

---

---

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

---

**FORM S-8  
REGISTRATION STATEMENT**  
*under the  
SECURITIES ACT OF 1933*

---

**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 02139**  
(Address, Including Zip Code, of Principal Executive Offices)

**SPERO THERAPEUTICS, INC. 2019 INDUCEMENT EQUITY INCENTIVE PLAN**  
(Full Title of the Plan)

**Ankit Mahadevia, M.D., Chief Executive Officer and President  
Spero Therapeutics, Inc.  
675 Massachusetts Avenue, 14th Floor  
Cambridge, Massachusetts 02139  
(857) 242-1600**  
(Name, Address and Telephone Number, Including Area Code, of Agent for Service)

---

Indicate by check mark whether the Registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer or a smaller reporting company. See definition of "large accelerated filer," "accelerated filer" and "smaller reporting company" in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer

Non-accelerated filer  (do not check if a smaller reporting company)

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 7(a)(2)(B) of the Securities Act.

---

**CALCULATION OF REGISTRATION FEE**

| <b>Title of Securities to be Registered</b> | <b>Amount to be Registered(1)</b> | <b>Proposed Maximum Offering Price Per Share(2)</b> | <b>Proposed Maximum Aggregate Offering Price(2)</b> | <b>Amount of Registration Fee</b> |
|---|-----------------------------------|---|---|-----------------------------------|
| Common Stock, \$0.001 par value             | 331,500 shares                    | \$11.95   | \$3,961,425.00                                      | \$480.13                          |

- (1) Spero Therapeutics, Inc., a Delaware corporation (the “Registrant”), is filing this Registration Statement to register 331,500 shares of common stock, \$0.001 par value (the “Common Stock”), of the Registrant for issuance under the Spero Therapeutics, Inc. 2019 Inducement Equity Incentive Plan (the “Inducement Plan”). The maximum number of shares which may be sold upon the exercise of options or stock-based awards granted under the Inducement Plan is subject to adjustment in accordance with certain anti-dilution and other provisions of the Inducement Plan. Accordingly, pursuant to Rule 416 under the Securities Act of 1933, as amended (the “Securities Act”), this Registration Statement covers, in addition to the number of shares stated above, an indeterminate number of shares which may be subject to grant or otherwise issuable after the operation of any such anti-dilution and other provisions.
- (2) This calculation is made solely for the purpose of determining the registration fee pursuant to the provisions of Rule 457(c) and (h) under the Securities Act. The offering price per share and the aggregate offering price for shares reserved for future grant or issuance under the Inducement Plan are based on the average of the high and low sale prices per share of the Common Stock as reported on The Nasdaq Global Select Market as of a date (March 8, 2019) within five business days prior to filing this Registration Statement.
- 
-

---

EXPLANATORY NOTE

In accordance with the instructional Note to Part I of Form S-8 as promulgated by the Securities and Exchange Commission, the information specified by Part I of Form S-8 has been omitted from this Registration Statement on Form S-8 for offers of Common Stock pursuant to the Inducement Plan. The documents containing the information specified in Part I will be delivered to the participants in the Inducement Plan covered by this Registration Statement as required by Rule 428(b)(1) under the Securities Act.

**PART II**

**INFORMATION REQUIRED IN THE REGISTRATION STATEMENT**

**Item 3. Incorporation of Certain Documents by Reference.**

The following documents filed by the Registrant with the Commission are incorporated herein by reference:

(a) The Registrant's annual report on Form 10-K for the fiscal year ended December 31, 2018, filed with the Commission on March 14, 2019; and

(b) The description of the Common Stock contained in the Registrant's Registration Statement on Form S-3 (File No. 333-228661) filed under the Securities Exchange Act of 1934, as amended (the "Exchange Act"), filed with the Commission on December 3, 2018, including any amendment or report filed for the purpose of updating such description.

All reports and other documents filed by the Registrant after the date hereof pursuant to Sections 13(a), 13(c), 14 and 15(d) of the Exchange Act prior to the filing of a post-effective amendment which indicates that all securities offered hereby have been sold or which deregisters all securities then remaining unsold, shall be deemed to be incorporated by reference herein and to be part hereof from the date of filing of such reports and documents.

**Item 4. Description of Securities.**

Not applicable.

**Item 5. Interests of Named Experts and Counsel.**

Not applicable.

**Item 6. Indemnification of Directors and Officers.**

Incorporated by reference from the Registrant's Registration Statement on Form S-1, as amended (File No. 333-220858).

**Item 7. Exemption from Registration Claimed.**

Not applicable.

