
**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 Rule 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:



675 Massachusetts Avenue, 14th Floor
Cambridge, Massachusetts 02139

April 26, 2019

To Our Stockholders:

You are cordially invited to attend the 2019 annual meeting of stockholders of Spero Therapeutics, Inc. to be held at 9:00 a.m. Eastern Time on Wednesday, June 5, 2019 at the offices of Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C. at One Financial Center, Boston, MA 02111.

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, two 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, 2019. 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".

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

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

April 26, 2019

NOTICE OF 2019 ANNUAL MEETING OF STOCKHOLDERS

TIME: 9:00 a.m. Eastern Time

DATE: Wednesday, June 5, 2019

PLACE: Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C., One Financial Center, Boston, MA 02111

PURPOSES:

1. To elect two directors to serve three-year terms expiring in 2022;
2. To ratify the appointment of PricewaterhouseCoopers LLP as the Company's independent registered public accounting firm for the fiscal year ending December 31, 2019; 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 April 8, 2019.

If you are a stockholder of record, you may vote in one of the following ways:

- **Vote over the Internet**, by following the "Vote by Internet" instructions on the enclosed proxy card;
- **Vote by telephone**, by following the "Vote by Phone" instructions on the enclosed proxy card;
- **Vote by mail**, by returning the proxy card (signed and dated); or
- **Vote in person at the 2019 annual meeting.**

If your shares are held in "street name," that is, held for your account by a broker or other nominee, you will receive instructions from the holder of record that you must follow for your shares to be voted.

A list of stockholders of record will be available at the annual meeting at Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C., One Financial Center, Boston, MA 02111, 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 by following the instructions in the Notice of Internet Availability of Proxy Materials that you previously received and submit your proxy by the Internet, telephone or mail 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



Joel Sendek
Chief Financial Officer and Secretary

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

PROXY STATEMENT FOR SPERO THERAPEUTICS, INC.
2019 ANNUAL MEETING OF STOCKHOLDERS TO BE HELD ON JUNE 5, 2019

This proxy statement, along with the accompanying Notice of 2019 Annual Meeting of Stockholders, contains information about the 2019 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 9:00 a.m. Eastern Time on Wednesday, June 5, 2019 at the offices of Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C. at One Financial Center, Boston, MA 02111.

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 May 3, 2019, 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, which includes our financial statements for the fiscal year ended December 31, 2018.

**IMPORTANT NOTICE REGARDING THE AVAILABILITY OF PROXY MATERIALS FOR THE
SHAREHOLDER MEETING TO BE HELD ON JUNE 5, 2019**

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 12-digit control number(s) available that appears on your proxy card.

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, 2018 on the website of the Securities and Exchange Commission, or 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 2019 Annual Meeting of stockholders to be held at the offices of Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C. at One Financial Center, Boston, MA 02111 on Wednesday, June 5, 2019 at 9:00 a.m. Eastern Time, and any adjournments of the meeting. 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, 2018 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 May 3, 2019.

Who Can Vote?

Only stockholders who owned our common stock at the close of business on April 8, 2019 are entitled to vote at the Annual Meeting. On this record date, there were 17,422,878 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 the appointment of PricewaterhouseCoopers LLP as the Company's independent registered public accounting firm for the fiscal year ending December 31, 2019. If you properly submit a proxy without giving specific voting instructions, your 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.

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- **In person at the meeting.** If you attend the meeting, you may deliver a completed proxy card in person or you may vote by completing a ballot, which will be available at the meeting.

Telephone and Internet voting facilities for stockholders of record will be available 24 hours a day and will close at 11:59 p.m. Eastern Time on June 4, 2019.

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 and bring it to the Annual Meeting 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, 2019.

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 in person and voting in person. Attending the Annual Meeting in person 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 both of the nominees, WITHHOLD your vote from both of the nominees or WITHHOLD your vote from either one 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 2019, 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

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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 9:00 a.m. Eastern Time on Wednesday, June 5, 2019 at the offices of Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C. at One Financial Center, Boston, MA 02111. When you arrive at One Financial Center, signs will direct you to the appropriate meeting rooms. 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 joint proxy statement/prospectus 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 or www.investorvote.com/SPRO 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 April 15, 2019 for (a) the executive officers named in the Summary Compensation Table on page 18 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 April 15, 2019 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 17,455,749 shares of common stock outstanding on April 15, 2019.

