program, including the identification of the primary risks associated with our business and periodic updates to such risks, and reports to our Board of Directors regarding these activities.

Stockholder Communications to the Board of Directors

Generally, stockholders who have questions or concerns should contact our Investor Relations department at 857-242-1547 or ir@sperotherapeutics.com. However, any stockholders who wish to address questions regarding our business directly with the Board of Directors, or any individual director, should direct his or her questions in writing to the Chairman of the Board of Directors at Spero Therapeutics, Inc., 675 Massachusetts Avenue, 14th Floor, Cambridge, Massachusetts 02139. Communications will be distributed to the Board of Directors, or to any individual director or directors as appropriate, depending on the facts and circumstances outlined in the communications. Items that are unrelated to the duties and responsibilities of the Board of Directors may be excluded, such as: junk mail and mass mailings; resumes and other forms of job

[Table of Contents](#)

inquiries; surveys; and solicitations or advertisements. In addition, any material that is unduly hostile, threatening, or illegal in nature may be excluded, provided that any communication that is filtered out will be made available to any outside director upon request.

Executive Officers

The following table sets forth certain information regarding our executive officers who are not also directors. We have employment agreements or consulting agreements with each of our executive officers.

<u>Name</u>	<u>Age</u>	<u>Position</u>
Stephen J. DiPalma	61	Chief Financial Officer (Interim)
Timothy Keutzer	52	Chief Development Officer
Cristina Larkin	50	Chief Operating Officer
David Melnick, M.D.	68	Chief Medical Officer

On September 4, 2019, Mr. Joel Sendek notified us of his resignation as the Company's Chief Financial Officer to pursue another opportunity closer to his home. Mr. Sendek's resignation was effective on November 8, 2019. Mr. Sendek's resignation was not as a result of any disagreement with our Board of Directors or any matter related to our operations, product candidates, policies or practices.

Stephen J. DiPalma has served as our interim Chief Financial Officer and Treasurer since November 2019. He is a Managing Director of Danforth Advisors, LLC, a financial consultancy that specializes in working with life sciences companies. Prior to and during his tenure at Danforth, Mr. DiPalma has served as interim Chief Financial Officer to several public and emerging companies in various stages of development. Mr. DiPalma joined Danforth in 2014 and served as Chief Financial Officer at Forum Pharmaceuticals from 2009 to 2014. He holds a B.S. from the University of Massachusetts and M.B.A. from Babson College.

Timothy Keutzer has served as our Chief Development Officer since June 2019. He has over 20 years' experience in the pharmaceutical industry, spanning multiple functional and therapeutic areas. Prior to joining Spero, Mr. Keutzer served in various roles at Cubist Pharmaceuticals, including Vice President of Program and Portfolio Management from May 2014 to July 2015. At Cubist Mr. Keutzer was the program leader for ceftolozane/tazobactam, which progressed rapidly from Phase 1 to Phase 3, and was approved in the FDA in December of 2014. Prior to that role, he also led several of Cubist's inlicensed development programs, and also led the commercial supply chain for Cubicin. His experience before Cubist spans multiple drug classes, and includes preclinical PK/PD and clinical operations at Genetics Institute, as well as global strategic marketing and program management at Wyeth. Tim began his career in contract toxicology labs. Mr. Keutzer earned his bachelor's degree from the University of Kentucky.

Cristina Larkin has served as our Chief Operating Officer since September 2017 and had previously served as our Chief Commercial Officer since March 2016. Ms. Larkin has over 26 years of experience developing strategic commercial insights for biopharmaceutical companies and their infectious disease products such as Avycaz[®], Dalvance[®], Teflaro[®], Levaquin[®] and Floxin[®]. Prior to joining us, Ms. Larkin founded CLC Insights, LLC. Prior to that, since 2004, she worked at Actavis, plc, formerly Forest Laboratories, Inc., where she served in various positions, including Assistant Vice President from 2014 to 2015. During that time, Ms. Larkin led the commercial hospital antibiotic franchise team and was responsible for the U.S. launch and execution strategy for several antibiotics. Additionally, she was a member of the business assessments and business development team and played an integral role in several strategic ventures, including the out-licensing of ceftaroline to AstraZeneca plc and the acquisition of Durata. From 1996 to 2002, Ms. Larkin served in various roles at Ortho-McNeil Pharmaceutical, LLC. Ms. Larkin received a bachelor's degree from Florida State University.

David Melnick, M.D. has served as our Chief Medical Officer since January 2018. Prior to joining Spero, Dr. Melnick served as Vice President of Clinical Development for Anti-Infectives at Allergan since 2015.

[Table of Contents](#)

In that capacity, he oversaw the development and regulatory approval of Teflaro[®], Avycaz[®], and Dalvance[®] in the United States. Prior to Allergan, Dr. Melnick served fifteen years at AstraZeneca in various levels of increasing responsibility, most recently as Vice President of Clinical Development for Anti-Infectives. In that capacity, he oversaw the late stage clinical development of Merrem[®], Teflaro[®], and Avycaz[®]. In addition, he served as the acting Vice President for early development at AstraZeneca. He received his medical training at Columbia University, followed by a Residency in Internal Medicine at The New York Hospital-Cornell Medical Center. Following a Fellowship in Infectious Disease at Yale University, he held faculty positions at the Boston University School of Medicine and the National Institute of Allergy and Infectious Diseases. He subsequently joined Kaiser-Permanente as a practicing Infectious Diseases specialist and as the Director of HIV Clinical Research at Kaiser Permanente Mid-Atlantic, with a faculty appointment at Georgetown University.

EXECUTIVE OFFICER AND DIRECTOR COMPENSATION

Summary Compensation Table

The following table shows the total compensation paid or accrued during the last two fiscal years ended December 31, 2019 and 2018 to our President and Chief Executive Officer and our two next most highly compensated executive officers who earned more than \$100,000 during the fiscal year ended December 31, 2019 and were serving as executive officers as of such date.

Name and Principal Position	Year	Salary (\$)	Bonus (\$)(1)	Stock Awards (\$)(2)	Option Awards (\$)(3)	Non-Equity Incentive Plan Compensation (\$)(4)	All other Compensation (\$)(5)	Total (\$)
Ankit Mahadevia, M.D. <i>Chief Executive Officer</i>	2019	497,083	—	285,023	752,778	250,000	792	1,785,676
	2018	465,000	—	—	—	255,750	574	721,324
Christina Larkin <i>Chief Operating Officer</i>	2019	394,167	—	118,493	271,837	158,000	792	943,289
	2018	385,000	—	—	—	148,225	574	533,799
David Melnick, M.D. <i>Chief Medical Officer</i>	2019	389,167	—	118,493	271,837	156,000	792	936,288
	2018	375,680	10,000	—	1,082,146	146,300	20,235	1,634,361

- (1) Consists of a sign-on bonus to Dr. Melnick in connection with his commencement of employment in January 2018.
- (2) These amounts represent the aggregate grant date fair value for performance-based stock awards computed in accordance with Financial Accounting Standards Board Accounting Standards Codification Topic 718, or ASC 718. A discussion of the assumptions used in determining grant date fair value may be found in Note 9 to our consolidated financial statements included in our Annual Report on Form 10-K for the fiscal year ended December 31, 2019.
- (3) These amounts represent the aggregate grant date fair value for option awards computed in accordance with Financial Accounting Standards Board Accounting Standards Codification Topic 718, or ASC 718. A discussion of the assumptions used in determining grant date fair value may be found in Note 9 to our consolidated financial statements for the year ended December 31, 2019.
- (4) Amounts represent cash bonuses earned for the applicable fiscal year.
- (5) Consists of the dollar value of life insurance premiums the Company paid with respect to term life insurance for the benefit of the executive officers named in the table above. With respect to Dr. Melnick, this amount also includes the reimbursement of certain relocation expenses in the amount of \$19,661 paid in 2018.

