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. 2017 STOCK 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 (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, 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		Accelerated filer	X
Non-accelerated filer	☐ (Do not check if a smaller reporting company)	Smaller reporting company	X
		Emerging growth company	X

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

Title of Securities to be Registered	Amount to be Registered (1)	Proposed Maximum Offering Price Per Share (2)	Proposed Maximum Aggregate Offering Price (2)	Amount of Registration Fee
Common Stock, par value \$0.001 per share	607,324 shares	\$11.95	\$7,257,521.80	\$879.62

- (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. 2017 Stock Incentive Plan, as Amended (the "2017 Plan") by operation of the 2017 Plan's "evergreen" provision. The maximum number of shares which may be sold upon the exercise of such options or issuance of stock-based awards granted under the 2017 Plan are subject to adjustment in accordance with certain anti-dilution and other provisions of the 2017 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 calculating the amount of the registration fee pursuant to Rule 457(c) and Rule 457(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 2017 Plan are based on the average of the high and the low price of Registrant's 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

This Registration Statement registers an aggregate of 607,324 additional shares of the Registrant's common stock reserved under the Spero Therapeutics, Inc. 2017 Stock Incentive Plan, as Amended (the "2017 Plan"), representing an increase of 607,324 shares reserved under the 2017 Plan effective January 1, 2019 by operation of the 2017 Plan's "evergreen" provision. This Registration Statement registers additional securities of the same class as other securities for which a registration statement filed on Form S-8 of the Registrant relating to an employee benefit plan is effective (SEC File No. 333-222060). The information contained in the Registrant's registration statement on Form S-8 (SEC File No. 333-222060) 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	Form of Common Stock Certificate of the Registrant.		S-1 (Exhibit 4.1)	10/6/2017	333-220858	
4.2	Amended and Restated Certificate of Incorporation of the Registrant.		8-K (Exhibit 3.1)	11/6/2017	001-38266	
4.3	Amended and Restated Bylaws of the Registrant.		8-K (Exhibit 3.2)	11/6/2017	001-38266	
4.4	2017 Stock Incentive Plan, as amended.		10-Q (Exhibit 10.1)	12/14/2017	001-38266	
4.5	Form of Stock Option Agreement under the 2017 Stock Incentive Plan, as amended.		10-Q (Exhibit 10.2)	12/14/2017	001-38266	
5.1	Opinion of Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C.	X				
23.1	Consent of Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C. (included in opinion of counsel filed as Exhibit 5.1).	X				
23.2	Consent of PricewaterhouseCoopers LLP, independent registered public accounting firm.	X				
24.1	Power of Attorney to file future amendments (set forth on the signature page of this Registration Statement).	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 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	
/s/ Ankit Mahadevia, M.D. Ankit Mahadevia, M.D.	Chief Executive Officer and President and Director (Principal Executive Officer)	March 14, 2019	
/s/ Joel Sendek Joel Sendek	Chief Financial Officer and Treasurer (Principal Financial Officer and Principal Accounting Officer)	March 14, 2019	
/s/ Milind Deshpande, Ph.D. Milind Deshpande, Ph.D.	Director	March 14, 2019	
/s/ Jean-François Formela, M.D. Jean-François Formela, M.D.	Director	March 14, 2019	
/s/ John C. Pottage, M.D. John C. Pottage, M.D.	Director	March 14, 2019	
/s/ David P. Southwell David P. Southwell	Director	March 14, 2019	
/s/ Frank E. Thomas Frank E. Thomas	Director	March 14, 2019	
/s/ Patrick Vink, M.D. 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 607,324 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. 2017 Stock Incentive Plan (the "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 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 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.

MINTZ, LEVIN, COHN, FERRIS, GLOVSKY AND POPEO, P.C.

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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