Name of Beneficial Owner	Number of Shares Beneficially Owned	Percent of Shares Beneficially Owned
Principal Stockholders		
S.R. One, Limited(1)	1,934,006	11.08%
Entities affiliated with BVF Inc.(2)	1,815,146	9.99%
Atlas Venture Fund IX, L.P.(3)	1,376,968	7.89%
GV 2015, L.P.(4)	1,112,473	6.37%
Lundbeckfond Invest A/S(5)	1,091,774	6.25%
Entities affiliated with Aquilo Capital Management, LLC(6)	1,031,947	5.91%
Atlas Venture Fund X, LLC(7)	1,031,160	5.91%
MRL Ventures Fund, LLC(8)	935,942	5.36%
Named Executive Officers and Directors		
Ankit Mahadevia, M.D.(9)	477,755	2.67%
Cristina Larkin(10)	83,719	*
David Melnick, M.D.(11)	47,813	*
Milind Deshpande, Ph.D.(12)	47,265	*
Jean-François Formela, M.D.(13)	2,414,201	13.83%
John C. Pottage, Jr., M.D.(14)	2,699	*
Cynthia Smith(15)	674	*
Frank E. Thomas(16)	20,059	*
Patrick Vink, M.D.(17)	24,146	*
All current executive officers and directors as a group (11 persons) (18)	3,342,901	18.34%

* Indicates beneficial ownership of less than 1%.

- (1) Consists of 1,934,006 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 September 19, 2018, which reported ownership as of August 14, 2018.
- (2) Includes (i) 1,404,711 shares of common stock held by Biotechnology Value Fund, L.P., or BVF, (ii) 298,102 shares of common stock held by Biotechnology Value Fund II, L.P., or BVF II, and

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(iii) 60,345 shares of common stock held by Biotechnology Value Trading Fund OS LP, or Trading Fund OS. BVF Partners OS Ltd, or Partners OS, as general partner of Trading Fund OS, may be deemed to beneficially own 60,345 shares of common stock beneficially owned by Trading Fund OS. BVF Partners L.P., or Partners, as general partner of BVF, BVF II, the investment manager of Trading Fund OS, and the sole member of Partners OS, may be deemed to beneficially own the 1,815,146 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 51,988 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 1,815,146 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 1,815,146 shares of common stock beneficially owned by BVF, Inc. Together, BVF, BVF II, Trading Fund OS, Partners OS, Partners, BVF Inc. and Mark N. Lampert (the "BVF Entities") hold 2,220 shares of Series A Convertible Preferred Stock ("Series A Preferred") convertible for an aggregate of 2,220,000 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, 2018, the Series A Blocker limited the aggregate conversion of Series A Preferred to 972,000 of the 2,220,000 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 April 15, 2019 is the maximum number of shares of common stock issuable upon conversion of Series A Preferred 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 April 15, 2019, the Series B Blocker limits 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. Partners OS disclaims beneficial ownership of the shares of common stock beneficially owned by Trading Fund OS. 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 14, 2019, which reported ownership as of December 31, 2018.

- (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 8, 2019, which reported ownership as of December 31, 2018.
- (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.