Narrative Disclosure to Summary Compensation Table

Our employment arrangements with our named executive officers are described below.

Ankit Mahadevia, M.D.

On March 2, 2015, Dr. Mahadevia executed an offer letter with respect to his employment as our Chief Executive Officer beginning on the same date. Under the terms of the offer letter, Dr. Mahadevia's annual base salary was \$360,500 in 2016 and \$400,000 effective on May 19, 2017. Under the offer letter, he was eligible to receive an annual incentive bonus determined at the discretion of our Board of Directors or Compensation Committee, with a target bonus opportunity of 30% of his then-current base salary.

Dr. Mahadevia entered into a new employment agreement on October 20, 2017. This agreement provides for the following increased severance payments upon termination by us without Cause (as defined

Table of Contents

below) or by Dr. Mahadevia for Good Reason (as defined below): (i) payment of his then current base salary for a period of 12 months following termination; (ii) a pro-rated target bonus for the period during which Dr. Mahadevia was employed in the year of termination; and (iii) continued coverage under our group health insurance plan until the earlier of 12 months from termination or the date Dr. Mahadevia becomes eligible for medical benefits with another employer. Further, the new agreement provides that upon termination by us without Cause or by Dr. Mahadevia for Good Reason within 90 days prior to the earlier to occur of a Change of Control (as defined below) or the execution of a definitive agreement the consummation of which would result in a Change of Control or one year following a Change of Control (a "Change of Control Termination"), Dr. Mahadevia will be entitled to receive (i) a lump sum payment equal to 12 months of his then-current base salary plus a pro-rated target bonus for the period during which Dr. Mahadevia was employed in the year of termination; (ii) acceleration of all unvested equity awards as of the date of termination; and (iii) continued coverage under our group health insurance plan until the earlier of 12 months from termination or the date Dr. Mahadevia becomes eligible for medical benefits with another employer. Payment in each case is subject to Dr. Mahadevia's execution of a release satisfactory to us following such termination.

In addition, if Dr. Mahadevia's employment terminates as a result of disability or death, he shall be entitled to receive a pro-rated target bonus for the period during which Dr. Mahadevia was employed in the year of termination. The new agreement also provides that Dr. Mahadevia shall serve as a member of our Board of Directors during his employment with us until the term of his directorship expires and he is not re-elected or his earlier resignation or removal from our Board of Directors.

In December 2017, Dr. Mahadevia's base salary was increased, effective January 1, 2018, to \$465,000 with a target bonus opportunity of 50% of base salary. In December 2018, Dr. Mahadevia's base salary was increased, effective February 1, 2019, to \$500,000 with a target bonus opportunity of 50% of his base salary. In December 2019, Dr. Mahadevia's base salary was increased, effective February 1, 2020, to \$540,000, with a target bonus opportunity of 50% of his base salary.

Cristina Larkin

In February 2016, Cristina Larkin, our then Chief Commercial Officer, executed an offer letter with respect to her employment beginning on March 7, 2016. In September 2017, Ms. Larkin was promoted to Chief Operating Officer, in connection with which her bonus target was increased from 25% to 30% of her then-current base salary. In October 2017, we entered into a new employment agreement with Ms. Larkin, which provided for a base salary of \$345,000 and eligibility for an annual incentive bonus, with a target bonus opportunity of 30% of her then-current base salary. In December 2017, Ms. Larkin's base salary was increased, effective January 1, 2018, to \$385,000 with a target bonus opportunity of 35% of base salary. In December 2018, Ms. Larkin's base salary was increased, effective February 1, 2019, to \$395,000 with a target bonus opportunity of 40% of base salary. In December 2019, Ms. Larkin's base salary was increased, effective February 1, 2020, to \$404,875 with a target bonus opportunity of 40% of her base salary.

The agreement also provides for the following severance payments upon termination by us without Cause or by Ms. Larkin for Good Reason: (i) payment of her then-current base salary for a period of nine months following termination; (ii) a pro-rated target bonus for the period during which Ms. Larkin was employed in the year of termination; and (iii) continued coverage under our group health insurance plan until the earlier of 12 months from termination or the date Ms. Larkin becomes eligible for medical benefits with another employer. Further, the agreement provides that upon termination by us without Cause or by Ms. Larkin for Good Reason within 90 days prior to the earlier to occur of a Change of Control or the execution of a definitive agreement the consummation of which would result in a Change of Control or one year following a Change of Control (a "Change of Control Termination"), Ms. Larkin will be entitled to receive: (i) a lump sum payment equal to 12 months of her then-current base salary plus a pro-rated target bonus for the period during which Ms. Larkin was employed in the year of termination; (ii) acceleration of (A) all unvested equity awards as of the date of termination if Ms. Larkin's employment commenced at least 24 months prior to a Change of Control (B) 50% of

[Table of Contents](#)

all unvested equity awards as of the date of termination if Ms. Larkin's employment commenced fewer than 24 months but at least 12 months prior to a Change of Control or (C) 25% of all unvested equity awards as of the date of termination if Ms. Larkin's employment commenced fewer than 12 months prior to a Change of Control; and (iii) continued coverage under our group health insurance plan until the earlier of 12 months from termination or the date Ms. Larkin becomes eligible for medical benefits with another employer. Payment in each case is subject to Ms. Larkin's execution of a release satisfactory to us following such termination. In addition, if Ms. Larkin's employment terminates as a result of disability or death, she shall be entitled to receive a pro-rated target bonus for the period during which Ms. Larkin was employed in the year of termination.

David Melnick, M.D.

On December 13, 2017, we entered into an agreement with Dr. Melnick with respect to his employment as our Chief Medical Officer commencing on January 4, 2018. The terms of Mr. Melnick's agreement provided for an annual base salary of \$380,000 prorated for fiscal year 2018, and eligibility for an annual incentive bonus, with a target bonus opportunity of 35% of his then-current base salary. In December 2018, Dr. Melnick's base salary was increased, effective February 1, 2019, to \$390,000 with a target bonus opportunity of 40% of base salary. In addition, Dr. Melnick was granted an option to purchase 135,000 shares of common stock and received a sign-on bonus of \$10,000. In December 2019, Dr. Melnick's base salary was increased, effective February 1, 2020, to \$413,400 with a target bonus opportunity of 40% of his base salary.

