

---

---

**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**  
(Address of Principal Executive Offices)

**02139**  
(Zip Code)

**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**  
(Name and address of agent of service)

**(857) 242-1600**  
(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   
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.

---

**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	3,170,254 shares	\$18.46	\$58,522,888.84	\$6,384.85

- (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”). 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 (September 15, 2021) within five business days prior to filing this Registration Statement.

---

## EXPLANATORY NOTE

This registration statement registers an aggregate of 3,170,254 additional shares of the Registrant's common stock reserved under the 2017 Plan, representing an increase of 3,170,254 shares reserved under the 2017 Plan effective August 17, 2021. 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. 333-222060) 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 December 14, 2017 (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.**

<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 Registrant.</a>		Form S-1 (Exhibit 4.1)	10/6/2017	333-220858
4.2	<a href="#">Amended and Restated Certificate of Incorporation of the Registrant.</a>		Form 8-K (Exhibit 3.1)	11/6/2017	001-38266
4.3	<a href="#">Certificate of Amendment to Amended and Restated Certificate of Incorporation of the Registrant.</a>		Form 8-K (Exhibit 3.1)	8/18/2021	001-38266
4.4	<a href="#">Amended and Restated Bylaws of the Registrant.</a>		Form 8-K (Exhibit 3.2)	11/6/2017	001-38266
4.5	<a href="#">2017 Stock Incentive Plan, as amended.</a>		Form 8-K (Exhibit 10.1)	8/18/2021	001-38266
4.6	<a href="#">Form of Stock Option Agreement under the 2017 Stock Incentive Plan, as amended.</a>	X			
4.7	<a href="#">Form of Restricted Stock Unit Agreement under the 2017 Stock Incentive Plan, as amended.</a>		Form 8-K (Exhibit 10.1)	8/30/21	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 PricewaterhouseCoopers LLP, independent registered public accounting firm.</a>	X			
23.2	<a href="#">Consent of Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C. (included in opinion of counsel filed Exhibit 5.1).</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 September 20, 2021.

### 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 Satyavrat Shukla, and each of them singly, his or her true and lawful attorneys-in-fact and agents, with full power of substitution and resubstitution in each of them singly, for him or her and in his or her 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 or she 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>	September 20, 2021
<u>/s/ Satyavrat Shukla</u> Satyavrat Shukla	Chief Financial Officer and Treasurer <i>(Principal Financial Officer and Principal Accounting Officer)</i>	September 20, 2021
<u>/s/ Milind Deshpande, Ph.D.</u> Milind Deshpande, Ph.D.	Director	September 20, 2021
<u>/s/ Jean-François Formela, M.D.</u> Jean-François Formela, M.D.	Director	September 20, 2021
<u>/s/ Scott Jackson</u> Scott Jackson	Director	September 20, 2021
<u>/s/ John C. Pottage, M.D.</u> John C. Pottage, M.D.	Director	September 20, 2021
<u>/s/ Cynthia Smith</u> Cynthia Smith	Director	September 20, 2021
<u>/s/ Frank E. Thomas</u> Frank E. Thomas	Director	September 20, 2021
<u>/s/ Patrick Vink, M.D.</u> Patrick Vink, M.D.	Director	September 20, 2021

**SPERO THERAPEUTICS, INC.**

**Stock Option Grant Notice**

Stock Option Grant under the Company's  
2017 Stock Incentive Plan (As Amended on August 17, 2021)

- 1. Name and Address of Participant: \_\_\_\_\_  
\_\_\_\_\_
- 2. Date of Option Grant: \_\_\_\_\_
- 3. Type of Grant: \_\_\_\_\_
- 4. Maximum Number of Shares for which this Option is exercisable: \_\_\_\_\_
- 5. Exercise (purchase) price per share: \_\_\_\_\_
- 6. Option Expiration Date: \_\_\_\_\_
- 7. Vesting Start Date: \_\_\_\_\_

8. Vesting Schedule: This Option shall become exercisable (and the Shares issued upon exercise shall be vested) as follows provided the Participant is an Employee, director or Consultant of the Company or of an Affiliate on the applicable vesting date:

[25% of the Shares shall be vested on the first anniversary of the Vesting Start Date, and thereafter the remainder of the Shares not yet vested shall vest in equal monthly installments for 36 months beginning on the first anniversary of the Vesting Start Date.]

