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

FORM 10-K/A
(Amendment No. 1)

(Mark One)

ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the fiscal year ended December 31, 2020

or

TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the transition period from _____ to _____

Commission file number 001-38266

SPERO THERAPEUTICS, INC.

(Exact name of registrant as specified in its charter)

Delaware
State or other jurisdiction of
incorporation or organization

46-4590683
(I.R.S. Employer
Identification No.)

675 Massachusetts Avenue, 14th Floor
Cambridge, Massachusetts
(Address of principal executive offices)

02139
(Zip Code)

Registrant's telephone number, including area code (857) 242-1600

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, \$0.001 par value per share	SPRO	The Nasdaq Global Select Market

Securities registered pursuant to Section 12(g) of the Act:

None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes No

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 15(d) of the Act. Yes No

Indicate by check mark whether the registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes No

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes No

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

Large accelerated filer
Non-accelerated filer

Accelerated filer
Smaller reporting company
Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report.

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Act). Yes No

The aggregate market value of Common Stock held by non-affiliates of the registrant computed by reference to the price of the registrant's Common Stock as of June 30, 2020, the last business day of the registrant's most recently completed second fiscal quarter, was approximately \$256.2 million (based on the last reported sale price on the Nasdaq Global Market as of such date). As of March 8, 2021, there were 29,504,257 shares of the registrant's Common Stock, \$0.001 par value per share, outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

None.

EXPLANATORY NOTE

This Amendment No. 1 on Form 10-K/A (this “Amendment”) amends the Annual Report on Form 10-K of Spero Therapeutics, Inc. (the “Company,” “we,” “our,” “us” or “Spero”) for the fiscal year ended December 31, 2020, as originally filed with the Securities and Exchange Commission (the “SEC”) on March 11, 2021 (the “Original 10-K”). The purpose of this Amendment is to include information required by Part III of the Annual Report on Form 10-K that was intentionally omitted from Part III of the Original 10-K. In addition, this Amendment amends Item 15 of Part IV of the Original 10-K to update the exhibit list and to include new certifications by our principal executive officer and principal financial officer under Section 302 of the Sarbanes-Oxley Act of 2002, as required by Rule 12b-15 under the Securities Exchange Act of 1934, as amended (the “Exchange Act”).

Except as described above, no other changes have been made to the Original 10-K. The Original 10-K continues to speak as of the dates described in the Original 10-K, and we have not updated the disclosures contained therein to reflect any events that occurred subsequent to such dates. Accordingly, this Amendment should be read in conjunction with the Company’s filings made with the SEC subsequent to the filing of the Original 10-K, as information in such filings may update or supersede certain information contained in this Amendment. As used in this Amendment, unless otherwise stated or the context otherwise indicates, references to “Spero,” the “Company,” “we,” “our,” “us” or similar terms refer to Spero Therapeutics, Inc. and our subsidiaries.

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Forward-Looking Information

This Amendment contains forward-looking statements that involve risks and uncertainties. We make such forward-looking statements pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995 and other federal securities laws. All statements other than statements of historical facts contained in this Amendment are forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as “may,” “will,” “should,” “expects,” “intends,” “plans,” “anticipates,” “believes,” “estimates,” “predicts,” “potential,” “continue” or the negative of these terms or other comparable terminology. These forward-looking statements include, but are not limited to, statements about:

- the initiation, timing, design, progress and results of, including interim data from, our preclinical studies and clinical trials, and our research and development programs;
- the timing and outcome of the New Drug Application approval process for tebipenem HBr;
- our ability to retain the continued service of our key professionals and to identify, hire and retain additional qualified professionals;
- our ability to advance product candidates into, and successfully complete, clinical trials;
- the timing or likelihood of regulatory filings and approvals;
- the direct and indirect impact of the pandemic caused by an outbreak of a new strain of coronavirus, or COVID-19, on our business and operations, including manufacturing, research and development costs, clinical trials, regulatory processes and employee expenses;
- the commercialization of our product candidates, if approved;
- the pricing, coverage and reimbursement of our product candidates, if approved;
- the implementation of our business model and strategic plans for our business and product candidates;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our product candidates;
- our ability to enter into strategic arrangements and/or collaborations and the potential benefits of such arrangements;
- our estimates regarding expenses, capital requirements and needs for additional financing;
- our ability to continue as a going concern;
- our financial performance;
- developments relating to our competitors and our industry; and
- other risks and uncertainties, including those listed under Part I, Item 1A. “Risk Factors” of the Original 10-K.

Any forward-looking statements in this Amendment reflect our current views with respect to future events or to our future financial performance and involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by these forward-looking statements. Factors that may cause actual results to differ materially from current expectations include, among other things, those listed under Part I Item 1A. “Risk Factors” of the Original 10-K. Given these uncertainties, you should not place undue reliance on these forward-looking statements. Except as required by law, we assume no obligation to update or revise these forward-looking statements for any reason, even if new information becomes available in the future.

This Amendment also contains estimates, projections and other information concerning our industry, our business, and the markets for certain diseases, including data regarding the estimated size of those markets, and the incidence and prevalence of certain medical conditions. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances reflected in this information. Unless otherwise expressly stated, we obtained this industry, business, market and other data from reports, research surveys, studies and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data and similar sources.

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PART III**Item 10. Directors, Executive Officers and Corporate Governance.****Directors**

Set forth below are the names of our directors, 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 that each person listed below should serve as a director is set forth below:

<u>Name</u>	<u>Age</u>	<u>Position with the Company</u>
Milind Deshpande, Ph.D.	64	Chairman of the Board of Directors
Jean-François Formela, M.D.	64	Director
Scott Jackson	56	Director
Ankit Mahadevia, M.D.	40	Chief Executive Officer, President and Director
John C. Pottage, Jr., M.D.	68	Director
Cynthia Smith	52	Director
Frank E. Thomas	51	Director
Patrick Vink, M.D.	57	Director

Our Board of Directors has reviewed the materiality of any relationship that each of our directors has with Spero Therapeutics, Inc., either directly or indirectly. Based upon this review, our Board of Directors has determined that the following members of the Board of Directors are "independent directors" as defined by The Nasdaq Stock Market: Milind Deshpande, Ph.D., Jean-François Formela, M.D., Scott Jackson, John C. Pottage, Jr., M.D., Cynthia Smith, Frank E. Thomas, and Patrick Vink, M.D. See "Item 13. Certain Relationships and Related Transactions, and Director Independence."

Milind Deshpande, Ph.D. has served on our Board of Directors since January 2014 and currently serves as chairman of our Board of Directors. Dr. Deshpande is the President and Chief Executive Officer at Nayan Therapeutics since February 2019, and President and Chief Executive Officer of Avilar Therapeutics since January 2020. He is also a Venture Partner at RA Capital, where he has served since October 2018. Dr. Deshpande served as President and Chief Executive Officer of Achillion Pharmaceuticals, Inc. and served on the board of directors from May 2013 until May 2018. He joined Achillion 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, Executive Vice President of Research and Chief Scientific Officer in June 2007 and President of Research and Development in October 2010. Prior to joining Achillion, Dr. Deshpande was Associate Director of Lead Discovery and Early Discovery Chemistry at the Pharmaceutical Research Institute at Bristol-Myers Squibb Co. from 1991 to 2001, where he managed the identification of new clinical candidates to treat infectious and neurological diseases. From 1988 to 1991, he held a faculty position at Boston University Medical School. Dr. Deshpande received his Ph.D. in Organic Chemistry from Ohio University, following his undergraduate education in India. We believe that Dr. Deshpande is qualified to serve on our Board of Directors due to his extensive experience in the life sciences industry.