The agreement also provides for the following severance payments upon termination by us without Cause or by Dr. Melnick for Good Reason: (i) payment of his then-current base salary for a period of nine months following termination; (ii) a pro-rated target bonus for the period during which Dr. Melnick was employed in the year of termination; and (iii) continued coverage under our group health insurance plan until the earlier of 12 months from termination or the date Dr. Melnick becomes eligible for medical benefits with another employer. Further, the agreement provides that upon termination by us without Cause or by Dr. Melnick for Good Reason within 90 days prior to the earlier to occur of a Change of Control or the execution of a definitive agreement the consummation of which would result in a Change of Control or one year following a Change of Control (a "Change of Control Termination"), Dr. Melnick will be entitled to receive: (i) a lump sum payment equal to 12 months of his then-current base salary plus a pro-rated target bonus for the period during which Dr. Melnick was employed in the year of termination; (ii) acceleration of (A) all unvested equity awards as of the date of termination if Dr. Melnick's employment commenced at least 24 months prior to a Change of Control (B) 50% of all unvested equity awards as of the date of termination if Melnick's employment commenced fewer than 24 months but at least 12 months prior to a Change of Control and (C) 25% of all unvested equity awards as of the date of termination if Dr. Melnick's employment commenced fewer than 12 months prior to a Change of Control; and (iii) continued coverage under our group health insurance plan until the earlier of 12 months from termination or the date Dr. Melnick becomes eligible for medical benefits with another employer. Payment in each case is subject to Dr. Melnick's execution of a release satisfactory to us following such termination. In addition, if Dr. Melnick's employment terminates as a result of disability or death, he shall be entitled to receive a pro-rated target bonus for the period during which Dr. Melnick was employed in the year of termination.

Under each of the employment agreements, Cause means (i) the executive's conviction of (A) a felony or (B) any misdemeanor involving moral turpitude, deceit, dishonesty or fraud; (ii) the executive's willful failure or refusal to comply with lawful directions of our Board of Directors, with respect to Dr. Mahadevia, or of our Chief Executive Officer, with respect to Dr. Melnick and Ms. Larkin, which failure or refusal continues for more than thirty days after written notice is given to the executive by our Board of Directors, with respect to Dr. Mahadevia, or by our Chief Executive Officer, with respect to Dr. Melnick and Ms. Larkin, which notice sets forth in reasonable detail the nature of such failure or refusal; (iii) willful and material breach by the executive of a written company policy applicable to the executive or the executive's covenants and/or obligations under his or her employment agreement or the material breach of the executive's proprietary information and inventions assignment agreement; and/or (iv) material misconduct by the executive that seriously discredits or damages us or any of our affiliates.

[Table of Contents](#)

Under each of the employment agreements, Good Reason means (i) relocation of the executive's principal business location to a location more than thirty (30) miles from the executive's then-current business location; (ii) a material diminution in the executive's duties, authority or responsibilities; (iii) a material reduction in the executive's base salary; (iv) willful and material breach by us of our covenants and/or obligations under the executive's employment agreement; or (v) within one year following a Change of Control, the executive is not an executive of the parent company, provided that the executive's roles responsibilities and scope of authority within the subsidiary is not comparable to the executive's roles, responsibilities and scope of authority with us prior to the Change of Control.

Under each of the employment agreements, Change of Control means (i) any person (as such term is used in Sections 13(d) and 14(d) of the Exchange Act) becomes the beneficial owner, directly or indirectly, of securities of the Company representing fifty percent (50%) or more of the total voting power represented by the Company's then outstanding voting securities (excluding for this purpose any such voting securities held by the Company, or any affiliate, parent or subsidiary of the Company, or by any employee benefit plan of the Company) pursuant to a transaction or a series of related transactions; (ii) a merger or consolidation of the Company other than a merger or consolidation which would result in the voting securities of the Company outstanding immediately prior thereto continuing to represent (either by remaining outstanding or by being converted into voting securities of the surviving entity or the parent of such corporation) at least fifty percent (50%) of the total voting power represented by the voting securities of the Company or such surviving entity or parent of such corporation, as the case may be, outstanding immediately after such merger or consolidation; (iii) our stockholders approve an agreement for the sale or disposition by the Company of all or substantially all of our assets; or (iv) a change in the composition of our Board of Directors, as a result of which fewer than a majority of the directors are incumbent directors.

All of our executive officers have entered into our standard proprietary information and inventions assignment agreement.

Outstanding Equity Awards at 2019 Fiscal Year-End

On June 30, 2017, we completed a series of transactions pursuant to which Spero Therapeutics, LLC merged with and into Spero Therapeutics, Inc., with Spero Therapeutics, Inc. continuing as the surviving corporation (the "2017 Reorganization"). As part of the 2017 Reorganization, each of the capital units of Spero Therapeutics, LLC issued and outstanding prior to the 2017 Reorganization was cancelled and converted into and exchanged for one share of Spero Therapeutics, Inc. capital stock of the same class and/or series, and each of the incentive units of Spero Therapeutics, LLC was terminated and cancelled. Promptly after the 2017 Reorganization, previous holders of incentive units who were still employed by us at the time of the Reorganization received stock options under the 2017 Plan. Such stock options were granted for the same number of shares of our common stock as the number of incentive units cancelled, and the stock options were granted with continued vesting on the same terms and with similar rights and restrictions as the incentive units. All such stock options have an exercise price of \$5.90.

[Table of Contents](#)

The following table shows grants of stock options outstanding on the last day of the fiscal year ended December 31, 2019 to each of the executive officers named in the Summary Compensation Table.

Name	Option Awards					Stock Awards			Equity incentive plan awards: market or payout value of unearned shares, units or other rights that have not vested (\$)
	Number of Securities Underlying Unexercised Options (#) Exercisable		Number of Securities Underlying Unexercised Options (#) Unexercisable	Option Exercise Price (\$)	Option Expiration Date	Number of Shares or Units of Stock That Have not Vested (#)	Market Value of Shares or Units of Stock that Have not Vested (\$)	Equity incentive plan awards: number of unearned shares, units or other rights that have not vested	
Ankit Mahadevia, M.D.	22,213	(1)	—	\$ 5.90	7/5/2027	—	—	—	—
	93,028	(2)	8,460	\$5.90	7/5/2027	—	—	—	—
	118,888	(3)	—	\$5.90	7/5/2027	—	—	—	—
	179,572	(4)	117,648	\$5.90	7/5/2027	—	—	—	—
	62,539	(5)	62,540	\$11.63	12/12/2027	—	—	—	—
	—		180,000	\$6.26	1/1/2029	—	—	—	—
	—		43,901	\$12.81	3/29/2029	—	—	—	—
		—	—	—	—	—	22,250	(8)	285,023
Cristina Larkin	18,907	(9)	1,527	\$ 5.90	7/5/2027	—	—	—	—
	5,949	(10)	541	\$5.90	7/5/2027	—	—	—	—
	42,758	(4)	28,021	\$5.90	7/5/2027	—	—	—	—
	31,270	(5)	31,270	\$11.63	12/12/2027	—	—	—	—
	—		65,000	\$6.26	1/1/2029	—	—	—	—
	—		15,854	\$12.81	3/29/2029	—	—	—	—
		—	—	—	—	—	9,250	(8)	118,493
David Melnick, M.D.	64,688	(11)	70,312	\$ 12.14	1/3/2028	—	—	—	—
	—		65,000	\$6.26	1/1/2029	—	—	—	—
	—		15,854	\$12.81	3/29/2029	—	—	—	—
		—	—	—	—	—	9,250	(8)	118,493

(1) 100% of these options vested on August 24, 2019.

