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

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**FORM S-8  
REGISTRATION STATEMENT  
UNDER  
THE SECURITIES ACT OF 1933**

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**SPERO THERAPEUTICS, INC.**

(Exact name of registrant as specified in its charter)

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**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)

**SPERO THERAPEUTICS, INC. 2019 INDUCEMENT EQUITY INCENTIVE PLAN, AS AMENDED**  
(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**  
(Name and address of agent for service)

**(857) 242-1600**  
(Telephone number, including area code, of agent for service)

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

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**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, par value \$0.001 per share	700,000 shares	\$11.92	\$8,344,000	\$1,083.05

- (1) The number of shares of common stock, par value \$0.001 per share (“Common Stock”), of Spero Therapeutics, Inc. (the “Registrant”) stated above consists of additional shares of common stock available for issuance under the Spero Therapeutics, Inc. 2019 Inducement Equity Incentive Plan, as amended (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) Estimated solely for the purpose of determining the registration fee pursuant to Rule 457(c) and (h) promulgated 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 (July 31, 2020) within five business days prior to filing this Registration Statement.

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## EXPLANATORY NOTE

This registration statement registers an aggregate of 700,000 additional shares of the Registrant's common stock reserved under the Inducement Plan, representing an increase of 700,000 shares reserved under the Inducement Plan effective June 23, 2020. This registration statement registers additional securities of the same class as other securities for which a registration statement filed on Form S-8 (File No. 333-230283) relating to an employee benefit plan is effective. The information contained in the Registrant's registration statement on Form S-8 filed with the Securities and Exchange Commission on March 14, 2019 (File No. 333-230283) is hereby incorporated by reference pursuant to General Instruction E of Form S-8.

**PART II**  
**INFORMATION REQUIRED IN THE REGISTRATION STATEMENT**

**Item 8. Exhibits.**

Exhibit Number	Exhibit Description	Filed Herewith	Incorporated by Reference herein from Form or Schedule	Filing Date	SEC File/Reg. Number
4.1	<a href="#">Form of Common Stock Certificate of the Registrant.</a>		S-1 (Exhibit 4.1)	10/6/2017	333-220858
4.2	<a href="#">Amended and Restated Certificate of Incorporation of the Registrant.</a>		8-K (Exhibit 3.1)	11/6/2017	001-38266
4.3	<a href="#">Amended and Restated Bylaws of the Registrant.</a>		8-K (Exhibit 3.2)	11/6/2017	001-38266
4.4	<a href="#">2019 Inducement Equity Incentive Plan, as amended.</a>		10-Q (Exhibit 10.1)	08/6/2020	001-38266
4.5	<a href="#">Form of Stock Option Agreement under the 2019 Inducement Equity Incentive Plan, as amended.</a>		10-Q (Exhibit 10.2)	08/6/2020	001-38266
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			

## 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 the City of Cambridge, Commonwealth of Massachusetts, on August 6, 2020.

### 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 Stephen J. DiPalma, 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.

<u>Signature</u>	<u>Title</u>	<u>Date</u>
<u>/s/ Ankit Mahadevia, M.D.</u> Ankit Mahadevia, M.D.	Chief Executive Officer and President and Director <i>(Principal Executive Officer)</i>	August 6, 2020
<u>/s/ Stephen J. DiPalma</u> Stephen J. DiPalma	Interim Chief Financial Officer and Treasurer <i>(Principal Financial Officer and Principal Accounting Officer)</i>	August 6, 2020
<u>/s/ Milind Deshpande, Ph.D.</u> Milind Deshpande, Ph.D.	Director	August 6, 2020
<u>/s/ Jean-François Formela, M.D.</u> Jean-François Formela, M.D.	Director	August 6, 2020
<u>/s/ Scott T. Jackson</u> Scott T. Jackson	Director	August 6, 2020
<u>/s/ John C. Pottage, M.D.</u> John C. Pottage, M.D.	Director	August 6, 2020
<u>/s/ Cynthia Smith</u> Cynthia Smith	Director	August 6, 2020
<u>/s/ Frank E. Thomas</u> Frank E. Thomas	Director	August 6, 2020
<u>/s/ Patrick Vink, M.D.</u> Patrick Vink, M.D.	Director	August 6, 2020



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

August 6, 2020

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 700,000 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, as amended (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.

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

August 6, 2020

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 16, 2020 relating to the financial statements, which appears in Spero Therapeutics, Inc.'s Annual Report on Form 10-K for the year ended December 31, 2019.

/s/ PricewaterhouseCoopers LLP  
Boston, Massachusetts  
August 6, 2020