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

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

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

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

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

Frank E. Thomas has served on our Board of Directors since July 2017. Mr. Thomas is currently President and Chief Operating Officer of Orchard Therapeutics, a development-stage biotechnology company based in the United Kingdom, where he served as Chief Financial Officer and Chief Business Officer from January 2018 to December 2019. Prior to Orchard, Mr. Thomas served as the President and Chief Operating Officer of AMAG Pharmaceuticals, Inc., a publicly traded commercial-stage pharmaceutical company, from April 2015 to April 2017, as AMAG's Executive Vice President and Chief Operating Officer from May 2012 through April 2015 and as Executive Vice President, Chief Financial Officer and Treasurer from August 2011 through May 2012. Prior to AMAG, he served as Senior Vice President, Chief Operating Officer and Chief Financial Officer for Molecular Biometrics, Inc., a commercial-stage medical diagnostics company, from October 2008 to July 2011. Prior to Molecular Biometrics, Mr. Thomas spent four years at Critical Therapeutics, Inc., a public biopharmaceutical company, from April 2004 to March 2008, where he was promoted to President in June 2006 and Chief Executive Officer in December 2006 from the position of Senior Vice President and Chief Financial Officer.

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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 and Larimar Therapeutics Inc, which he joined in May 2020. Mr. Thomas holds a B.B.A. from the University of Michigan, Ann Arbor. We believe that Mr. Thomas' extensive commercial and operational management experience at biopharmaceutical companies and with financial matters qualifies him to serve on our Board of Directors.

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

Term of Office of Directors

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

- (1) Cynthia Smith, John C. Pottage, Jr., M.D. and Scott Jackson constitute our Class I directors with a term ending at the 2021 annual meeting;
- (2) Patrick Vink, M.D. and Frank E. Thomas constitute our Class II directors with a term ending at the 2022 annual meeting; and
- (3) 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 2023 annual meeting.

Committees of the Board of Directors and Meetings

Meeting Attendance. During the fiscal year ended December 31, 2020, there were five meetings of our Board of Directors, and the various committees of the Board of Directors met a total of eight times. No director attended fewer than 75% of the total number of meetings of the Board of Directors and of committees of the Board of Directors on which such director served during the fiscal year ended December 31, 2020. The Board of Directors has adopted a policy under which each member of the Board of Directors makes every effort to but is not required to attend each annual meeting of our stockholders.

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

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

Compensation Committee. Our Compensation Committee met four times during the fiscal year ended December 31, 2020. This committee currently has four members, Patrick Vink, M.D. (Chairman), Jean-François Formela, M.D., Milind Deshpande, Ph.D., and Cynthia Smith. Our Compensation Committee’s role and responsibilities are set forth in the Compensation Committee’s written charter and include reviewing, approving and making recommendations regarding our compensation policies, practices and procedures to ensure that legal and fiduciary responsibilities of the Board of Directors are carried out and that such policies, practices and procedures contribute to our success. Our Compensation Committee also administers the Spero Therapeutics, Inc. 2017 Stock Incentive Plan, as amended, or the 2017 Plan and our 2019 Inducement Equity Incentive Plan, as amended. The Compensation Committee is responsible for the determination of the compensation of our chief executive officer and shall conduct its decision-making process with respect to that issue without the chief executive officer present. All members of the Compensation Committee qualify as independent under the definition promulgated by The Nasdaq Stock Market.

In July 2019, the Compensation Committee retained Meridian Compensation Partners, LLC (“Meridian”) as an independent advisor to the Compensation Committee to provide executive compensation consulting services. Meridian did not provide any services to the Company other than executive compensation consulting services during the fiscal year ended December 31, 2020. In compliance with the SEC and the corporate governance rules of The Nasdaq Stock Market, Meridian provided the Compensation Committee with a letter addressing each of the six independence factors. Their responses affirm the independence of Meridian and the partners, consultants, and employees who service the Compensation Committee on executive compensation matters and governance issues.

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

Nominating and Corporate Governance Committee. Our Nominating and Corporate Governance Committee (“Nominating Committee”) did not meet during the fiscal year ended December 31, 2020 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
- 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.

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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, which apply to our principal executive officer, our principal financial and accounting officer and all of our other employees, 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.

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.

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.

Delinquent Section 16(a) Reports. Section 16(a) of the Exchange Act requires directors, executive officers, and persons owning more than 10% of any class of a company's equity securities registered under Section 12 of the Exchange Act to file reports on a timely basis on the initiation of their status as a reporting person and any changes with respect to their beneficial ownership of such equity securities with the SEC. Executive officers, directors and greater than 10% stockholders are required by SEC regulations to furnish those companies copies of all Section 16(a) forms they file.

Our records reflect that all reports which were required to be filed pursuant to Section 16(a) of the Exchange Act were filed on a timely basis during the year ended December 31, 2020, with the exception of a Form 4 filing for Ankit Mahadevia, M.D. related to transactions that occurred on June 22, 2020, June 23, 2020 and June 24, 2020, which was inadvertently filed late on June 29, 2020.

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.

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

Board Leadership Structure and Role in Risk Oversight

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

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

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

Stockholder Communications to the Board of Directors

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

Executive Officers

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

<u>Name</u>	<u>Age</u>	<u>Position</u>
Tamara Joseph	58	Chief Legal Officer
Timothy Keutzer	53	Chief Development Officer
Cristina Larkin	50	Chief Operating Officer
David Melnick, M.D.	69	Chief Medical Officer
Satyavrat Shukla	49	Chief Financial Officer

Satyavrat Shukla joined the Company as its Chief Financial Officer on January 4, 2021. Effective as of such date, Stephen J. DiPalma resigned as the Company's Interim Chief Financial Officer. Mr. DiPalma's resignation was not as a result of any disagreement with our Board of Directors or any matter related to our operations, product candidates, policies or practices.

Tamara Joseph has served as our Chief Legal Officer since November 2020. She has over 20 years of leadership roles in the biotechnology sector, overseeing legal, public and government affairs, compliance and risk management. Ms. Joseph most recently served as General Counsel at Millendo Therapeutics, Inc. and previously served as General Counsel at Enzyvant Therapeutics Ltd., InVivo Therapeutics Holdings Corp., Cubist Pharmaceuticals, Inc., Mayne Pharma Ltd., and Transkaryotic Therapies, Inc. Her experience also includes establishing and leading the ex-US operations of the Biogen Idec Inc. legal and public affairs departments. Ms. Joseph received her B.A. in economics from Duke University, her J.D. from the University of Michigan Law School and her L.L.M. degrees from the College of Europe in Belgium and the University of Paris.

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

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

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

Satyavrat Shukla has served as our Chief Financial Officer since January 2021. He has over 20 years of strategic and financial leadership experience. He was most recently Chief Financial Officer at Ziopharm Oncology, Inc. from July 2019 to December 2020, where he directed all of Ziopharm's financial aspects, including financial planning, analysis and reporting, treasury and tax functions, capital strategy and investor relations. Prior to Ziopharm, Mr. Shukla was Vice President and Global Head of Corporate Finance for Vertex Pharmaceuticals, Inc. from July 2012 to July 2019, where he managed financial planning, analysis and budgeting, and led the annual long-range planning process encompassing Vertex's entire portfolio and operations across more than 30 countries. Previously, Mr. Shukla was a Principal at Cornerstone Research, where he led teams providing consulting services for life science clients ranging from start-ups to multi-billion-dollar corporations. Prior to Cornerstone, he worked for finance consulting firms LECG Corporation and Putnam, Hayes & Bartlett, Inc. Mr. Shukla earned a B.A. in Economics from Harvard University and an M.B.A. in Finance and Strategy from Yale University. He also holds the Chartered Financial Analyst designation.