(2) As part of the 2017 Reorganization, Dr. Mahadevia was granted options to replace his previously awarded incentive units in Spero Therapeutics, LLC. The options vest in accordance with the vesting terms of Dr. Mahadevia's previously held incentive units: 25% of the underlying shares were deemed vested April 28, 2017, the first anniversary of the vesting commencement date, with an additional 1/36th of the remaining shares vesting monthly thereafter until the option is fully vested. In addition, in the event of a Change of Control Termination, the vesting of these options will accelerate in accordance with the terms of the option and his employment agreement.

(3) 100% of these options vested on July 6, 2017.

(4) 25% of the options vested on July 6, 2018 and an additional 1/36th of the remaining shares vest monthly until the option is fully vested. In addition, in the event of a Change of Control Termination, the vesting of these options will accelerate in accordance with the terms of the option and his or her employment agreement.

Table of Contents

- (5) 25% of the options vested on December 13, 2018 and an additional 1/36th of the remaining shares vest monthly until the option is fully vested. In addition, in the event of a Change of Control Termination, the vesting of these options will accelerate in accordance with the terms of the option and his or her employment agreement.
- (6) 25% of the options vest on January 2, 2020 and an additional 1/36th of the remaining shares vest monthly until the option is fully vested. In addition, in the event of a Change of Control Termination, the vesting of these options will accelerate in accordance with the terms of the option and his or her employment agreement.
- (7) These performance-based options, which were granted in March 2019, vest in four equal installments upon the achievement, within the performance period ending December 31, 2020, of certain performance goals, which are more fully described below under “Performance-Based Equity Incentive Awards,” and are contingent on the executive remaining an employee, director or consultant of Spero as of each such date.
- (8) These performance-based restricted stock units, which were granted in March 2019, vest in four equal installments upon the achievement, within the performance period ending December 31, 2020, of certain performance goals, which are more fully described below under “Performance-Based Equity Incentive Awards,” and are contingent on the executive remaining an employee, director or consultant of Spero as of each such date.
- (9) As part of the Company’s 2017 Reorganization, Ms. Larkin was granted options to replace her previously awarded incentive units in Spero Therapeutics, LLC. The options vest in accordance with the vesting terms of Ms. Larkin’s previously held incentive units: 25% of the underlying shares were deemed vested on March 7, 2017, the first anniversary of the vesting commencement date, with an additional 1/36th of the remaining shares vesting monthly thereafter until the option is fully vested. In addition, in the event of a Change of Control Termination, the vesting of these options will accelerate in accordance with the terms of the option and her employment agreement.
- (10) As part of the Reorganization, Ms. Larkin was granted options to replace her previously awarded incentive units in Spero Therapeutics, LLC. The options vest in accordance with the vesting terms of Ms. Larkin’s previously held incentive units: 25% of the underlying shares were deemed vested April 28, 2017, the first anniversary of the vesting commencement date, with an additional 1/36th of the remaining shares vesting monthly thereafter until the option is fully vested. In addition, in the event of a Change of Control Termination, the vesting of these options will accelerate in accordance with the terms of the option and her employment agreement.
- (11) 25% of the options vested on January 4, 2019 and an additional 1/36th of the remaining shares vest monthly until the option is fully vested. In addition, in the event of a Change of Control Termination, the vesting of these options will accelerate in accordance with the terms of the option and his employment agreement.

Performance-Based Equity Incentive Awards

Historically, we have generally granted stock options with time-based vesting to our executives at the time of hire and on an annual basis thereafter. In March 2019, in addition to the foregoing, we granted an aggregate of 150,000 performance-based options and restricted stock units (“RSUs”) to our senior executives. These options and RSUs (the “Performance Awards”) are subject to performance-based vesting eligibility and a subsequent partial time-based vesting schedule. Specifically, the Performance Awards are eligible for vesting based on the achievement of performance criteria, each representing a 25% vesting opportunity if achieved within a specified time during the performance period (the “Performance Period”), and relating to (i) the release of tebipenem HBr top-line data; (ii) FDA acceptance of a tebipenem HBr New Drug Application; (iii) non-dilutive financing; and (iv) equity financing. Following the Performance Period, Performance Awards determined to be eligible for

[Table of Contents](#)

vesting as a result of achievement of the performance criteria will vest as follows: (a) 50% of the eligible award will vest immediately, and (b) the remaining eligible award will vest (i) in the case of options, in equal monthly instalments ending two years after the Performance Period expiration, and (ii) in the case of RSUs, on such two year anniversary. The Performance Awards will be subject to provisions of the executives' employment agreements regarding acceleration of vesting in the event of certain termination events following a change in control only to the extent previously determined to be eligible for vesting as a result of achievement of the performance criteria. We believe the achievement of the performance criteria will require significant execution and effort by the executives with no assurance of achievement guaranteed. Awards for which the performance criteria has not been achieved as specified during the Performance Period will lapse.

Potential Payments upon Termination or Change-In-Control

The employment agreements provide for the following severance payments upon termination by us without Cause or by the employee for Good Reason: (i) payment of the employee's then-current base salary for a period of nine months following termination (12 months in the case of the Chief Executive Officer); (ii) a pro-rated target bonus for the period during which the employee was employed in the year of termination; and (iii) continued coverage under our group health insurance plan until the earlier of 12 months from termination or the date the employee becomes eligible for medical benefits with another employer.

Further, the agreements provide that upon termination by us without Cause or by the employee for Good Reason within 90 days prior to or one year following the earlier to occur of a Change of Control (as defined in the executive's employment agreements) or the execution of a definitive agreement the consummation of which would result in a Change of Control, the employee will be entitled to receive: (i) a lump sum payment equal to 12 months of the employee's then-current base salary plus a pro-rated target bonus for the period during which the employee was employed in the year of termination; (ii) acceleration of unvested equity awards as of the date of termination in accordance with the terms of the executive's employment agreement, as described above under "Narrative Disclosure to Summary Compensation Table;" and (iii) continued coverage under our group health insurance plan until the earlier of 12 months from termination or the date the employee becomes eligible for medical benefits with another employer. Payment in each case is subject to the employee's execution of a release satisfactory to us following such termination. In addition, if the employee's employment terminates as a result of disability or death, he or she shall be entitled to receive a pro-rated target bonus for the period during which the employee was employed in the year of termination.

Director Compensation

The following table shows the total compensation paid or accrued during the fiscal year ended December 31, 2019 to each of our current and former non-employee directors. Scott Jackson joined our Board of Directors in April 2020. Directors who are employed by us are not compensated for their service on our Board of Directors.