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- (5) The board of directors of Lundbeckfond Invest A/S consists of Jørgen Huno Rasmussen, Steffen Kragh, Lars Holmqvist, Susanne Krüger Kjær, Michael Kjær, Peter Schütze, Gunhild Waldemar, Vagn Flink Møller Pedersen, Henrik Sindal Jensen, and Peter Adler Würtzen, who have shared investment and voting control with respect to the shares held by Lundbeckfond Invest A/S and may exercise such control only with the support of a majority of the members of the Lundbeckfond Invest Ventures A/S board of directors. No individual member of the Lundbeckfond Invest A/S board of directors is deemed to hold any beneficial ownership or reportable pecuniary interest in the shares held by Lundbeckfond Invest A/S. Casper Breum, one of our directors, is a partner of Lundbeckfond Ventures, a division within Lundbeckfond Invest A/S, and is not deemed to beneficially own the shares held by Lundbeckfond Invest A/S. The address for Lundbeckfond Invest A/S is Scherfigsvej 7, 2100 Copenhagen Ø, Denmark. This information is based solely on a Schedule 13G filed by Lundbeckfond Invest A/S with the SEC on February 14, 2018, which reported ownership as of December 31, 2017.
- (6) 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, 2019, which reported ownership as of such date.
- (7) All shares are 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. The address for Atlas Venture Fund X, is 400 Technology Square, 10th Floor, Cambridge, Massachusetts 02139. 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.
- (8) All shares are held directly by MRL Ventures Fund, LLC, or MRL Ventures Fund, which is a subsidiary of Merck Sharp & Dohme Corp. Reza Halse is the President of MRL Ventures. Dr. Halse was also a member of our Board of Directors until his resignation immediately prior to the effectiveness of the registration statement filed in connection with our initial public offering. Dr. Halse disclaims beneficial ownership of such shares, except to the extent of his pecuniary interest therein, if any. The address for MRL Ventures Fund, LLC is 320 Bent Street, Cambridge, Massachusetts 02141. This information is based solely on a Schedule 13G filed by Merck & Co., Inc., Merck Sharp & Dohme Corp., and MRL Ventures Fund LLC with the SEC on November 15, 2017, which reported ownership as of such date.
- (9) Consists of (i) 65,817 shares of common stock held by Mahadevia-Mehta Family Trust, of which Dr. Mahadevia is the trustee, and (ii) 411,938 shares of common stock underlying options that are exercisable as of April 15, 2019 or will become exercisable within 60 days after such date held by Dr. Mahadevia.
- (10) Consists of (i) 1,500 shares of common stock and (ii) 82,219 shares of common stock underlying options that are exercisable as of April 15, 2019 or will become exercisable within 60 days after such date held by Ms. Larkin.

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- (11) Consists of 47,813 shares of common stock underlying options that are exercisable as of April 15, 2019 or will become exercisable within 60 days after such date held by Dr. Melnick, our Chief Medical Officer.
- (12) Consists of (i) 16,454 shares of common stock and (ii) 30,811 shares of common stock underlying options that are exercisable as of April 15, 2019 or will become exercisable within 60 days after such date held by Dr. Deshpande.
- (13) See footnotes 3 and 7. Also includes 6,073 shares of common stock underlying options that are exercisable as of April 15, 2019 or will become exercisable within 60 days after such date held by Dr. Formela.
- (14) Consists of 2,699 shares of common stock underlying options that are exercisable as of April 15, 2019 or will become exercisable within 60 days after such date held by Dr. Pottage.
- (15) Consists of 674 shares of common stock underlying options that are exercisable as of April 15, 2019 or will become exercisable within 60 days after such date held by Ms. Smith.
- (16) Consists of 20,059 shares of common stock underlying options that are exercisable as of April 15, 2019 or will become exercisable within 60 days after such date held by Mr. Thomas.
- (17) Consists of 24,146 shares of common stock underlying options that are exercisable as of April 15, 2019 or will become exercisable within 60 days after such date held by Dr. Vink.
- (18) See notes 3, 7 and 9 through 17 above; also includes Joel Sendek and Thomas Parr Jr., Ph.D., 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 seven members, classified into three classes as follows:

- (1) Patrick Vink, M.D. and Frank E. Thomas constitute our Class II directors with a term ending at the upcoming 2019 Annual Meeting;
- (2) 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 2020 annual meeting; and
- (3) Cynthia Smith and John C. Pottage, Jr., M.D. constitute our Class I directors with a term ending at the 2021 annual meeting.

On March 29, 2019, our Board of Directors accepted the recommendation of the Nominating and Corporate Governance Committee and voted to nominate Patrick Vink, M.D. and Frank E. Thomas for election at the Annual Meeting for a term of three years to serve until the 2022 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:

Name	Age	Position with the Company
Milind Deshpande, Ph.D.	62	Chairman of the Board of Directors
Jean-François Formela, M.D.	62	Director
Ankit Mahadevia, M.D.	38	Chief Executive Officer, President and Director
John C. Pottage, Jr., M.D.	66	Director
Cynthia Smith	50	Director
Frank E. Thomas	49	Director
Patrick Vink, M.D.	55	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., 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 currently the President and Chief Executive Officer at Nayan Therapeutics, where he has served since February 2019. 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, 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 new advances in biology and drug discovery technologies as well as novel therapeutics. Dr. Formela joined Atlas Venture in 1993 to build its U.S. life sciences franchise. Prior to joining Atlas, he worked at Schering-Plough Corporation, where he directed U.S. Phase 4 clinical trials in all therapeutic areas. Before that, he was responsible for the marketing of Intron A, Schering-Plough's alpha-interferon. Dr. Formela began his career as a medical doctor and practiced emergency medicine at Necker University Hospital in Paris. Dr. Formela serves as chair of the board of directors of IFM Therapeutics, and serves on the boards of directors of Intellia Therapeutics, F-Star Biotechnology Ltd., KDAC, Korro, KYN Therapeutics, Inc., Korro, Triplet, and Translate Bio, which he co-founded. Dr. Formela 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.