Item 11. Executive Compensation.

Summary Compensation Table

The following table shows the total compensation paid or accrued during the last two fiscal years ended December 31, 2020 and 2019 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, 2020 and were serving as executive officers as of such date.

Name and Principal Position	Year	Salary (\$)	Bonus (\$)	Stock Awards (\$)(1)	Option Awards (\$)(2)	Non-Equity Incentive Plan Compensation (\$)(3)	All other Compensation (\$)(4)(5)	Total (\$)
Ankit Mahadevia, M.D. Chief Executive Officer	2020	536,667	—	—	1,153,962	424,049	6,110	2,120,788
	2019	497,083	—	285,023	752,778	250,000	4,490	1,789,374
Christina Larkin Chief Operating Officer	2020	404,052	—	—	352,600	225,968	9,342	991,962
	2019	394,167	—	118,493	271,837	158,000	5,486	947,983
David Melnick, M.D. Chief Medical Officer	2020	411,450	—	—	352,600	229,548	6,315	999,913
	2019	389,167	—	118,493	271,837	156,000	4,292	939,789

- (1) These amounts represent the aggregate grant date fair value for performance-based stock awards computed in accordance with Financial Accounting Standards Board Accounting Standards Codification Topic 718, or ASC 718. A discussion of the assumptions used in determining grant date fair value may be found in Note 9 to our consolidated financial statements for the year ended December 31, 2020.

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- (2) These amounts represent the aggregate grant date fair value for option awards computed in accordance with Financial Accounting Standards Board Accounting Standards Codification Topic 718, or ASC 718. A discussion of the assumptions used in determining grant date fair value may be found in Note 9 to our consolidated financial statements for the year ended December 31, 2020.
- (3) Amounts represent annual cash bonuses earned for the applicable fiscal year. The annual cash bonuses are paid in the first quarter of the calendar year following the year in which the cash bonus relates.
- (4) Amounts in this column for the year ended December 31, 2020 include (i) in the case of Mr. Mahadevia, \$792 consists of the dollar value of life insurance premiums the Company paid with respect to term life insurance and \$5,318 in a Company matching contribution under our 401(k) plan, (ii) in the case of Ms. Larkin, \$792 consists of the dollar value of life insurance premiums the Company paid with respect to term life insurance and \$8,550 in a Company matching contribution under our 401(k) plan and (iii) in the case of Mr. Melnick, \$792 consists of the dollar value of life insurance premiums the Company paid with respect to term life insurance and \$5,523 in a Company matching contribution under our 401(k) plan.
- (5) Amounts in this column for the year ended December 31, 2019 include (i) in the case of Mr. Mahadevia, \$792 consists of the dollar value of life insurance premiums the Company paid with respect to term life insurance and \$3,698 in a Company matching contribution under our 401(k) plan, (ii) in the case of Ms. Larkin, \$792 consists of the dollar value of life insurance premiums the Company paid with respect to term life insurance and \$4,694 in a Company matching contribution under our 401(k) plan and (iii) in the case of Mr. Melnick, \$792 consists of the dollar value of life insurance premiums the Company paid with respect to term life insurance and \$3,500 in a Company matching contribution under our 401(k) plan.

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

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

In December 2017, Dr. Mahadevia's base salary was increased, effective January 1, 2018, to \$465,000 with a target bonus opportunity of 50% of base salary. In December 2018, Dr. Mahadevia's base salary was increased, effective February 1, 2019, to \$500,000 with a target bonus opportunity of 50% of his base salary. In December 2019, Dr. Mahadevia's base salary was increased, effective February 1, 2020, to \$540,000, with a target bonus opportunity of 50% of his base salary. In December 2020, Dr. Mahadevia's base salary was increased, effective February 1, 2021, to \$565,000, with a target bonus opportunity of 50% of his base salary.

Cristina Larkin

In February 2016, Cristina Larkin, our then Chief Commercial Officer, executed an offer letter with respect to her employment beginning on March 7, 2016. In September 2017, Ms. Larkin was promoted to Chief Operating Officer, in connection with which her bonus target was increased from 25% to 30% of her then-current base salary. In October 2017, we entered into a new employment agreement with Ms. Larkin, which provided for a base salary of \$345,000 and eligibility for an annual incentive bonus, with a target bonus opportunity of 30% of her then-current base salary. In December 2017, Ms. Larkin's base salary was increased, effective January 1, 2018, to \$385,000 with a target bonus opportunity of 35% of base salary. In December 2018, Ms. Larkin's base salary was increased, effective February 1, 2019, to \$395,000 with a target bonus opportunity of 40% of base salary. In December 2019, Ms. Larkin's base salary was increased, effective February 1, 2020, to \$404,875 with a target bonus opportunity of 40% of her base salary. In December 2020, Ms. Larkin's base salary was increased, effective February 1, 2021, to \$430,000 with a target bonus opportunity of 40% of her base salary.

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

David Melnick, M.D.

On December 13, 2017, we entered into an agreement with Dr. Melnick with respect to his employment as our Chief Medical Officer commencing on January 4, 2018. The terms of Mr. Melnick's agreement provided for an annual base salary of \$380,000 prorated for fiscal year 2018, and eligibility for an annual incentive bonus, with a target bonus opportunity of 35% of his then-current base salary. In December 2018, Dr. Melnick's base salary was increased, effective February 1, 2019, to \$390,000 with a target bonus opportunity of 40% of base salary. In addition, Dr. Melnick was granted an option to purchase 135,000 shares of common stock and received a sign-on bonus of \$10,000. In December 2019, Dr. Melnick's base salary was increased, effective February 1, 2020, to \$413,400 with a target bonus opportunity of 40% of his base salary. In December 2020, Dr. Melnick's base salary was increased, effective February 1, 2021, to \$430,000 with a target bonus opportunity of 40% of his base salary.

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

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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.

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 2020 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.

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The following table shows grants of stock options outstanding on the last day of the fiscal year ended December 31, 2020 to each of the executive officers named in the Summary Compensation Table.