Name	Fees Earned	Option	Total(\$)
	or Paid in	Awards*	
	Cash (\$)	(\$)	
Milind Deshpande, Ph.D.	77,500	45,374(3)	122,874
Jean-François Formela, M.D.	44,000	45,374(3)	89,374
John C. Pottage, Jr., M.D.	52,500	45,374(3)	97,874
Cynthia Smith (1)	31,264	151,135(3)(4)	182,399
David P. Southwell (2)	10,625	—	10,625
Frank E. Thomas	54,000	45,374(3)	99,374
Patrick Vink, M.D.	52,500	45,374(3)	99,874

[Table of Contents](#)

* These amounts represent the aggregate grant date fair value of options granted to each director in the fiscal year ended December 31, 2019, computed in accordance with FASB ASC Topic 718. A discussion of the assumptions used in determining grant date fair value may be found in Note 9 to our consolidated financial statements, included in our Annual Report on Form 10-K for the fiscal year ended December 31, 2019.

- (1) Ms. Smith joined our Board of Directors in March 2019.
- (2) Mr. Southwell resigned from our Board of Directors in April 2019.
- (3) Represents an option to purchase 6,073 shares of common stock at an exercise price of \$10.67. The shares underlying the option award vest and become fully exercisable on June 5, 2020, subject to the individual's continued service as of such date.
- (4) Represents an option to purchase 12,146 shares of common stock at an exercise price of \$12.81. The shares underlying the option award vest in thirty-six equal monthly installments at the end of each successive month following March 29, 2019, subject to the individual's continued service as of such date.
- (5) As of December 31, 2019, the aggregate number of options held by each of our non-employee directors was as follows (representing both exercisable and unexercisable option awards, none of which have been exercised):

<u>Name</u>	<u>Number of Shares Underlying Outstanding Stock Options</u>
Milind Deshpande, Ph.D.	60,627
Jean François Formela, M.D.	12,146
John C. Pottage, Jr., M.D.	18,219
Cynthia Smith	18,219
Frank E. Thomas	42,661
Patrick Vink, M.D.	42,660

Non-Employee Director Compensation Policy

Under our Non-Employee Director Compensation Policy, as amended, each non-employee director is eligible to receive compensation for his or her service consisting of annual cash retainers and equity awards. Our non-employee directors receive the following annual retainers for their service:

<u>Position</u>	<u>Retainer</u>
Board Member	\$ 35,000
Board Chairperson (additional retainer)	30,000
Lead Director, if any (additional retainer)	18,750
Audit Committee Chair	15,000
Compensation Committee Chair	10,000
Nominating and Governance Committee Chair	7,500
Audit Committee Member	7,500
Compensation Committee Member	5,000
Nominating and Governance Committee Member	4,000

In December 2019 we amended our Non-Employee Director Compensation Policy to provide the following with respect to equity awards to non-employee directors: (i) the initial equity award consisting of a non-qualified stock option to purchase shares of our common stock upon first appointment to our Board of

[Table of Contents](#)

Directors and vesting in equal monthly installments until the third anniversary of the grant date subject to the non-employee director's continued service, was increased from 12,146 shares to 15,000 shares, and (ii) annual equity awards consisting of a non-qualified stock option to purchase shares of our common stock vesting on the first anniversary of the grant date subject to the non-employee director's continued service, were increased from 6,073 shares to 7,500 shares,. The policy was further amended to provide that, prior to the beginning of each calendar year, a non-employee director may elect to receive all or a portion of his or her base annual fee for service on our Board of Directors (i.e., \$35,000) in the form of a non-qualified stock option to purchase a number of shares of our common stock based on the Black-Scholes value of such option, which option will be granted on the first business day of the calendar year. These options vest in four quarterly installments on the last day of each calendar quarter during the calendar year, subject to the continued service of the non-employee director.

Directors may be reimbursed for travel, food, lodging and other expenses directly related to their service as directors. Directors are also entitled to the protection provided by their indemnification agreements and the indemnification provisions in our amended and restated certificate of incorporation and amended and restated By-Laws.

EQUITY COMPENSATION PLANS AND OTHER BENEFIT PLANS**Equity Compensation Plan Information**

The following table provides certain aggregate information with respect to all of the Company's equity compensation plans in effect as of December 31, 2019.

Plan category	(a) Number of securities to be issued upon exercise of outstanding options, warrants and rights	(b) Weighted-average exercise price of outstanding options, warrants and rights	(c) Number of securities remaining for future issuance under equity compensation plans (excluding securities reflected in column (a))
Equity compensation plans approved by stockholders (1)	2,829,678	\$ 7.94	329,457(3)
Equity compensation plans not approved by stockholders (2)	171,300	\$ 11.42	160,200
Total:	3,000,978	\$ 8.13	489,657

- (1) This plan category consists of the Company's 2017 Stock Incentive Plan, as amended.
- (2) This plan category consists of the Company's 2019 Inducement Equity Incentive Plan, as amended.
- (3) Under the Company's 2017 Stock Incentive Plan, the number of shares of common stock that may be issued automatically increases on an annual basis on the first day of each fiscal year, beginning with the fiscal year until and including the fiscal year ending December 31, 2027, by an amount equal to the lesser of (i) 607,324 shares of common stock, (ii) 4% of the number of outstanding shares of our common stock on such date, or (iii) an amount determined by our Board of Directors or Compensation Committee.

Benefits Programs

Each named executive employee is eligible to participate in our benefits programs, which include health, life, disability and dental insurance and a 401(k) retirement savings plan.

Spero Therapeutics, Inc.'s 2017 Stock Incentive Plan

We adopted the Spero Therapeutics, Inc. 2017 Stock Incentive Plan on June 28, 2017, as amended on October 18, 2017 (the "2017 Plan"). The 2017 Plan will expire on June 30, 2027. Under the 2017 Plan, we may grant incentive stock options, non-qualified stock options, restricted and unrestricted stock awards and other stock-based awards.

Since its adoption, there have been 3,911,049 shares of our common stock authorized for issuance under the 2017 Plan, which amount includes the automatic increase effective as of January 1, 2020. As of September 1, 2020, a total of 304,022 shares are available for future grant under the 2017 Plan.

Our Board of Directors is authorized to administer the 2017 Plan. In accordance with the provisions of the 2017 Plan, our Board of Directors determines the terms of the options and other awards issued pursuant thereto, including the following:

- which employees, directors and consultants shall be granted awards;
- the number of shares of common stock subject to options and other awards;

Table of Contents

- the exercise price of each option, which generally shall not be less than fair market value of the common stock on the date of grant;
- the termination or cancellation provisions applicable to the options;
- the terms and conditions of other awards, including conditions for repurchase, termination or cancellation, issue price and repurchase price; and
- all other terms and conditions upon which each award may be granted in accordance with the 2017 Plan.

No participant may receive awards for more than 1,000,000 shares of our common stock in any fiscal year.

In addition, our Board of Directors or any committee to which our Board of Directors delegates authority may, with the consent of the affected plan participants, amend outstanding awards consistent with the terms of the 2017 Plan.