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 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 has served as Senior Vice President and Chief Scientific and Medical Officer of ViiV Healthcare since November 2009. 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, Akebia Therapeutics, and Nivalis 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 has served as Chief Financial Officer and Chief Business Officer of Orchard Therapeutics Limited since January 2018, a development-stage biotechnology company based in the United Kingdom. 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 Acacia Pharma Ltd, Arch Biopartners, Concordia International Corp., NMD Pharma, Piquar AG, and Santhera Pharmaceuticals Ag., and is Chairman of the board of directors of Targovax Oy. 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, 2018, there were five meetings of our Board of Directors, and the various committees of the Board of Directors met a total of eleven 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 he served during fiscal 2018. 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 five times during fiscal 2018. This committee currently has three members, Frank E. Thomas (Chairman), John C. Pottage, Jr., M.D., and Patrick Vink, M.D. 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 Securities and Exchange Commission 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 Securities and Exchange Commission 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 fiscal 2018. 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 includes reviewing, approving 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. 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 engaged Pearl Meyer & Partners, LLC ("Pearl Meyer") as an independent advisor to the Compensation Committee providing executive compensation consulting services. Pearl Meyer was engaged by and reports 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 fiscal year 2018. In compliance with the

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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.

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 twice during fiscal 2018 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;
- 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.

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

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- 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 Nasdaq 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;
- 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

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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 inquiries
- surveys
- 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 with each of the executive officers of the Company.

Name	Age	Position
Joel Sendek	52	Chief Financial Officer
Cristina Larkin	48	Chief Operating Officer
David Melnick, M.D.	67	Chief Medical Officer
Thomas Parr Jr., Ph.D.	65	Chief Scientific Officer

Joel Sendek has served as our Chief Financial Officer since May 2017. Mr. Sendek has nearly 30 years of experience in the life sciences sector, including 18 years as a senior sell-side research analyst covering biotechnology. Prior to joining us, Mr. Sendek was the Chief Financial Officer at Forward Pharma A/S since August 2014. As an analyst, he served as a Managing Director at Stifel Financial Corp. from January 2012 to July 2014, where he led the firm's healthcare equity research group, and previously he was a Managing Director at Lazard Ltd. since January 2000, where he established the firm's healthcare equity research effort. Prior to his career in equity research, Mr. Sendek worked as Senior Director of Corporate Development at Progenics Pharmaceuticals, Inc. and as an investment banking analyst at Goldman, Sachs & Co. Mr. Sendek holds a B.A. in Biochemistry from Rice University.

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 24 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. 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.

Thomas Parr Jr., Ph.D. has served as our Chief Scientific Officer since April 2014. He has more than 30 years of drug discovery experience across both large pharmaceutical and small biotechnology companies. Prior to joining Spero, from 2012 to 2014, Dr. Parr was the Chief Scientific Officer at Fedora Pharmaceuticals, Inc. where the company moved novel diazabicyclooctane beta-lactamase inhibitors toward development partnerships. Prior to Fedora, he was the Chief Scientific Officer at Targanta Therapeutics, now part of The Medicines Company. Dr. Parr earned his Ph.D. from the University of Calgary and conducted a postdoctoral fellowship at the University of British Columbia. He was an Assistant Professor in the Department of Microbiology and Biochemistry at the University of Ottawa before beginning his drug discovery and development career.

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, 2018 and 2017 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, 2018 and were serving as executive officers as of such date.

Name and Principal Position	Year	Salary (\$)	Bonus (\$)(1)	Option Awards (\$)(2)	Non-Equity Incentive Plan Compensation (\$)(3)	All other Compensation (\$)(4)	Total (\$)
Ankit Mahadevia, M.D.	2018	465,000	—	—	255,750	574	721,324
Chief Executive Officer	2017	389,574	—	2,679,616	114,000	1,087	3,184,277
Cristina Larkin	2018	385,000	—	—	148,225	574	533,799
Chief Operating Officer	2017	330,669	—	796,800	98,325	734	1,226,528
David Melnick, M.D.	2018	375,680	10,000	1,082,146	146,300	20,235	1,634,361
Chief Medical Officer	2017	—	—	—	—	—	—

(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 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 8 to our consolidated financial statements for the year ended December 31, 2018.