Name	Option Awards				Stock Awards			
	Number of Securities Underlying Unexercised Options (#) Exercisable	Number of Securities Underlying Unexercised Options (#) Unexercisable	Option Exercise Price (\$)	Option Expiration Date	Number of Shares or Units of Stock That Have not Vested (#)	Market Value of Shares or Units of Stock that Have not Vested (\$)	Equity incentive plan awards: number of unearned shares, units or other rights that have not vested	Equity incentive plan awards: market or payout value of unearned shares, units or other rights that have not vested (\$)
Ankit Mahadevia, M.D.	22,213 (1)	—	\$ 5.90	7/5/2027	—	—	—	—
	101,488 (2)	—	\$ 5.90	7/5/2027	—	—	—	—
	118,888 (3)	—	\$ 5.90	7/5/2027	—	—	—	—
	208,874 (4)	43,346 (4)	\$ 5.90	7/5/2027	—	—	—	—
	93,809 (5)	31,270 (5)	\$ 11.63	12/12/2027	—	—	—	—
	86,250 (6)	93,750 (6)	\$ 6.26	1/1/2029	—	—	—	—
	—	32,925 (7)	\$ 12.81	3/29/2029	—	—	—	—
	—	180,000 (8)	\$ 9.34	2/2/2030	—	—	—	—
	—	—	—	—	—	16,687 (9)	213,760	
Cristina Larkin	8,434 (10)	—	\$ 5.90	7/5/2027	—	—	—	—
	6,490 (11)	—	\$ 5.90	7/5/2027	—	—	—	—
	60,454 (4)	10,325 (4)	\$ 5.90	7/5/2027	—	—	—	—
	46,905 (5)	15,635 (5)	\$ 11.63	12/12/2027	—	—	—	—
	31,146	33,854 (6)	\$ 6.26	1/1/2029	—	—	—	—
	—	11,890 (7)	\$ 12.81	3/29/2029	—	—	—	—
	—	55,000 (8)	\$ 9.34	2/2/2030	—	—	—	—
	—	—	—	—	—	6,937 (9)	88,863	
David Melnick, M.D.	98,438 (12)	36,562 (12)	\$ 12.14	1/3/2028	—	—	—	—
	31,146 (6)	33,854 (6)	\$ 6.26	1/1/2029	—	—	—	—
	— (7)	11,890 (7)	\$ 12.81	3/29/2029	—	—	—	—
	—	55,000 (8)	\$ 9.34	2/2/2030	—	—	—	—
	—	—	—	—	—	6,937 (9)	88,863	

- (1) 100% of these options vested on August 24, 2019.
- (2) As part of the 2017 Reorganization, Dr. Mahadevia was granted options to replace his previously awarded incentive units in Spero Therapeutics, LLC. The options vest in accordance with the vesting terms of Dr. Mahadevia's previously held incentive units: 25% of the underlying shares were deemed vested April 28, 2017, the first anniversary of the vesting commencement date, with an additional 1/36th of the remaining shares vesting monthly thereafter until the option is fully vested. In addition, in the event of a Change of Control Termination, the vesting of these options will accelerate in accordance with the terms of the option and his employment agreement.
- (3) 100% of these options vested on July 6, 2017.
- (4) 25% of the options vested on July 6, 2018 and an additional 1/36th of the remaining shares vest monthly until the option is fully vested. In addition, in the event of a Change of Control Termination, the vesting of these options will accelerate in accordance with the terms of the option and his or her employment agreement.
- (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.

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- (6) 25% of the options vested on January 2, 2020 and an additional 1/36th of the remaining shares vest monthly until the option is fully vested. In addition, in the event of a Change of Control Termination, the vesting of these options will accelerate in accordance with the terms of the option and his or her employment agreement.
- (7) These performance-based options, which were granted in March 2019, vest in four equal installments upon the achievement, within the performance period ending December 31, 2020, of certain performance goals, which are more fully described below under “Performance-Based Equity Incentive Awards,” and are contingent on the executive remaining an employee, director or consultant of Spero as of each such date.
- (8) 25% of the options vest on February 3, 2021 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.
- (9) These performance-based restricted stock units, which were granted in March 2019, vest in four equal installments upon the achievement, within the performance period ending December 31, 2020, of certain performance goals, which are more fully described below under “Performance-Based Equity Incentive Awards,” and are contingent on the executive remaining an employee, director or consultant of Spero as of each such date. In January 2021, the performance-based awards were cancelled due to the non-achievement of the performance-based vesting criteria.
- (10) 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.
- (11) 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.
- (12) 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.

The following table shows number of shares acquired and the value realized upon exercises of share options during the fiscal year ended December 31, 2020 by each of the executive officers named in the Summary Compensation Table.

Name	Option Awards	
	Number of Shares Acquired on Exercise (#)	Value Realized on Exercise (\$)(1)
Ankit Mahadevia, M.D.	45,000	378,598
Cristina Larkin	12,000	157,200
David Melnick, M.D.	—	—

- (1) The value realized on exercise is based on the market price of the shares at exercise less the applicable option exercise price.

Performance-Based Equity Incentive Awards

Historically, we have generally granted stock options with time-based vesting to our executives at the time of hire and on an annual basis thereafter. In March 2019, in addition to the foregoing, we granted an aggregate of 150,000 performance-based options and restricted stock units (“RSUs”) to our senior executives. These options and RSUs (the “Performance Awards”) are subject to performance-based vesting eligibility and a subsequent partial time-based vesting schedule. Specifically, the Performance Awards are eligible for vesting based on the achievement of performance criteria, each representing a 25% vesting opportunity if achieved within a specified time during the performance period (the “Performance Period”), and relating to (i) the release of tebipenem HBr top-line data; (ii) FDA acceptance of a tebipenem HBr New Drug Application; (iii) non-dilutive financing; and (iv) equity financing. Following the Performance Period, Performance Awards determined to be eligible for vesting as a result of achievement of the performance criteria will vest as follows: (a) 50% of the eligible award will vest immediately, and (b) the remaining eligible award will vest (i) in the case of options, in equal monthly instalments ending two years after the Performance Period expiration, and (ii) in the case of RSUs, on such two year anniversary. The Performance Awards will be subject to provisions of the executives’ employment agreements regarding acceleration of vesting in the event of certain termination events following a change in control only to the extent

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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.

In January 2021, the performance-based awards were cancelled due to the non-achievement of the performance-based vesting criteria, and the awards were added back to the shares of common stock available for issuance under the 2017 Plan. None of the outstanding options and awards had vested as of December 31, 2020.

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, 2020 to each of our current and former non-employee directors. Scott Jackson joined our Board of Directors in April 2020. Directors who are employed by us are not compensated for their service on our Board of Directors.

Name	Fees Earned or Paid in Cash (\$)	Option Awards* (\$)(6)	Total(\$)
Milind Deshpande, Ph.D.	42,500	109,418 (2)(5)	151,918
Jean-François Formela, M.D.	9,000	109,418 (2)(5)	118,418
Scott Jackson (1)	30,104	291,356 (4)(5)	321,460
John C. Pottage, Jr., M.D.	52,500	74,426 (5)	126,926
Cynthia Smith	40,000	74,426 (5)	114,426
Frank E. Thomas	36,500	91,922 (3)(5)	128,422
Patrick Vink, M.D.	17,500	109,418 (2)(5)	126,918

* These amounts represent the aggregate grant date fair value of options granted to each director in the fiscal year ended December 31, 2020, computed in accordance with FASB ASC Topic 718. A discussion of the assumptions used in determining grant date fair value may be found in Note 9 to our consolidated financial statements, included in the Original Form 10-K.

- (1) Mr. Jackson joined our Board of Directors in April 2020.
- (2) Represents an option to purchase 5,408 shares of common stock at an exercise price of \$9.87. The shares underlying the option award vest and became fully exercisable on December 31, 2020, subject to the individual's continued service as of such date.
- (3) Represents an option to purchase 2,704 shares of common stock at an exercise price of \$9.87. The shares underlying the option award vest and became fully exercisable on December 31, 2020, subject to the individual's continued service as of such date.
- (4) Represents an option to purchase 15,000 shares of common stock at an exercise price of \$13.94. The shares underlying the option award vest in thirty-six equal monthly installments at the end of each successive month following June 23, 2020, subject to the individual's continued service as of such date.