Upon a merger, consolidation, or sale of all or substantially all of our assets, our Board of Directors or any committee to which our Board of Directors delegates authority, or the Board of Directors of any corporation assuming the our obligations, may, in its sole discretion, take any one or more of the following actions pursuant to the 2017 Plan, as to some or all outstanding awards, to the extent not otherwise agreed under any individual agreement:

- provide that outstanding options will be assumed or substituted for options of the successor corporation;
- provide that the outstanding options must be exercised within a certain number of days, either to the extent the options are then exercisable, or at our Board of Directors' discretion, any such options being made partially or fully exercisable;
- terminate outstanding options in exchange for a cash payment of an amount equal to the difference between (a) the consideration payable upon consummation of the corporate transaction to a holder of the number of shares into which such option would have been exercisable to the extent then exercisable, or in our Board of Directors' discretion, any such options being made partially or fully exercisable, and (b) the aggregate exercise price of those options;
- provide that outstanding stock grants will be substituted for shares of the successor corporation or consideration payable with respect to our outstanding stock in connection with the corporate transaction; and
- terminate outstanding stock grants in exchange for payment of an amount equal to the consideration payable upon consummation of the corporate transaction to a holder of the same number of shares comprising the stock grant, to the extent the stock grant is no longer subject to any forfeiture or repurchase rights, or at our Board of Directors' discretion, all forfeiture and repurchase rights being waived upon the corporate transaction. For purposes of determining such payments, in the case of a corporate transaction the consideration for which, in whole or in part, is other than cash, the consideration other than cash shall be valued at the fair market value thereof as determined in good faith by our Board of Directors.

In connection with the Company's 2017 Reorganization, all outstanding incentive units issued under Spero Therapeutics, LLC's operating agreement were cancelled. Any incentive unit holders who were

[Table of Contents](#)

employees, directors or consultants of the Company at the time of the 2017 Reorganization were issued options under the 2017 Plan with continued vesting on the same schedule and the same terms as such person's incentive units.

Spero Therapeutics, Inc.'s 2019 Inducement Equity Incentive Plan

On March 11, 2019, the Board of Directors adopted Spero Therapeutics, Inc.'s 2019 Inducement Equity Incentive Plan, as amended on June 23, 2020 (the "2019 Inducement Plan"). The Board of Directors initially reserved 331,500 shares and in June 2020 reserved an additional 700,000 shares of our common stock under the 2019 Inducement Plan to be used exclusively for grants of awards to individuals that were not previously employees or directors of the Company, as an inducement to the individual's entry into employment with the Company within the meaning of Rule 5635(c)(4) of the Nasdaq Listing Rules. The 2019 Inducement Plan was adopted without stockholder approval pursuant to Rule 5635(c)(4). The 2019 Inducement Plan provides for the grant of equity-based awards, including options, restricted and unrestricted stock awards, and other stock-based awards, and its terms are substantially similar to the 2017 Plan, but with such other terms and conditions intended to comply with the Nasdaq inducement award exception.

As of September 1, 2020, there were 336,900 shares outstanding and 694,600 shares available for grant under the 2019 Inducement Plan.

Rule 10b5-1 Sales Plans

Our directors and executive officers may adopt written plans, known as Rule 10b5-1 plans, in which they will contract with a broker to buy or sell shares of our common stock on a periodic basis. Under a Rule 10b5-1 plan, a broker executes trades pursuant to parameters established by the director or officer when entering into the plan, without further direction from the director or officer. The director or officer may amend or terminate the plan in limited circumstances. Our directors and executive officers may also buy or sell additional shares of our common stock outside of a Rule 10b5-1 plan when they are not in possession of material, nonpublic information.

REPORT OF AUDIT COMMITTEE

The Audit Committee of the Board of Directors, which consists entirely of directors who meet the independence and experience requirements of The Nasdaq Stock Market has furnished the following report:

The Audit Committee assists the Board of Directors in overseeing and monitoring the integrity of our financial reporting process, compliance with regulatory requirements and the quality of internal and external audit processes. This committee's role and responsibilities are set forth in our charter adopted by the Board of Directors, which is available on our website at www.sperotherapeutics.com. This committee reviews and reassesses our charter annually and recommends any changes to the Board of Directors for approval. The Audit Committee is responsible for overseeing our overall financial reporting process, and for the appointment, compensation, retention, and oversight of the work of PricewaterhouseCoopers LLP. In fulfilling its responsibilities for the financial statements for fiscal year ended December 31, 2019, the Audit Committee took the following actions:

- Reviewed and discussed the audited financial statements for the fiscal year ended December 31, 2019 with management and PricewaterhouseCoopers LLP, our independent registered public accounting firm;
- Discussed with PricewaterhouseCoopers LLP the matters required to be discussed by the Public Company Accounting Oversight Board in accordance with Auditing Standard No. 1301, Communications with Audit Committees; and
- Received written disclosures and the letter from PricewaterhouseCoopers LLP regarding its independence as required by applicable requirements of the Public Company Accounting Oversight Board regarding PricewaterhouseCoopers LLP communications with the Audit Committee and the Audit Committee further discussed with PricewaterhouseCoopers LLP their independence. The Audit Committee also considered the status of pending litigation, taxation matters and other areas of oversight relating to the financial reporting and audit process that the committee determined appropriate.

Based on the Audit Committee's review of the audited financial statements and discussions with management and PricewaterhouseCoopers LLP, the Audit Committee recommended to the Board of Directors that the audited financial statements be included in our Annual Report on Form 10-K for the fiscal year ended December 31, 2019 for filing with the SEC.

Members of the Spero Therapeutics, Inc. Audit Committee

Frank E. Thomas (Chairman)
Scott Jackson
John C. Pottage, Jr., M.D.
Patrick Vink, M.D.

CERTAIN RELATIONSHIPS AND RELATED PERSON TRANSACTIONS

The following is a description of transactions since January 1, 2018, to which we have been a party, in which the amount involved exceeds \$120,000, and in which any of our directors, executive officers or holders of more than 5% of our capital stock, or an affiliate or immediate family member thereof, had or will have a direct or indirect material interest. We refer to such transactions as “related party transactions” and such persons as “related parties.” With the approval of our Board of Directors, we have engaged in the related party transactions described below. We believe the terms obtained or consideration that we paid or received, as applicable, in connection with the transactions described below were comparable to terms available or the amounts that would be paid or received, as applicable, from unaffiliated third parties.

Investors’ Rights Agreement

We entered into an investors’ rights agreement with the purchasers of our outstanding preferred stock, including entities with which certain of our directors are affiliated. The investors’ rights agreement provides these holders the right, after April 30, 2018, to demand that we file a registration statement or request that their shares be covered by a registration statement that we are otherwise filing.