The foregoing rights are cumulative and are subject to the other terms and conditions of this Agreement.

The Company and the Participant acknowledge receipt of this Stock Option Grant Notice and agree to the terms of the Stock Option Agreement attached hereto and incorporated by reference herein and the Company's 2017 Stock Incentive Plan, as amended.

**SPERO THERAPEUTICS, INC.**

By: \_\_\_\_\_  
Name:  
Title:

\_\_\_\_\_  
Participant

**SPERO THERAPEUTICS, INC.**

**STOCK OPTION AGREEMENT—INCORPORATED TERMS AND CONDITIONS**

AGREEMENT made as of the date of grant set forth in the Stock Option Grant Notice by and between Spero Therapeutics, Inc. (the “Company”), a Delaware corporation, and the individual whose name appears on the Stock Option Grant Notice (the “Participant”).

WHEREAS, the Company desires to grant to the Participant an Option to purchase shares of its common stock, \$0.001 par value per share (the “Shares”), under and for the purposes set forth in the Company’s 2017 Stock Incentive Plan, as amended (the “Plan”);

WHEREAS, the Company and the Participant understand and agree that any terms used and not defined herein have the same meanings as in the Plan; and

WHEREAS, the Company and the Participant each intend that the Option granted herein shall be of the type set forth in the Stock Option Grant Notice.

NOW, THEREFORE, in consideration of the mutual covenants hereinafter set forth and for other good and valuable consideration, the parties hereto agree as follows:

1. GRANT OF OPTION.

The Company hereby grants to the Participant the right and option to purchase all or any part of an aggregate of the number of Shares set forth in the Stock Option Grant Notice, on the terms and conditions and subject to all the limitations set forth herein, under United States securities and tax laws, and in the Plan, which is incorporated herein by reference. The Participant acknowledges receipt of a copy of the Plan.

2. EXERCISE PRICE.

The exercise price of the Shares covered by the Option shall be the amount per Share set forth in the Stock Option Grant Notice, subject to adjustment, as provided in the Plan, in the event of a stock split, reverse stock split or other events affecting the holders of Shares after the date hereof (the “Exercise Price”). Payment shall be made in accordance with Paragraph 9 of the Plan.

3. EXERCISABILITY OF OPTION.

Subject to the terms and conditions set forth in this Agreement and the Plan, the Option granted hereby shall become vested and exercisable as set forth in the Stock Option Grant Notice and is subject to the other terms and conditions of this Agreement and the Plan.

4. TERM OF OPTION.

This Option shall terminate on the Option Expiration Date as specified in the Stock Option Grant Notice and, if this Option is designated in the Stock Option Grant Notice as an ISO and the Participant owns as of the date hereof more than 10% of the total combined voting power of all classes of capital stock of the Company or an Affiliate, such date may not be more than five years from the date of this Agreement, but shall be subject to earlier termination as provided herein or in the Plan.

If the Participant ceases to be an Employee, director or Consultant of the Company or of an Affiliate for any reason other than the death or Disability of the Participant, or termination of the Participant for Cause (the "Termination Date"), the Option to the extent then vested and exercisable pursuant to Section 3 hereof as of the Termination Date, and not previously terminated in accordance with this Agreement, may be exercised within three months after the Termination Date, or on or prior to the Option Expiration Date as specified in the Stock Option Grant Notice, whichever is earlier, but may not be exercised thereafter except as set forth below. In such event, the unvested portion of the Option shall not be exercisable and shall expire and be cancelled on the Termination Date.

If this Option is designated in the Stock Option Grant Notice as an ISO and the Participant ceases to be an Employee of the Company or of an Affiliate but continues after termination of employment to provide service to the Company or an Affiliate as a director or Consultant, this Option shall continue to vest in accordance with Section 3 above as if this Option had not terminated until the Participant is no longer providing services to the Company. In such case, this Option shall automatically convert and be deemed a Non-Qualified Option as of the date that is three months from termination of the Participant's employment and this Option shall continue on the same terms and conditions set forth herein until such Participant is no longer providing service to the Company or an Affiliate.

Notwithstanding the foregoing, in the event of the Participant's Disability or death within three months after the Termination Date, the Participant or the Participant's Survivors may exercise the Option within one year after the Termination Date, but in no event after the Option Expiration Date as specified in the Stock Option Grant Notice.