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- (5) Represents an option to purchase 7,500 shares of common stock at an exercise price of \$13.52. The shares underlying the option award vest and became fully exercisable on October 27, 2021, subject to the individual's continued service as of such date.
- (6) As of December 31, 2020, the aggregate number of options held by each of our non-employee directors was as follows (representing both exercisable and unexercisable option awards, none of which have been exercised):

<u>Name</u>	<u>Number of Shares Underlying Outstanding Stock Options</u>
Milind Deshpande, Ph.D.	73,535
Jean François Formela, M.D.	25,054
Scott Jackson	22,500
John C. Pottage, Jr., M.D.	25,719
Cynthia Smith	25,719
Frank E. Thomas	52,865
Patrick Vink, M.D.	55,568

Non-Employee Director Compensation Policy

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

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

In December 2019 we amended our Non-Employee Director Compensation Policy to provide the following with respect to equity awards to non-employee directors: (i) the initial equity award consisting of a non-qualified stock option to purchase shares of our common stock upon first appointment to our Board of Directors and vesting in equal monthly installments until the third anniversary of the grant date subject to the non-employee director's continued service, was increased from 12,146 shares to 15,000 shares, and (ii) annual equity awards consisting of a non-qualified stock option to purchase shares of our common stock vesting on the first anniversary of the grant date subject to the non-employee director's continued service, were increased from 6,073 shares to 7,500 shares. The policy was further amended to provide that, prior to the beginning of each calendar year, a non-employee director may elect to receive all or a portion of his or her base annual fee for service on our Board of Directors (i.e., \$35,000) in the form of a non-qualified stock option to purchase a number of shares of our common stock based on the Black-Scholes value of such option, which option will be granted on the first business day of the calendar year. These options vest in four quarterly installments on the last day of each calendar quarter during the calendar year, subject to the continued service of the non-employee director.

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

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters.

The following table sets forth certain information with respect to the beneficial ownership of our common stock as of March 8, 2021 for (a) the executive officers named in the Summary Compensation Table on Item 11 of this Amendment, (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 March 8, 2021 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 29,504,257 shares of common stock outstanding on March 8, 2021.

Name of Beneficial Owner	Number of Shares Beneficially Owned	Percent of Shares Beneficially Owned
Principal Stockholders		
Entities affiliated with Aquilo Capital Management, LLC (1)	3,932,209	13.33%
Entities affiliated with BVF Inc. (2)	2,768,278	9.99%
S.R. One, Limited (3)	1,740,606	5.90%
BlackRock, Inc. (4)	1,731,600	5.87%
Named Executive Officers and Directors		
Ankit Mahadevia, M.D. (5)	813,724	2.76%
Christina Larkin (6)	191,475	*
David Melnick, M.D. (7)	167,605	*
Milind Deshpande, Ph.D. (8)	81,263	*
Jean-François Formela, M.D. (9)	2,425,682	8.22%
Scott Jackson (10)	4,167	*
John C. Pottage, Jr., M.D. (11)	16,532	*
Cynthia Smith (12)	15,165	*
Frank E. Thomas (13)	43,787	*
Patrick Vink, M.D. (14)	47,512	*
All current executive officers and directors as a group (13 persons) (15)	3,916,391	13.27%

* Indicates beneficial ownership of less than 1%.

(1) 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 LO, L.P. (previously known as 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 16, 2021, which reported ownership as of December 31, 2020.

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- (2) Includes (i) 1,649,735 shares of common stock held by Biotechnology Value Fund, L.P., or BVF, (ii) 950,942 shares of common stock held by Biotechnology Value Fund II, L.P., or BVF II, and (iii) 134,912 shares of common stock held by Biotechnology Value Trading Fund OS LP, or Trading Fund OS. BVF I GP LLC, or BVF GP, as general partner of BVF, may be deemed to beneficially own 1,649,735 shares of common stock beneficially owned by BVF. BVF II GP LLC, or BVF II GP, as general partner of BVF II, may be deemed to beneficially own 950,942 shares of common stock beneficially owned by BVF II. BVF Partners OS Ltd, or Partners OS, as general partner of Trading Fund OS, may be deemed to beneficially own 134,912 shares of common stock beneficially owned by Trading Fund OS. BVF GP Holdings LLC, or BVF GPH, as the sole member of BVF GP and BVF II GP, may be deemed to beneficially own 2,600,677 shares of common stock beneficially owned in the aggregate by BVF GP and BVF II GP. BVF Partners L.P., or Partners, as investment manager of BVF, BVF II and Trading Fund OS, and the sole member of Partners OS, may be deemed to beneficially own the 2,768,278 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 32,689 shares of common stock held in the Partners Managed Accounts. BVF Inc., as the general partner of Partners, may be deemed to beneficially own the 2,768,278 shares of common stock owned by Partners. Mark N. Lampert is a director and officer of BVF Inc., and may be deemed to beneficially own the 2,768,278 shares of common stock beneficially owned by BVF, Inc. Together, BVF, BVF II, BVF GP, BVF II GP, Trading Fund OS, BVF GPH, Partners OS, Partners, BVF Inc. and Mark N. Lampert (the “BVF Entities”) hold 1,000 shares of Series B Convertible Preferred Stock (“Series B Preferred”) convertible for an aggregate of 1,000,000 shares of common stock. The Series B Preferred may not be converted if, after such conversion, the BVF Entities would beneficially own more than 9.99% of the common stock then issued and outstanding (the “Series B Blocker”). As of December 31, 2020, the Series B Blocker limited the aggregate conversion of Series B Preferred to 525,000 of the 1,000,000 shares of common stock underlying the Series B Preferred. As a result of the Series B Blocker, included in the percentage of shares beneficially owned as of December 31, 2020 is the maximum number of shares of common stock issuable upon conversion of Series B Preferred up to the limit imposed by the Series B Blocker, and excluded are the remaining shares of common stock issuable upon conversion of Series B Preferred that are prevented from converting due to the Series B Blocker. Together the BVF Entities also hold 2,287 shares of Series C Convertible Preferred Stock (the “Series C Preferred”) convertible for an aggregate of 2,287,000 shares of common stock. The Series C 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 C Blocker”). As of December 31, 2020, the Series C Blocker limits the aggregate conversion of Series C Preferred by the BVF Entities to 0 out of the 2,287,000 shares of common stock underlying the Series C Preferred. Together the BVF Entities also hold 3,215,000 shares of Series D Convertible Preferred Stock (the “Series D Preferred”) convertible for an aggregate of 3,215,000 shares of common stock. The Series D 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 D Blocker”). As of December 31, 2020, the Series D Blocker limits the aggregate conversion of Series D Preferred by the BVF Entities to 0 out of the 3,215,000 shares of common stock underlying the Series D Preferred. BVF GP disclaims beneficial ownership of the shares of common stock beneficially owned by BVF. BVF II GP disclaims beneficial ownership of the shares of common stock beneficially owned by BVF II. Partners OS disclaims beneficial ownership of the shares of common stock beneficially owned by Trading Fund OS. BVF GPH disclaims beneficial ownership of the shares of common stock beneficially owned by BVF GP and BVF II GP. Each of Partners, BVF Inc. and Mr. Lampert disclaims beneficial ownership of the shares of common stock beneficially owned by BVF, BVF II, Trading Fund OS, and the Partners Management Accounts. The address of the principal business and office of BVF Inc. and certain of its affiliates is 1 Sansome Street, 30th Floor, San Francisco, California, 94194. This information is based solely on a Schedule 13G/A filed with the SEC on February 16, 2021, which reported ownership as of December 31, 2020.
- (3) Consists of 1,740,606 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 December 7, 2020, which reported ownership as of November 5, 2020.
- (4) Consists of 1,731,600 shares of common stock owned by BlackRock, Inc. The address for BlackRock, Inc. is 55 East 52nd Street, New York, New York 10055. This information is based solely on a Schedule 13G filed by BlackRock, Inc. with the SEC on February 2, 2021, which reported ownership as of December 31, 2020.
- (5) Consists of (i) 65,817 shares of common stock held by Mahadevia-Mehta Family Trust, of which Dr. Mahadevia is the trustee, and (ii) 797,583 shares of common stock underlying options that are exercisable as of March 8, 2021 or will become exercisable within 60 days after such date held by Dr. Mahadevia.
- (6) Consists of (i) 1,500 shares of common stock and (ii) 205,975 shares of common stock underlying options that are exercisable as of March 8, 2021 or will become exercisable within 60 days after such date held by Ms. Larkin.
- (7) Consists of 167,605 shares of common stock underlying options that are exercisable as of March 8, 2021 or will become exercisable within 60 days after such date held by Dr. Melnick.