Participation in Our July 2018 Public Offering

On July 17, 2018, we completed an underwritten public offering of (i) 3,780,000 shares of our common stock at a price to the public of \$12.50 per share, and (ii) 2,220 shares of our non-voting Series A Convertible Preferred Stock (the “Series A Preferred Stock”) at a price to the public of \$12,500.00 per share, with each share of Series A Preferred Stock convertible into 1,000 shares of our common stock, subject to certain ownership restrictions. Entities affiliated with BVF Inc. (“BVF”), which beneficially owns more than 5% of our outstanding common stock, purchased all 2,220 shares of Series A Preferred Stock for a total purchase price of \$27,500,000, before deducting underwriting discounts and commissions and expenses related to the offering. On November 15, 2018, we entered into an agreement with BVF to exchange 1,000,000 shares of our common stock held by BVF for 1,000 shares of our non-voting Series B Convertible Preferred Stock, each share of which is convertible into 1,000 shares of our common stock, subject to certain ownership restrictions. See footnote 2 to the beneficial ownership table in the section “Security Ownership of Certain Beneficial Owners and Management.”

Participation in Our March 2020 Rights Offering

On March 5, 2020, we completed a rights offering of (i) 1,046,249 shares of our common stock and (ii) 2,287 shares of our non-voting Series C Convertible Preferred Stock (the “Series C Preferred Stock”), with each share of Series C Preferred Stock convertible into 1,000 shares of our common stock, subject to certain ownership restrictions. Entities affiliated with BVF, which beneficially owns more than 5% of our outstanding common stock, purchased all 2,287 shares of Series C Preferred Stock for a total purchase price of \$20,583,000, before deducting expenses related to the offering.

Participation in Our September 2020 Public Offering

On September 15, 2020, we completed an underwritten public offering of (i) 4,785,000 shares of our common stock and (ii) 3,215,000 shares of our non-voting Series D Convertible Preferred Stock (the “Series D Preferred Stock”), each at a price to the public of \$10.00 per share, with the shares of Series D Preferred Stock convertible on a one-to-one basis into shares of our common stock, subject to certain ownership restrictions.

Certain of our existing stockholders and their affiliated entities purchased an aggregate of approximately \$60 million of shares of our common stock and Series D Preferred Stock in our September 2020 offering at the public offering price. The table below sets forth the aggregate number of shares of our common stock and Series

[Table of Contents](#)

D Preferred Stock issued to our holders of more than 5% of our capital stock, or an affiliate thereof, at the time of the transaction:

	Shares of Common Stock	Shares of Series D Preferred Stock	Aggregate Purchase Price
Entities Affiliated with Aquilo Capital Management, LLC	2,500,000	—	\$ 25,000,000
Entities Affiliated with BVF Inc.	285,000	3,215,000	\$ 35,000,000

Indemnification Agreements with Officers and Directors and Directors' and Officers' Liability Insurance

We have entered into indemnification agreements with each of our executive officers and directors. The indemnification agreements, our amended and restated certificate of incorporation and our amended and restated By-Laws require us to indemnify our directors to the fullest extent not prohibited by Delaware law. Subject to certain limitations, our amended and restated certificate of incorporation also requires us to advance expenses incurred by our directors and officers, subject to limited exceptions. We also maintain a general liability insurance policy which covers certain liabilities of directors and officers of the Company arising out of claims based on acts or omissions in their capacities as directors or officers.

Policies and Procedures for Related Party Transactions

We have adopted a written policy that requires all future transactions between us and any director, executive officer, holder of 5% or more of any class of our capital stock or any member of the immediate family of, or entities affiliated with, any of them, or any other related persons, as defined in Item 404 of Regulation S-K, or their affiliates, in which the amount involved is equal to or greater than the threshold amount proscribed by Item 404 of Regulation S-K, be approved in advance by our Audit Committee. Any request for such a transaction must first be presented to our Audit Committee for review, consideration and approval. In approving or rejecting any such proposal, our Audit Committee is to consider the relevant facts and circumstances available and deemed relevant to the Audit Committee, including, but not limited to, the extent of the related party's interest in the transaction, and whether the transaction is on terms no less favorable to us than terms we could have generally obtained from an unaffiliated third party under the same or similar circumstances.

PROPOSAL 1: ELECTION OF DIRECTORS

The Board of Directors has nominated Milind Deshpande, Ph.D., Jean-François Formela, M.D. and Ankit Mahadevia, M.D. for re-election at the Annual Meeting. The Board of Directors currently consists of eight members, classified into three classes as follows: (i) Cynthia Smith, Scott Jackson and John C. Pottage, Jr., M.D. constitute our Class I directors with a term ending at the 2021 annual meeting; (ii) Patrick Vink, M.D. and Frank E. Thomas constitute our Class II directors with a term ending at the 2022 annual meeting; and (iii) Milind Deshpande, Ph.D., Jean-François Formela, M.D., and Ankit Mahadevia, M.D. constitute our Class III directors with a term ending at the upcoming Annual Meeting. At each annual meeting of stockholders, directors are elected for a full term of three years to succeed those directors whose terms are expiring.

The Board of Directors has voted to nominate Milind Deshpande, Ph.D., Jean-François Formela, M.D. and Ankit Mahadevia, M.D. for election at the Annual Meeting as Class III directors for a term of three years to serve until the 2023 annual meeting of stockholders, and until their respective successors are elected and qualified. The Class I directors (Cynthia Smith, Scott Jackson and John C. Pottage, Jr., M.D.) and the Class II directors (Patrick Vink, M.D. and Frank E. Thomas) will serve until the annual meeting of stockholders to be held in 2021 and 2022, respectively, and until their respective successors have been elected and qualified.

Unless authority to vote for any of these nominees is withheld, the shares represented by the enclosed proxy will be voted **FOR** the election as directors of Milind Deshpande, Ph.D., Jean-François Formela, M.D. and Ankit Mahadevia, M.D. In the event that either nominee becomes unable or unwilling to serve, the shares represented by the enclosed proxy will be voted for the election of such other person as the Board of Directors may recommend in that nominee's place. We have no reason to believe that any nominee will be unable or unwilling to serve as a director.

A plurality of the votes cast **FOR** each nominee at the Annual Meeting is required to elect each nominee as a director.

We have no formal policy regarding diversity of our board members, but our Corporate Governance Guidelines provide that the background and qualifications of the members of our Board of Directors considered as a group should provide a significant breadth of experience, knowledge, and ability to assist our Board of Directors in fulfilling its responsibilities. Our priority in selection of board members is identification of members who will further the interests of our stockholders through their established records of professional accomplishment, the ability to contribute positively to the collaborative culture among our board members, knowledge of our business, understanding of the competitive landscape in which we operate and adherence to high ethical standards.

THE BOARD OF DIRECTORS RECOMMENDS THE ELECTION OF MILIND DESHPANDE, PH.D., JEAN-FRANÇOIS FORMELA, M.D. AND ANKIT MAHADEVIA, M.D. AS DIRECTORS, AND PROXIES SOLICITED BY THE BOARD OF DIRECTORS WILL BE VOTED IN FAVOR THEREOF UNLESS A STOCKHOLDER HAS INDICATED OTHERWISE ON THE PROXY.