**Item 8. Exhibits.**

| <u>Exhibit Number</u> | <u>Exhibit Description</u>   | <u>Filed Herewith</u> | <u>Incorporated by Reference herein from Form or Schedule</u> | <u>Filing Date</u> | <u>SEC File/Reg. Number</u> |
|-----------------------|--|-----------------------|---|--------------------|-----------------------------|
| 4.1                   | <a href="#">Form of Common Stock Certificate of the Registrant.</a>                  |                       | S-1<br>(Exhibit 4.1)  | 10/6/2017          | 333-220858                  |
| 4.2                   | <a href="#">Amended and Restated Certificate of Incorporation of the Registrant.</a> |                       | 8-K<br>(Exhibit 3.1)  | 11/6/2017          | 001-38266                   |
| 4.3                   | <a href="#">Amended and Restated Bylaws of the Registrant.</a>                       |                       | 8-K<br>(Exhibit 3.2)  | 11/6/2017          | 001-38266                   |

| <u>Exhibit Number</u> | <u>Exhibit Description</u>  | <u>Filed Herewith</u> | <u>Incorporated by Reference herein from Form or Schedule</u> | <u>Filing Date</u> | <u>SEC File/Reg. Number</u> |
|-----------------------|---|-----------------------|---|--------------------|-----------------------------|
| 5.1                   | <a href="#">Opinion of Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C.</a>  | X                     |   |                    |                             |
| 23.1                  | <a href="#">Consent of Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C. (included in opinion of counsel filed as Exhibit 5.1).</a> | X                     |   |                    |                             |
| 23.2                  | <a href="#">Consent of PricewaterhouseCoopers LLP, independent registered public accounting firm.</a>                                 | X                     |   |                    |                             |
| 24.1                  | <a href="#">Power of Attorney to file future amendments (set forth on the signature page of this Registration Statement).</a>         | X                     |   |                    |                             |
| 99.1                  | <a href="#">2019 Inducement Equity Incentive Plan.</a>  |                       | 10-K<br>(Exhibit 10.3)  | 3/14/2019          | 001-38266                   |
| 99.2                  | <a href="#">Form of Stock Option Agreement under the 2019 Inducement Equity Incentive Plan.</a>                                       |                       | 10-K<br>(Exhibit 10.4)  | 3/14/2019          | 001-38266                   |

Item 9. Undertakings.

(a) The undersigned Registrant hereby undertakes:

(1) To file, during any period in which offers or sales are being made, a post-effective amendment to this Registration Statement:

(i) To include any prospectus required by Section 10(a)(3) of the Securities Act of 1933;

(ii) To reflect in the prospectus any facts or events arising after the effective date of the Registration Statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represents a fundamental change in the information set forth in the Registration Statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the Commission pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than a 20% change in the maximum aggregate offering price set forth in the "Calculation of Registration Fee" table in the effective Registration Statement.

(iii) To include any material information with respect to the plan of distribution not previously disclosed in the Registration Statement or any material change to such information in the Registration Statement;

*Provided, however,* that paragraphs (a)(1)(i) and (a)(1)(ii) do not apply if the Registration Statement is on Form S-3, Form S-8 or Form F-3, and the information required to be included in a post-effective amendment by those paragraphs is contained in periodic reports filed with or furnished to the Commission by the Registrant pursuant to Section 13 or Section 15(d) of the Securities Exchange Act of 1934 that are incorporated by reference in this Registration Statement.

---

(2) That, for the purpose of determining any liability under the Securities Act of 1933, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

(3) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.

- (b) The undersigned Registrant hereby undertakes that, for purposes of determining any liability under the Securities Act of 1933, each filing of the Registrant's annual report pursuant to Section 13(a) or Section 15(d) of the Securities Exchange Act of 1934 that is incorporated by reference in this Registration Statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.
- (c) Insofar as indemnification for liabilities arising under the Securities Act of 1933 may be permitted to directors, officers and controlling persons of the Registrant pursuant to the foregoing provisions, or otherwise, the Registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the Registrant of expenses incurred or paid by a director, officer or controlling person of the Registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the Registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Act and will be governed by the final adjudication of such issue.

---

**SIGNATURES**

Pursuant to the requirements of the Securities Act of 1933, the Registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-8 and has duly caused this Registration Statement to be signed on its behalf by the undersigned, thereunto duly authorized, in Cambridge, Massachusetts on March 14, 2019.

**SPERO THERAPEUTICS, INC.**

By: /s/ Ankit Mahadevia, M.D.  
Ankit Mahadevia, M.D.  
Chief Executive Officer and President

Each person whose signature appears below constitutes and appoints Ankit Mahadevia, M.D. and Joel Sendek, and each of them singly, his true and lawful attorneys-in-fact and agents, with full power of substitution and resubstitution in each of them singly, for him and in his name, place and stead, and in any and all capacities, to sign any and all amendments (including post-effective amendments) to this Registration Statement on Form S-8 of Spero Therapeutics, Inc., and to file the same, with all exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting to the attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite or necessary to be done in connection therewith, as fully to all intents and purposes as he might or could do in person, hereby ratifying and confirming all that the attorneys-in-fact and agents or any of each of them or their substitute may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act of 1933, this Registration Statement has been signed by the following persons in the capacities and on the dates indicated.