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- (8) Consists of (i) 16,454 shares of common stock and (ii) 64,809 shares of common stock underlying options that are exercisable as of March 8, 2021 or will become exercisable within 60 days after such date held by Dr. Deshpande.
- (9) Includes 1,376,968 shares 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 2, 2021, which reported ownership as of December 31, 2020. Also includes 1,031,160 shares held directly by Atlas Venture Fund X, LLC, or Atlas Fund X. Atlas Venture Associates X, L.P., or AVA X LP, is the general partner of Atlas Venture Fund X, and Atlas Venture Associates X, LLC, or AVA X LLC, is the general partner of AVA X LP. Peter Barrett, Bruce Booth, Jean-François Formela, M.D., David Gragzel and Jason Rhodes are the members of AVA X LLC and collectively make investment decisions on behalf of Atlas Venture Fund X. Dr. Formela is also a member of our Board of Directors. Dr. Formela disclaims beneficial ownership of such shares, except to the extent of his pecuniary interest therein, if any. This information is based solely on a Schedule 13D/A filed by Atlas Venture Fund X, L.P. with the SEC on February 16, 2021, which reported ownership as of such date. Also includes 17,554 shares of common stock underlying options that are exercisable as of March 8, 2021 or will become exercisable within 60 days after such date held by Dr. Formela.
- (10) Consists of 4,167 shares of common stock underlying options that are exercisable as of March 8, 2021 or will become exercisable within 60 days after such date held by Mr. Jackson.
- (11) Consists of 16,532 shares of common stock underlying options that are exercisable as of March 8, 2021 or will become exercisable within 60 days after such date held by Dr. Pottage.
- (12) Consists of 15,165 shares of common stock underlying options that are exercisable as of March 8, 2021 or will become exercisable within 60 days after such date held by Ms. Smith.
- (13) Consists of 43,787 shares of common stock underlying options that are exercisable as of March 8, 2021 or will become exercisable within 60 days after such date held by Mr. Thomas.
- (14) Consists of 47,512 shares of common stock underlying options that are exercisable as of March 8, 2021 or will become exercisable within 60 days after such date held by Dr. Vink.
- (15) See 5 through 14 above; also includes Tamara Joseph, Timothy Keutzer and Satyavrat Shukla, who are executive officers but not a named executive officers.

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, 2020:

<u>Plan category</u>	<u>(a)</u> <u>Number of securities to be issued upon exercise of outstanding options, warrants and rights (#)</u>	<u>(b)</u> <u>Weighted-average exercise price of outstanding options, warrants and rights (\$)</u>	<u>(c)</u> <u>Number of securities remaining for future issuance under equity compensation plans (excluding securities reflected in column (a)) (#)</u>
Equity compensation plans approved by stockholders ⁽¹⁾⁽³⁾	3,137,233	8.42	288,432
Equity compensation plans not approved by stockholders ⁽²⁾	545,000	12.96	481,500
Total:	3,682,233	9.10	769,932

(1) This plan category consists of the Company's 2017 Stock Incentive Plan.

(2) This plan category consists of the Company's 2019 Inducement Equity Incentive Plan.

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

Benefits Programs

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

Spero Therapeutics, Inc.'s 2017 Stock Incentive Plan

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

Since its adoption, there have been 4,518,373 shares of our common stock authorized for issuance under the 2017 Plan, which amount includes the automatic increase effective as of January 1, 2021. As of March 8, 2021, a total of 146,296 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;
- 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, as amended on June 23, 2020 (the “2019 Inducement Plan”). The Board of Directors initially reserved 331,500 shares of our common stock under the 2019 Inducement Plan. As previously disclosed, in June 2020, the Board of Directors reserved an additional 700,000 shares of our common stock under the 2019 Inducement Plan to be used exclusively for grants of awards to individuals that were not previously employees or directors of the Company, as an inducement to the individual’s entry into employment with the Company within the meaning of Rule 5635(c)(4) of the Nasdaq Listing Rules. The 2019 Inducement Plan was adopted without stockholder approval pursuant to Rule 5635(c)(4). The 2019 Inducement Plan provides for the grant of equity-based awards, including options, restricted and unrestricted stock awards, and other stock-based awards, and its terms are substantially similar to the 2017 Plan, but with such other terms and conditions intended to comply with the Nasdaq inducement award exception.

As of March 8, 2021, there were 692,050 shares outstanding and 334,450 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.

Item 13. Certain Relationships and Related Transactions, and Director Independence.

Related Party Transactions

The following is a description of transactions since January 1, 2019, to which we have been a party, in which the amount involved exceeds \$120,000, and in which any of our directors, executive officers or holders of more than 5% of our capital stock, or an affiliate or immediate family member thereof, had or will have a direct or indirect material interest. We refer to such transactions as “related party transactions” and such persons as “related parties.” With the approval of our Board of Directors, we have engaged in the related party transactions described below. We believe the terms obtained or consideration that we paid or received, as applicable, in connection with the transactions described below were comparable to terms available or the amounts that would be paid or received, as applicable, from unaffiliated third parties.

Investors’ Rights Agreement

We entered into an investors’ rights agreement at the time of our initial public offering with the purchasers of our outstanding preferred stock, including entities with which certain of our directors are affiliated. The investors’ rights agreement contains piggyback registration rights that are applicable in certain circumstances and expire on the 5th anniversary of our initial public offering.

Participation in Our March 2020 Rights Offering

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

Participation in Our September 2020 Public Offering

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

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Certain of our existing stockholders and their affiliated entities purchased an aggregate of approximately \$60 million of shares of our common stock and Series D Preferred Stock in our September 2020 offering at the public offering price. The table below sets forth the aggregate number of shares of our common stock and Series D Preferred Stock issued to our holders of more than 5% of our capital stock, or an affiliate thereof, at the time of the transaction:

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

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

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

Policies and Procedures for Related Party Transactions

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

Director Independence

Our Board of Directors undertook a review of the composition of our Board of Directors and independence of each director. Based upon information requested from and provided by each director concerning his or her background, employment and affiliations, including family relationships, our Board of Directors has determined that each of Milind Deshpande, Ph.D., Jean-Francois Formela, M.D., Scott Jackson, John C. Pottage, Jr., M.D., Cynthia Smith, Frank E. Thomas and Patrick Vink, M.D. would qualify as "independent" as that term is defined by Nasdaq Listing Rule 5605(a)(2). Ankit Mahadevia, M.D. would not qualify as "independent" under applicable Nasdaq Listing Rules applicable to the Board of Directors generally or to separately designated Board committees because he currently serves as our Chief Executive Officer. In making such determinations, our Board of Directors considered the relationships that each of our non-employee directors has with our company and all other facts and circumstances deemed relevant in determining independence, including the beneficial ownership of our capital stock by each non-employee director.