In the event the Participant's service is terminated by the Company or an Affiliate for Cause, the Participant's right to exercise any unexercised portion of this Option even if vested shall cease immediately as of the time the Participant is notified his or her service is terminated for Cause, and this Option shall thereupon terminate. Notwithstanding anything herein to the contrary, if subsequent to the Participant's termination, but prior to the exercise of the Option, the Administrator determines that, either prior or subsequent to the Participant's termination, the Participant engaged in conduct which would constitute Cause, then the Participant shall immediately cease to have any right to exercise the Option and this Option shall thereupon terminate.

In the event of the Disability of the Participant, as determined in accordance with the Plan, the Option shall be exercisable within one year after the Participant's termination of service due to Disability or, if earlier, on or prior to the Option Expiration Date as specified in the Stock Option Grant Notice. In such event, the Option shall be exercisable:

- (a) to the extent that the Option has become exercisable but has not been exercised as of the date of the Participant's termination of service due to Disability; and
- (b) in the event rights to exercise the Option accrue periodically, to the extent of a pro rata portion through the date of the Participant's termination of service due to Disability of any additional vesting rights that would have accrued on the next vesting date had the Participant not become Disabled. The proration shall be based upon the number of days accrued in the current vesting period prior to the date of the Participant's termination of service due to Disability.

In the event of the death of the Participant while an Employee, director or Consultant of the Company or of an Affiliate, the Option shall be exercisable by the Participant's Survivors within one year after the date of death of the Participant or, if earlier, on or prior to the Option Expiration Date as specified in the Stock Option Grant Notice. In such event, the Option shall be exercisable:

- (x) to the extent that the Option has become exercisable but has not been exercised as of the date of death; and

- (y) in the event rights to exercise the Option accrue periodically, to the extent of a pro rata portion through the date of death of any additional vesting rights that would have accrued on the next vesting date had the Participant not died. The proration shall be based upon the number of days accrued in the current vesting period prior to the Participant's date of death.

#### 5. METHOD OF EXERCISING OPTION.

Subject to the terms and conditions of this Agreement, the Option may be exercised by written notice to the Company or its designee, in substantially the form of Exhibit A attached hereto (or in such other form acceptable to the Company, which may include electronic notice). Such notice shall state the number of Shares with respect to which the Option is being exercised and shall be signed by the person exercising the Option (which signature may be provided electronically in a form acceptable to the Company). Payment of the Exercise Price for such Shares shall be made in accordance with Paragraph 9 of the Plan. The Company shall deliver such Shares as soon as practicable after the notice shall be received, provided, however, that the Company may delay issuance of such Shares until completion of any action or obtaining of any consent, which the Company deems necessary under any applicable law (including, without limitation, state securities or "blue sky" laws). The Shares as to which the Option shall have been so exercised shall be registered in the Company's share register in the name of the person so exercising the Option (or, if the Option shall be exercised by the Participant and if the Participant shall so request in the notice exercising the Option, shall be registered in the Company's share register in the name of the Participant and another person jointly, with right of survivorship) and shall be delivered as provided above to or upon the written order of the person exercising the Option. In the event the Option shall be exercised, pursuant to Section 4 hereof, by any person other than the Participant, such notice shall be accompanied by appropriate proof of the right of such person to exercise the Option. All Shares that shall be purchased upon the exercise of the Option as provided herein shall be fully paid and nonassessable.

#### 6. PARTIAL EXERCISE.

Exercise of this Option to the extent above stated may be made in part at any time and from time to time within the above limits, except that no fractional share shall be issued pursuant to this Option.

#### 7. NON-ASSIGNABILITY.

The Option shall not be transferable by the Participant otherwise than by will or by the laws of descent and distribution. If this Option is a Non-Qualified Option then it may also be transferred (i) pursuant to a qualified domestic relations order as defined by the Code or Title I of the Employee Retirement Income Security Act or the rules thereunder or (ii) for no consideration to or for the benefit of the Participant's Immediate Family (including, without limitation, to a trust for the benefit of the Participant's Immediate Family or to a partnership or limited liability company for one or more members of the Participant's Immediate Family), and the transferee shall remain subject to all the terms and conditions applicable to the Option prior to such transfer and each such transferee shall so acknowledge in writing as a condition precedent to the effectiveness of such transfer. The term "Immediate Family" shall mean the Participant's spouse, former spouse, parents, children, stepchildren, adoptive relationships, sisters, brothers, nieces, nephews and grandchildren (and, for this purpose, shall also include the