(3) Amounts represent cash bonuses earned for the applicable fiscal year.

(4) 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.

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 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

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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 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.

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 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 offer letter 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 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 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.

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.

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.

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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 2018 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.

The following table shows grants of stock options outstanding on the last day of the fiscal year ended December 31, 2018 to each of the executive officers named in the Summary Compensation Table.

Name	Option Awards			
	Number of Securities Underlying Unexercised Options (#) Exercisable	Number of Securities Underlying Unexercised Options (#) Unexercisable	Option Exercise Price (\$)	Option Expiration Date
Ankit Mahadevia, M.D.	18,511(1)	3,702(1)	\$5.90	7/5/2027
	67,653(2)	33,835(2)	\$5.90	7/5/2027
	118,888(3)	—	\$5.90	7/5/2027
	105,270(4)	191,950(4)	\$5.90	7/5/2027
	31,269(5)	93,810(5)	\$11.63	12/12/2027
Cristina Larkin	12,798(6)	7,636(6)	\$5.90	7/5/2027
	4,326(7)	2,164(7)	\$5.90	7/5/2027
	25,066(4)	45,713(4)	\$5.90	7/5/2027
	15,635(5)	46,905(5)	\$11.63	12/12/2027
David Melnick, M.D.	—	135,000(8)	\$12.14	1/3/2028

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- (1) 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 August 24, 2016, 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.
- (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.
- (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) 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.
- (7) 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.
- (8) 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 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 SPR994 top-line data; (ii) FDA acceptance of a SPR994 New Drug Application; (iii) non-dilutive financing; and (iv) equity financing. Following the Performance Period, Performance Awards determined to be eligible for 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 installments 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, 2018 to each of our current and former non-employee directors. Cynthia Smith joined our Board of Directors in March 2019. Directors who are employed by us are not compensated for their service on our Board of Directors.

Name	Fees Earned or Paid in Cash (\$)	Option Awards* (\$)(7)	Total(\$)
Casper Breum(1)	18,913	—	18,913
Milind Deshpande, Ph.D.	73,886	48,146(2)	122,032
Jean-François Formela, M.D.	44,000	48,146(2)	92,146
Vikas Goyal(3)	—	—	—
John C. Pottage, Jr., M.D.	14,552	84,218(4)	98,770
David P. Southwell(5)		167,198(2)	
	32,583	(6)	199,781
Frank E. Thomas	54,000	48,146(2)	102,145
Patrick Vink, M.D.	52,500	48,146(2)	138,347

* These amounts represent the aggregate grant date fair value of options granted to each director in the fiscal year ended December 31, 2018, 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 8 to our consolidated financial statements for the year ended December 31, 2018.

- (1) Mr. Breum resigned from our Board of Directors in September 2018.
- (2) Represents an option to purchase 6,073 shares of common stock at an exercise price of \$11.54. The shares underlying the option award vest and become fully exercisable on June 5, 2019, subject to the individual's continued service as of such date.
- (3) Mr. Goyal resigned from our Board of Directors in February 2018.
- (4) Represents an option to purchase 12,146 shares of common stock at an exercise price of \$10.25. The shares underlying the option award vest in thirty-six equal monthly installments at the end of each successive month following September 21, 2018, subject to the individual's continued service as of such date.
- (5) Mr. Southwell resigned from our Board of Directors in April 2019.
- (6) Represents an option to purchase 12,146 shares of common stock at an exercise price of \$14.25. The shares underlying the option award vest in thirty-six equal monthly installments at the end of each successive month following March 30, 2018, subject to the individual's continued service as of such date.

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- (7) As of December 31, 2018, 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):

Name	Number of Shares Underlying Outstanding Stock Options
Milind Deshpande, Ph.D.	54,554
Jean François Formela, M.D.	6,073
John C. Pottage, Jr., M.D.	12,146
David P. Southwell	18,219
Frank E. Thomas	36,588
Patrick Vink, M.D.	36,587

Non-Employee Director Compensation Policy

Under our Non-Employee Director Compensation Policy, 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:

Position	Retainer
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

Equity awards for non-employee directors consist of (i) an initial equity award consisting of a non-qualified stock option to purchase 12,146 shares of our common stock upon first appointment to our Board of Directors and vesting in equal monthly installments until the third anniversary of the grant date, subject to the non-employee director's continued service, and (ii) annual equity awards commencing in 2018 consisting of a non-qualified stock option to purchase 6,073 shares of our common stock vesting on the first anniversary of the grant date, subject to the non-employee director's continued service.