PROPOSAL 2: INDEPENDENT PUBLIC ACCOUNTANTS

The Audit Committee has appointed PricewaterhouseCoopers LLP, or PwC, as our independent registered public accounting firm, to audit our financial statements for the fiscal year ending December 31, 2020. PricewaterhouseCoopers LLP was our independent registered public accounting firm for the fiscal years ended December 31, 2018 and 2019. The Board of Directors proposes that the stockholders ratify this appointment. We expect that representatives of PricewaterhouseCoopers LLP will be present at the Annual Meeting, will be able to make a statement if they so desire, and will be available to respond to appropriate questions.

In deciding to appoint PricewaterhouseCoopers LLP, the Audit Committee reviewed auditor independence issues and existing commercial relationships with PricewaterhouseCoopers LLP and concluded that PricewaterhouseCoopers LLP has no commercial relationship with the Company that would impair its independence for the fiscal year ending December 31, 2020.

The following table presents fees for professional audit services and other services rendered by PricewaterhouseCoopers LLP to the Company for the fiscal years ended December 31, 2019 and December 31, 2018.

	Fiscal Year 2019	Fiscal Year 2018
Audit Fees(1)	\$ 794,000	\$ 998,250
Audit-Related Fees(2)	45,000	50,000
Tax Fees(3)	29,000	62,000
All Other Fees(4)	2,800	2,800
Total	<u>\$ 870,800</u>	<u>\$ 1,113,050</u>

- (1) Audit fees consisted of audit work performed in the preparation of financial statements, the review of the interim consolidated financial statements, and related services that are normally provided in connection with registration statements.
- (2) Audit related fees consist of fees billed by PricewaterhouseCoopers LLP for assurance and related services that are reasonably related to the performance of the audit or review of our consolidated financial statements.
- (3) Tax fees incurred in 2019 and 2018 consist of fees for professional services, including tax consulting and compliance performed by PricewaterhouseCoopers LLP.
- (4) All other fees represent payment for access to the PricewaterhouseCoopers LLP online accounting research and financial disclosure databases.

Policy on Audit Committee Pre-Approval of Services

Consistent with SEC policies regarding auditor independence, the Audit Committee has responsibility for appointing, setting compensation and overseeing the work of our independent registered public accounting firm. In recognition of this responsibility, the Audit Committee reviews and pre-approves all audit and permissible non-audit services provided by our independent registered public accounting firm; provided, however, that de minimis non-audit services may instead be approved in accordance with applicable SEC rules.

In the event the stockholders do not ratify the appointment of PricewaterhouseCoopers LLP as our independent registered public accounting firm, the Audit Committee will reconsider its appointment.

[Table of Contents](#)

The affirmative vote of a majority in voting power of the shares of our common stock present or represented at the Annual Meeting and voting affirmatively or negatively is required to ratify the appointment of the independent registered public accounting firm.

THE BOARD OF DIRECTORS RECOMMENDS A VOTE TO RATIFY THE APPOINTMENT OF PRICEWATERHOUSECOOPERS LLP AS OUR INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM, AND PROXIES SOLICITED BY THE BOARD OF DIRECTORS WILL BE VOTED IN FAVOR OF SUCH RATIFICATION UNLESS A STOCKHOLDER INDICATES OTHERWISE ON THE PROXY.

CODE OF CONDUCT AND ETHICS

We have adopted a Code of Business Conduct and Ethics that applies to all of our employees, including our chief executive officer and chief financial and accounting officers. The text of the Code of Business Conduct and Ethics is posted on our website at www.sperotherapeutics.com and will be made available to stockholders without charge, upon request, in writing to the Secretary of the Company at Spero Therapeutics, Inc., 675 Massachusetts Avenue, 14th Floor, Cambridge, Massachusetts 02139. Disclosure regarding any amendments to, or waivers from, provisions of the Code of Business Conduct and Ethics that apply to our directors, principal executive and financial officers will be included in a Current Report on Form 8-K within four business days following the date of the amendment or waiver, unless website posting or the issuance of a press release of such amendments or waivers is then permitted by the rules of The Nasdaq Stock Market.

OTHER MATTERS

The Board of Directors knows of no other business which will be presented to the Annual Meeting. If any other business is properly brought before the Annual Meeting, proxies will be voted in accordance with the judgment of the persons named therein.

STOCKHOLDER PROPOSALS AND NOMINATIONS FOR DIRECTOR

To be considered for inclusion in the proxy statement relating to our 2021 annual meeting of stockholders (the “2021 Annual Meeting”), we must receive stockholder proposals (other than for director nominations) no later than June 29, 2021. To be considered for presentation at the 2021 Annual Meeting, although not included in the proxy statement, proposals (including director nominations that are not requested to be included in our proxy statement) must be received not less than 90 days nor more than 120 days prior to the first anniversary of this year’s Annual Meeting; provided, however, that in the event that the date of the 2021 Annual Meeting is advanced by more than 30 days, or delayed by more than 60 days, from the first anniversary of the this year’s Annual Meeting, a stockholder’s notice must be received not earlier than the 120th day prior to such annual meeting and not later than the close of business on the later of (A) the 90th day prior to such annual meeting and (B) the tenth day following the day on which notice of the date of such annual meeting was mailed or public disclosure of the date of such annual meeting was made, whichever first occurs.

Proposals that are not received in a timely manner will not be voted on at the 2021 Annual Meeting. If a proposal is received on time, the proxies that management solicits for the meeting may still exercise discretionary voting authority on the proposal under circumstances consistent with the proxy rules of the SEC. All stockholder proposals should be marked for the attention of Secretary, Spero Therapeutics, Inc., 675 Massachusetts Avenue, 14th Floor, Cambridge, Massachusetts 02139.

Cambridge, Massachusetts
September 30, 2020

The 2020 Annual Meeting of Stockholders of Spero Therapeutics, Inc. will be held on October 27, 2020 at 10:00 A.M. EST, virtually via the internet at www.meetingcenter.io/266420432.

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

The password for this meeting is – SPRO2020.

Important notice regarding the Internet availability of proxy materials for the Annual Meeting of Stockholders.
The material is available at: www.edocumentview.com/SPRO

	<p>Small steps make an impact. Help the environment by consenting to receive electronic delivery, sign up at www.investorvote.com/SPRO</p>	
---	--	---

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

Proxy – Spero Therapeutics, Inc.



Notice of 2020 Annual Meeting of Stockholders

Proxy Solicited by Board of Directors for Annual Meeting – October 27, 2020

Ankit Mahadevia, M.D. and Stephen J. DiPalma (the "Proxies"), or any 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 2020 Annual Meeting of Stockholders of Spero Therapeutics, Inc. to be held on October 27, 2020 or at any postponement or adjournment thereof.

Shares represented by this proxy will be voted as directed by the stockholder. If no such directions are indicated, the Proxies will have authority to vote FOR Milind Deshpande, Ph.D., FOR Jean-François Formela, M.D., FOR Ankit Mahadevia, M.D. and FOR Proposal 2, the ratification of PricewaterhouseCoopers LLP as independent auditors for Spero Therapeutics, Inc. for the fiscal year ending December 31, 2020.

In their discretion, the Proxies are authorized to vote upon such other business as may properly come before the meeting.

(Proposals to be voted on appear on reverse side)

C Non-Voting Items

Change of Address – Please print new address below.

Comments – Please print your comments below.