| Signature   | Title  | Date           |
|---|--|----------------|
| <u>/s/ Ankit Mahadevia, M.D.</u><br>Ankit Mahadevia, M.D.             | Chief Executive Officer and President and Director<br><i>(Principal Executive Officer)</i>                     | March 14, 2019 |
| <u>/s/ Joel Sendek</u><br>Joel Sendek                                 | Chief Financial Officer and Treasurer<br><i>(Principal Financial Officer and Principal Accounting Officer)</i> | March 14, 2019 |
| <u>/s/ Milind Deshpande, Ph.D.</u><br>Milind Deshpande, Ph.D.         | Director   | March 14, 2019 |
| <u>/s/ Jean-François Formela, M.D.</u><br>Jean-François Formela, M.D. | Director   | March 14, 2019 |
| <u>/s/ John C. Pottage, M.D.</u><br>John C. Pottage, M.D.             | Director   | March 14, 2019 |
| <u>/s/ David P. Southwell</u><br>David P. Southwell                   | Director   | March 14, 2019 |
| <u>/s/ Frank E. Thomas</u><br>Frank E. Thomas                         | Director   | March 14, 2019 |
| <u>/s/ Patrick Vink, M.D.</u><br>Patrick Vink, M.D.                   | Director   | March 14, 2019 |



One Financial Center  
Boston, MA 02111  
617-542-6000  
www.mintz.com

March 14, 2019

Spero Therapeutics, Inc.  
675 Massachusetts Avenue, 14th Floor  
Cambridge, Massachusetts 02139

Ladies and Gentlemen:

We have acted as legal counsel to Spero Therapeutics, Inc., a Delaware corporation (the “Company”), in connection with the preparation and filing with the Securities and Exchange Commission (the “Commission”) of a Registration Statement on Form S-8 (the “Registration Statement”), pursuant to which the Company is registering the issuance under the Securities Act of 1933, as amended (“Securities Act”), of an aggregate of 331,500 shares (the “Shares”) of the Company’s common stock, \$0.001 par value per share (“Common Stock”), in accordance with the terms of the Spero Therapeutics, Inc. 2019 Inducement Equity Incentive Plan (the “Inducement Plan”). This opinion is being rendered in connection with the filing of the Registration Statement with the Commission. All capitalized terms used herein and not otherwise defined shall have the respective meanings given to them in the Registration Statement.

In connection with this opinion, we have examined the Company’s Amended and Restated Certificate of Incorporation and Amended and Restated Bylaws, each as currently in effect; such other records of the corporate proceedings of the Company and certificates of the Company’s officers as we have deemed relevant; and the Registration Statement and the exhibits thereto.

In our examination, we have assumed the genuineness of all signatures, the legal capacity of natural persons, the authenticity of all documents submitted to us as originals, the conformity to original documents of all documents submitted to us as copies, the authenticity of the originals of such copies, and the truth and correctness of any representations and warranties contained therein. In addition, we have assumed that the Company will receive any required consideration in accordance with the terms of the Inducement Plan.

Our opinion expressed herein is limited to the General Corporation Law of the State of Delaware and we express no opinion with respect to the laws of any other jurisdiction. No opinion is expressed herein with respect to the qualification of the Shares under the securities or blue sky laws of any state or any foreign jurisdiction.

Please note that we are opining only as to the matters expressly set forth herein, and no opinion should be inferred as to any other matters. This opinion is based upon currently existing statutes, rules, regulations and judicial decisions, and we disclaim any obligation to advise you of any change in any of these sources of law or subsequent legal or factual developments which might affect any matters or opinions set forth herein.

Based upon the foregoing, we are of the opinion that the Shares, when issued and delivered in accordance with the terms of the Inducement Plan, will be validly issued, fully paid and non-assessable.

---

BOSTON   LONDON   LOS ANGELES   NEW YORK   SAN DIEGO   SAN FRANCISCO   WASHINGTON  
MINTZ, LEVIN, COHN, FERRIS, GLOVSKY AND POPEO, P.C.



March 14, 2019

Page 2

We understand that you wish to file this opinion with the Commission as an exhibit to the Registration Statement in accordance with the requirements of Item 601(b)(5) of Regulation S-K promulgated under the Securities Act, and we hereby consent thereto. In giving this consent, we do not admit that we are within the category of persons whose consent is required under Section 7 of the Securities Act or the rules and regulations of the Commission promulgated thereunder.

Very truly yours,

/s/ Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C.

Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C.

**CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM**

We hereby consent to the incorporation by reference in this Registration Statement on Form S-8 of Spero Therapeutics, Inc. of our report dated March 14, 2019 relating to the financial statements, which appears in Spero Therapeutics, Inc.'s Annual Report on Form 10-K for the year ended December 31, 2018.

/s/ PricewaterhouseCoopers LLP  
Boston, Massachusetts  
March 14, 2019