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, 2018.

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)	2,297,810	8.03	341,811(2)
Equity compensation plans not approved by stockholders	—	—	—
Total:	2,297,810	8.03	341,811

(1) This plan category consists of the 2017 Plan.

(2) Under the 2017 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 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 3,303,7254 shares of our common stock authorized for issuance under the 2017 Plan, which amount includes the automatic increase effective as of January 1, 2019. As of April 15, 2019, a total of 153,059 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;
- 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;

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- 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 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 (the “Inducement Plan”) and reserved 331,500 shares of our common stock 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 Inducement Plan was adopted without stockholder approval pursuant to Rule 5635(c)(4). The 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 April 15, 2019, there were no shares outstanding and 331,500 shares available for grant under the 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, 2018, the Audit Committee took the following actions:

- Reviewed and discussed the audited financial statements for the fiscal year ended December 31, 2018 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, 2018 for filing with the SEC.

Members of the Spero Therapeutics, Inc. Audit Committee

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

SECTION 16(a) BENEFICIAL OWNERSHIP REPORTING COMPLIANCE

Section 16(a) of the Securities Exchange Act of 1934, as amended, or the Exchange Act, requires our directors and executive officers, and persons who own more than ten percent of a registered class of our equity securities, to file with the SEC initial reports of ownership and reports of changes in ownership of our common stock and other equity securities. Officers, directors and greater than ten percent stockholders are required by SEC regulations to furnish us with copies of all Section 16(a) forms they file.

To our knowledge, based solely on a review of the copies of such reports furnished to us and written representations regarding the filing of required reports, we believe that all Section 16(a) filing requirements applicable to our directors, executive officers and greater-than-ten-percent beneficial owners with respect to fiscal year ended December 31, 2018 were met.

CERTAIN RELATIONSHIPS AND RELATED PERSON TRANSACTIONS

The following is a description of transactions since January 1, 2017, 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.

Equity Financings***Class C Preferred Unit Financing***

In March 2017, we issued an aggregate of 29,647,582 Class C preferred units, consisting of (i) 5,321,112 Class C preferred units in exchange for 8,500 bridge units and (ii) 24,326,470 Class C preferred units at a price per unit of \$1.7749 for an aggregate purchase price of approximately \$43,177,052. The following table sets forth the number of Class C preferred units purchased by our directors, executive officers and 5% stockholders and their affiliates at the time of or as a result of such issuance and the aggregate purchase price paid for such units.

Name	Bridge Units Exchanged	Class C Preferred Units Received in Exchange for Bridge Units	Class C Preferred Units Purchased	Aggregate Purchase Price
GV 2015, L.P.(1)	—	—	6,760,944	\$11,999,999
RA Capital Healthcare Fund, L.P.(2)	—	—	3,673,446	\$6,519,999
Atlas Venture Fund IX, L.P.(3)	1,833	1,147,691	1,971,942	\$3,500,000
S.R. One, Limited(4)	1,833	1,147,691	2,535,354	\$4,500,000
Lundbeckfond Invest A/S(5)	1,000	626,013	1,859,259	\$3,299,999
MRL Ventures Fund, LLC(6)	1,833	1,147,691	783,259	\$1,390,206
KPC Venture Capital LLC	750	469,510	429,326	\$762,011
Osage University Partners II, L.P.(7)	1,250	782,516	408,383	\$724,839
Atlas Venture Fund X, L.P.(8)	—	—	3,662,178	\$6,500,000

(1) GV 2015, L.P. beneficially owned, in the aggregate, more than 5% of our outstanding capital stock at the time of or as a result of the Class C preferred unit financing.