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Subject to some exceptions, Nasdaq Listing Rule 5605(a)(2) provides that a director will only qualify as an “independent director” if, in the opinion of our Board of Directors, that person does not have a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director, and that a director cannot be an “independent director” if (a) the director is, or in the past three years has been, an employee of ours; (b) a member of the director’s immediate family is, or in the past three years has been, an executive officer of ours; (c) the director or a member of the director’s immediate family has received more than \$120,000 per year in direct compensation from us within the preceding three years, other than for service as a director or benefits under a tax-qualified retirement plan or non-discretionary compensation (or, for a family member, as a non-executive employee); (d) the director or a member of the director’s immediate family is a current partner of our independent public accounting firm, or has worked for such firm in any capacity on our audit at any time during the past three years; (e) the director or a member of the director’s immediate family is, or in the past three years has been, employed as an executive officer of a company where one of our executive officers serves on the compensation committee; or (f) the director or a member of the director’s immediate family is an executive officer, partner or controlling stockholder of a company that makes payments to, or receives payments from, us in an amount which, in any 12-month period during our past three fiscal years, exceeds the greater of 5% of the recipient’s consolidated gross revenues for that year or \$200,000 (except for payments arising solely from investments in our securities or payments under non-discretionary charitable contribution matching programs). Additionally, in order to be considered an independent member of an audit committee under Rule 10A-3 under the Exchange Act, a member of an audit committee may not, other than in his or her capacity as a member of the audit committee, the Board of Directors, or any other committee of the Board of Directors, accept, directly or indirectly, any consulting, advisory, or other compensatory fee from the applicable company or any of its subsidiaries or otherwise be an affiliated person of the applicable company or any of its subsidiaries. To be considered an independent member of the compensation committee under Rule 10C-1 under the Exchange Act, the Board must consider and determine whether a director has a relationship to such company which is material to that director’s ability to be independent from management in connection with the duties of a compensation committee member, including, but not limited to: the source of compensation of the director, including any consulting advisory or other compensatory fee paid by such company to the director; and whether the director is affiliated with the company or any of its subsidiaries or affiliates.

Item 14. Principal Accounting Fees and Services.

PricewaterhouseCoopers LLP was our independent registered public accounting firm for the fiscal years ended December 31, 2020 and 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, 2020 and December 31, 2019:

	Fiscal Year 2020	Fiscal Year 2019
Audit Fees(1)	\$ 777,000	\$ 794,000
Audit-Related Fees(2)	55,000	45,000
Tax Fees(3)	—	29,000
All Other Fees(4)	2,800	2,800
Total	\$ 834,800	\$ 870,800

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

Policy on Audit Committee Pre-Approval of Services

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

PART IV**Item 15. Exhibits, Financial Statement Schedules.****(1) Consolidated Financial Statements**

No financial statements are filed with this Amendment No. 1 to our Annual Report on Form 10-K. See Index to Consolidated Financial Statements at Item 8 of the Original Form 10-K.

(2) Financial Statement Schedules

No financial statement schedules are filed with this Amendment No. 1 to our Annual Report on Form 10-K.

(3) Exhibits

The following is a list of exhibits filed as part of this Amendment No. 1 to our Annual Report on Form 10-K.

<u>Exhibit Number</u>	<u>Exhibit Description</u>	<u>Filed with this Report</u>	<u>Incorporated by Reference herein from Form or Schedule</u>	<u>Filing Date</u>	<u>SEC File / Registration Number</u>
3.1	Amended and Restated Certificate of Incorporation of the Registrant		Form 8-K (Exhibit 3.1)	11/6/2017	001-38266
3.2	Amended and Restated Bylaws of the Registrant		Form 8-K (Exhibit 3.2)	11/6/2017	001-38266
3.3	Certificate of Designation of Preferences, Rights and Limitations of Series A Convertible Preferred Stock		Form 8-K (Exhibit 3.1)	7/17/2018	001-38266
3.4	Certificate of Designation of Preferences, Rights and Limitations of Series B Convertible Preferred Stock		Form 8-K (Exhibit 3.1)	11/16/2018	001-38266
3.5	Certificate of Designation of Preferences, Rights and Limitations of Series C Convertible Preferred Stock		Form 8-K (Exhibit 3.1)	2/28/2020	001-38266
3.6	Certificate of Designation of Preferences, Rights and Limitations of Series D Convertible Preferred Stock		Form 8-K (Exhibit 3.1)	9/14/2020	001-38266
4.1	Form of Common Stock Certificate		Form S-1 (Exhibit 4.1)	10/6/2017	333-220858
4.2	Investors' Rights Agreement, dated as of June 30, 2017, by and between the Registrant and the other parties thereto		Form S-1 (Exhibit 4.2)	10/6/2017	333-220858
4.3	Description of Registrant's Securities		Form 10-K (Exhibit 4.3)	3/16/2020	001-38266
10.1#	2017 Stock Incentive Plan, as amended		Form 10-Q (Exhibit 10.1)	12/14/2017	001-38266
10.2#	Form of Stock Option Agreement under the 2017 Stock Incentive Plan, as amended		Form 10-Q (Exhibit 10.2)	12/14/2017	001-38266
10.3#	2019 Inducement Equity Incentive Plan, as amended		Form 10-Q (Exhibit 10.1)	8/6/2020	001-38266
10.4#	Form of Stock Option Agreement under the 2019 Inducement Equity Incentive Plan, as amended		Form 10-Q (Exhibit 10.2)	8/6/2020	001-38266
10.5#	Form of Director and Officer Indemnification Agreement		Form S-1 (Exhibit 10.4)	10/6/2017	333-220858
10.6#	Non-Employee Director Compensation Policy, as amended		Form 10-K (Exhibit 10.6)	3/16/2020	001-38266

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10.7#	<u>Employment Agreement, dated October 20, 2017, by and between the Registrant and Ankit Mahadevia, M.D.</u>	Form S-1/A (Exhibit 10.5)	10/23/2017	333-220858
10.8#	<u>Employment Agreement, dated December 9, 2020, by and between the Registrant and Satyavrat Shukla</u>	Form 10-K (Exhibit 10.8)	3/11/2021	001-38266
10.9#	<u>Amended and Restated Employment Agreement, dated April 22, 2020, by and between the Registrant and Thomas Parr Jr., Ph.D.</u>	Form 10-Q (Exhibit 10.3)	8/6/2020	001-38266
10.10#	<u>Employment Agreement, dated October 20, 2017, by and between the Registrant and Cristina Larkin</u>	Form S-1/A (Exhibit 10.8)	10/23/2017	333-220858
10.11#	<u>Employment Agreement, dated December 13, 2017, by and between the Registrant and David Melnick, M.D.</u>	Form 10-K (Exhibit 10.9)	4/2/2018	001-38266
10.12#	<u>Employment Agreement, dated January 1, 2020, by and between the Registrant and Timothy Keutzer</u>	Form 10-K (Exhibit 10.12)	3/16/2020	001-38266
10.13#	<u>Employment Agreement, dated November 6, 2020, by and between the Registrant and Tamara Joseph</u>	Form 10-K (Exhibit 10.13)	3/11/2021	001-38266
10.14#	<u>Consulting Agreement, dated April 18, 2019, by and between the Registrant and David P. Southwell</u>	Form 10-K (Exhibit 10.13)	3/16/2020	001-38266
10.15#	<u>Consulting Agreement, dated November 4, 2019, by and between the Registrant and Danforth Advisors, LLC</u>	Form 10-Q (Exhibit 10.1)	5/8/2020	001-38266
10.16#	<u>Lease Agreement, dated August 24, 2015, by and between the Registrant and U.S. REIF Central Plaza Massachusetts, LLC</u>	Form S-1 (Exhibit 10.11)	10/6/2017	333-220858
10.17	<u>First Amendment to Lease Agreement, dated January 17, 2018, by and between the Registrant and U.S. REIF Central Plaza Massachusetts, LLC</u>	Form 8-K (Exhibit 99.1)	1/23/2018	001-38266
10.18	<u>Second Amendment to Lease Agreement, dated December 16, 2019, by and between the Registrant and U.S. REIF Central Plaza Massachusetts, LLC</u>	Form 8-K (Exhibit 99.1)	12/19/2019	001-38266
10.19	<u>Third Amendment to Lease Agreement, dated May 4, 2020, by and between the Registrant and U.S. REIF Central Plaza Massachusetts, LLC</u>	Form 10-Q (Exhibit 10.4)	8/6/2020	001-38266
10.20	<u>Sublease, dated July 6, 2016, by and between the Registrant and Tetrphase Pharmaceuticals, Inc.</u>	Form S-1 (Exhibit 10.12)	10/6/2017	333-220858
10.21†	<u>Stock Purchase Agreement, dated June 6, 2016, by and among Spero Cantab, Inc., the Registrant, Spero Cantab UK Limited, PBB Distributions Limited, New Pharma License Holdings Limited, Cantab Anti-Infectives Ltd and Pro Bono Bio PLC, as amended by Amendment to Stock Purchase Agreement, dated July 18, 2017</u>	Form S-1 (Exhibit 10.13)	10/6/2017	333-220858
10.22†	<u>Assignment and License Agreement, dated May 9, 2016, by and among Spero Trinem, Inc., the Registrant and Vertex Pharmaceuticals Incorporated</u>	Form S-1/A (Exhibit 10.14)	10/23/2017	333-220858
10.23†	<u>License Agreement, dated June 14, 2017, by and between the Registrant and Meiji Seika Pharma Co., Ltd., as supplemented by Addendum to License Agreement, dated June 14, 2017</u>	Form S-1 (Exhibit 10.15)	10/6/2017	333-220858

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10.24†	Contract Award, dated July 12, 2018, issued by the Biomedical Advanced Research and Development Authority of the United States Department of Health and Human Services	Form 10-Q (Exhibit 10.1)	11/8/2018	001-38266
10.25††	Amended and Restated License Agreement, dated January 15, 2021, by and between the Registrant and Everest Medicines II Limited	Form 10-K (Exhibit 10.25)	3/11/2021	001-38266
10.26	Exchange Agreement, dated November 15, 2018, by and among Spero Therapeutics, Inc. and Biotechnology Value Fund, L.P., Biotechnology Value Fund II, L.P., Biotechnology Value Trading Fund OS, L.P. and MSI BVF SPV LLC	Form 8-K (Exhibit 10.1)	11/16/2018	001-38266
10.27	Controlled Equity Offering Sales Agreement, dated December 3, 2018, by and between the Registrant and Cantor Fitzgerald & Co.	Form S-3 (Exhibit 1.2)	12/3/2018	333-228661
10.28	Controlled Equity Offering Sales Agreement, dated March 11, 2021, by and between the Registrant and Cantor Fitzgerald & Co.	Form 10-K (Exhibit 10.28)	3/11/2021	001-38266
10.29	Securities Purchase Agreement, dated June 12, 2019, by and between the Registrant and Novo Holdings A/S	Form 10-Q (Exhibit 10.1)	8/8/2019	001-38266
10.30	Form of Proprietary Information and Inventions Assignment Agreement	Form S-1/A (Exhibit 10.17)	10/23/2017	333-220858
16.1	Letter of KPMG LLP, dated August 25, 2017, regarding changes in the Registrant's certifying accountants	Form S-1 (Exhibit 16.1)	10/6/2017	333-220858
21.1	List of Subsidiaries of the Registrant	Form 10-K (Exhibit 21.1)	3/16/2020	001-38266
23.1	Consent of PricewaterhouseCoopers LLP, independent registered public accounting firm	Form 10-K (Exhibit 23.1)	3/11/2021	001-38266
31.1	Certification of Principal Executive Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002	X		
31.2	Certification of Principal Financial Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002	X		
32*	Certification pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, by Principal Executive Officer and Principal Financial Officer	Form 10-K (Exhibit 32)	3/11/2021	001-38266

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101.INS	XBRL Instance Document - the instance document does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document	
101.SCH	Inline XBRL Taxonomy Extension Schema Document	Form 10-K (Exhibit 101.SCG)
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document	Form 10-K (Exhibit 101.CAL)
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document	Form 10-K (Exhibit 101.DEF)
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document	Form 10-K (Exhibit 101.LAB)
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document	Form 10-K (Exhibit 101.PRE)
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)	X

† Confidential treatment received as to portions of the exhibit. Confidential materials omitted and filed separately with the SEC.

†† Certain confidential portions of this Exhibit were omitted by means of marking such portions with brackets (“[***]”) because the identified confidential portions (i) are not material and (ii) would be competitively harmful if publicly disclosed.

Management contract or compensatory plan.

* The certification attached as Exhibit 32 that accompanies this Annual Report on Form 10-K is not deemed filed with the Securities and Exchange Commission and is not to be incorporated by reference into any filing of Spero Therapeutics, Inc. under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, whether made before or after the date of this Form 10-K, irrespective of any general incorporation language contained in such filing.

Item 16. Form 10-K Summary.

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

Date: March 23, 2021

SPERO THERAPEUTICS, INC.

By: /s/ Ankit Mahadevia, M.D.

Ankit Mahadevia, M.D.

President and Chief Executive Officer

CERTIFICATIONS UNDER SECTION 302

I, Ankit Mahadevia, M.D., certify that:

1. I have reviewed this Amendment No. 1 to Annual Report on Form 10-K/A of Spero Therapeutics, Inc.; and
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report.

Date: March 23, 2021

/s/ Ankit Mahadevia, M.D.

Ankit Mahadevia, M.D.

President and Chief Executive Officer

(Principal Executive Officer)

CERTIFICATIONS UNDER SECTION 302

I, Satyavrat Shukla, certify that:

1. I have reviewed this Amendment No. 1 to Annual Report on Form 10-K/A of Spero Therapeutics, Inc.; and
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report.

Date: March 23, 2021

/s/ Satyavrat Shukla

Satyavrat Shukla
Chief Financial Officer and Treasurer
(Principal Financial Officer and Principal Accounting
Officer)