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- (2) RA Capital Healthcare Fund, L.P. beneficially owned, in the aggregate, more than 5% of our outstanding capital stock at the time of or as a result of the Class C preferred unit financing.
- (3) Atlas Venture Fund IX, L.P. beneficially owned, in the aggregate, more than 5% of our outstanding capital stock at the time of or as a result of the Class C preferred unit financing. Jean-François Formela, M.D., a member of our Board of Directors, is a Partner at Atlas Venture.
- (4) S.R. One, Limited beneficially owned, in the aggregate, more than 5% of our outstanding capital stock at the time of or as a result of the Class C preferred unit financing. Vikas Goyal, a former member of our Board of Directors, is a Principal at S.R. One, Limited.
- (5) Lundbeckfond Invest A/S beneficially owned, in the aggregate, more than 5% of our outstanding capital stock at the time of or as a result of the Class C preferred unit financing. Casper Breum, a former member of our Board of Directors, is a Senior Partner at Lundbeckfond Ventures, an affiliate of Lundbeckfond Invest A/S.
- (6) MRL Ventures Fund, LLC beneficially owned, in the aggregate, more than 5% of our outstanding capital stock at the time of or as a result of the Class C preferred unit financing. Reza Halse, a former member of our Board of Directors until his resignation immediately prior to the effectiveness of the registration statement filed in connection with our initial public offering, serves as President of MRL Ventures Fund, LLC.
- (7) Osage University Partners II, L.P. beneficially owned, in the aggregate, more than 5% of our outstanding capital stock at the time of or as a result of the Class C preferred unit financing.
- (8) Atlas Venture Fund X, L.P. beneficially owned, in the aggregate, more than 5% of our outstanding capital stock at the time of or as a result of the Class C preferred unit financing. Jean-François Formela, M.D., a member of our Board of Directors, is a Partner at Atlas Venture.

Reorganization

On June 30, 2017, 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.

Series C Preferred Stock

In July 2017, after the consummation of the 2017 Reorganization, we sold to Joel Sendek, our Chief Financial Officer, 61,880 shares of Series C preferred stock of Spero Therapeutics, Inc., at a purchase price of \$1.7749 per share, for an aggregate purchase price of \$109,831. Such purchase and sale was made in accordance with the terms of Mr. Sendek's offer letter. In October 2017, Mr. Sendek transferred his 61,880 shares to a retained annuity trust that he established and of which he is a beneficiary.

Agreements with Stockholders

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.

Right of First Refusal and Co-Sale Agreement

We entered into a right of first refusal and co-sale agreement with certain holders of our common stock and preferred stock, including entities with which certain of our directors are affiliated. This agreement provided for rights of first refusal and co-sale relating to the shares of our common stock held by the parties to the agreement. The right of first refusal and co-sale agreement has terminated.

Voting Agreement

We entered into a voting agreement with certain holders of our common stock and preferred stock, including entities with which certain of our directors are affiliated. Under this agreement, our stockholders that were party to the agreement agreed to vote their shares to elect to our Board of Directors: (i) one director designated by Atlas Venture Fund IX, L.P. and Atlas Venture Fund X, L.P., (ii) one director designated by S.R. One, Limited, (iii) one director designated by Lundbeckfond Invest A/S, (iv) one director designated by MRL Ventures Fund, LLC, (v) after delivery of written notice from GV 2015, L.P. to the Company informing the Company that GV 2015, L.P. would designate a member of our Board of Directors, one director designated by GV 2015, L.P., (vi) the person who was the company's then-serving Chief Executive Officer, (vii) one director with relevant industry experience who was reasonably acceptable to a majority of the other directors then serving on our Board of Directors and (viii) two directors designated by the stockholders holding a majority of shares voting together as a single class on an as-converted to common stock basis. The voting agreement has terminated.

Participation in Our Initial Public Offering

In November 2017, in our initial public offering, we issued an aggregate of 5,971,498 shares of our common stock at a purchase price of \$14.00 per share, which included 471,498 shares of common stock issued upon exercise by the underwriters of their option to purchase additional shares. Gross proceeds from the offering were approximately \$83.6 million, prior to deducting \$9.4 million of underwriting discounts and commissions, and offering expenses paid by the Company.

Certain of our existing stockholders and their affiliated entities, including affiliates of our directors, purchased an aggregate of approximately \$30.0 million of our shares in our initial public offering at the initial public offering price. The table below sets forth the aggregate number of common shares issued to our directors, executive officers or holders of more than 5% of our capital stock at the time, or an affiliate or immediate family member thereof, at the time of the transaction:

	<u>Shares</u>	<u>Aggregate Purchase Price</u>
RA Capital Healthcare Fund, L.P.	484,000	\$6,776,000
Atlas Venture Fund X, L.P.	428,571	\$5,999,994
S.R. One, Ltd.	428,571	\$5,999,994
Rock Spring Capital Management, LP	250,000	\$3,500,000
Lundbeckfond Invest A/S	214,285	\$2,999,990
MRL Ventures Fund, LLC	192,857	\$2,699,998
Osage University Partners II, L.P.	89,285	\$1,249,990

Participation in Our July 2018 Public Offering

On July 17, 2018, we completed underwritten public offerings 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 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

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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 such BVF entities to exchange 1,000,000 shares of our common stock held by BVF for 1,000 shares of our 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.”

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 Patrick Vink, M.D. and Frank E. Thomas for re-election at the Annual Meeting. The Board of Directors currently consists of seven members, classified into three classes as follows: (i) Cynthia Smith 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 upcoming 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 2020 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 Patrick Vink, M.D. and Frank E. Thomas for election at the Annual Meeting as Class II directors for a term of three years to serve until the 2022 annual meeting of Stockholders, and until their respective successors are elected and qualified. The Class I directors (Cynthia Smith and John C. Pottage, Jr., M.D.) and the Class III directors (Milind Deshpande, Ph.D., Jean-François Formela, M.D., and Ankit Mahadevia) will serve until the annual meeting of Stockholders to be held in 2021 and 2020, 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 Patrick Vink, M.D. and Frank E. Thomas. 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 PATRICK VINK, M.D. AND FRANK E. THOMAS 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, 2019. PricewaterhouseCoopers LLP was our independent registered public accounting firm for the fiscal years ended December 31, 2017 and 2018. 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, 2019.

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, 2018 and December 31, 2017.

	Fiscal Year 2018	Fiscal Year 2017
Audit Fees(1)	\$ 998,250	\$ 1,490,605
Audit-Related Fees(2)	50,000	64,000
Tax Fees(3)	62,000	13,200
All Other Fees(4)	2,800	2,700
Total	\$ 1,113,050	\$ 1,570,505

- (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, including the registration statement for our initial public offering. Included in the 2017 audit fees is \$834,576 of fees billed in connection with our initial public offering in November 2017.
- (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 2018 and 2017 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.

Less than 1% of fees paid by the Company to PwC for non-audit services for the year ended December 31, 2017 were retrospectively approved by the Audit Committee pursuant to the de minimis exception under Rule 2-01(c)(7)(i)(C) of Regulation S-X. These fees relate to the use of an online financial disclosure database used in connection with the Company's periodic filings with the Securities and Exchange Commission.

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

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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.

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 2020 Annual Meeting of Stockholders, we must receive stockholder proposals (other than for director nominations) no later than January 4, 2020. To be considered for presentation at the 2020 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 2020 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 2020 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
April 26, 2019

**2019 Annual Meeting Admission Ticket
2019 Annual Meeting of Stockholders of Spero Therapeutics, Inc.**

**June 5, 2019, 9:00 a.m. Local Time
Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C.
One Financial Center, Boston, MA 02111**

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

From Points West: Take the Mass. Pike (I-90 East) to Exit 24A (South Station). Stay on Atlantic Avenue until you can take a left on Essex Street. One Financial Center is on the corner of Atlantic Avenue and Essex Street.

From Points North: Take I-93 South toward Boston. Take Exit 20B-A toward South Station. This is the I-90 West / Mass. Pike exit. Take Exit 20A, continuing toward South Station. Turn left on Essex Street. Look for a brown building with red awnings directly in front of you. One Financial Center will be on the left.

From Points South: Take the Southeast Expressway (I-93 North) to Exit 20 (Worcester / Logan I-90 – South Station).

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

	Small steps make an impact. Help the environment by consenting to receive electronic delivery, sign up at www.investorvote.com/SPRO	
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q IF VOTING BY MAIL, SIGN, DETACH AND RETURN THE BOTTOM PORTION IN THE ENCLOSED ENVELOPE. q

Proxy – Spero Therapeutics, Inc.



**Notice of 2019 Annual Meeting of Stockholders
Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C.
One Financial Center, Boston, MA 02111**

Proxy Solicited by Board of Directors for Annual Meeting – June 5, 2019

Ankit Mahadevia, M.D. and Joel Sendek (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 2019 Annual Meeting of Stockholders of Spero Therapeutics, Inc. to be held on June 5, 2019 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 Patrick Vink, M.D., FOR Frank E. Thomas, and FOR Proposal 2, the ratification of PricewaterhouseCoopers LLP as independent auditors for Spero Therapeutics, Inc. for the fiscal year ending December 31, 2019.

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.