Participant). Except as provided above in this paragraph, the Option shall be exercisable, during the Participant's lifetime, only by the Participant (or, in the event of legal incapacity or incompetency, by the Participant's guardian or representative) and shall not be assigned, pledged or hypothecated in any way (whether by operation of law or otherwise) and shall not be subject to execution, attachment or similar process. Any attempted transfer, assignment, pledge, hypothecation or other disposition of the Option or of any rights granted hereunder contrary to the provisions of this Section 7, or the levy of any attachment or similar process upon the Option shall be null and void.

#### 8. NO RIGHTS AS STOCKHOLDER UNTIL EXERCISE.

The Participant shall have no rights as a stockholder with respect to Shares subject to this Agreement until registration of the Shares in the Company's share register in the name of the Participant. Except as is expressly provided in the Plan with respect to certain changes in the capitalization of the Company, no adjustment shall be made for dividends or similar rights for which the record date is prior to the date of such registration.

#### 9. ADJUSTMENTS.

The Plan contains provisions covering the treatment of Options in a number of contingencies such as stock splits and mergers. Provisions in the Plan for adjustment with respect to stock subject to Options and the related provisions with respect to successors to the business of the Company are hereby made applicable hereunder and are incorporated herein by reference.

#### 10. TAXES.

The Participant acknowledges and agrees that (i) any income or other taxes due from the Participant with respect to this Option or the Shares issuable upon exercise of this Option shall be the Participant's responsibility; (ii) the Participant was free to use professional advisors of his or her choice in connection with this Agreement, has received advice from his or her professional advisors in connection with this Agreement, understands its meaning and import, and is entering into this Agreement freely and without coercion or duress; (iii) the Participant has not received and is not relying upon any advice, representations or assurances made by or on behalf of the Company or any Affiliate or any employee of or counsel to the Company or any Affiliate regarding any tax or other effects or implications of the Option, the Shares or other matters contemplated by this Agreement; and (iv) neither the Administrator, the Company, its Affiliates, nor any of its officers or directors, shall be held liable for any applicable costs, taxes, or penalties associated with the Option if, in fact, the Internal Revenue Service were to determine that the Option constitutes deferred compensation under Section 409A of the Code.

If this Option is designated in the Stock Option Grant Notice as a Non-Qualified Option or if the Option is an ISO and is converted into a Non-Qualified Option and such Non-Qualified Option is exercised, the Participant agrees that the Company may withhold from the Participant's remuneration, if any, the minimum statutory amount of federal, state and local withholding taxes attributable to such amount that is considered compensation includable in such person's gross income. At the Company's discretion, the amount required to be withheld may be withheld in cash from such remuneration, or in kind from the Shares otherwise deliverable to the Participant on exercise of the Option. The Participant further agrees that, if the Company does not withhold an amount from the Participant's remuneration sufficient to satisfy the Company's income tax withholding obligation, the Participant will reimburse the Company on demand, in cash, for the amount under-withheld.

11. PURCHASE FOR INVESTMENT.

Unless the offering and sale of the Shares to be issued upon the particular exercise of the Option shall have been effectively registered under the Securities Act, the Company shall be under no obligation to issue the Shares covered by such exercise unless the Company has determined that such exercise and issuance would be exempt from the registration requirements of the Securities Act and until the following conditions have been fulfilled:

- (a) The person(s) who exercise the Option shall warrant to the Company, at the time of such exercise, that such person(s) are acquiring such Shares for their own respective accounts, for investment, and not with a view to, or for sale in connection with, the distribution of any such Shares, in which event the person(s) acquiring such Shares shall be bound by the provisions of the following legend which shall be endorsed upon any certificate(s) evidencing the Shares issued pursuant to such exercise:

“The shares represented by this certificate have been taken for investment and they may not be sold or otherwise transferred by any person, including a pledgee, unless (1) either (a) a Registration Statement with respect to such shares shall be effective under the Securities Act of 1933, as amended, or (b) the Company shall have received an opinion of counsel satisfactory to it that an exemption from registration under such Act is then available, and (2) there shall have been compliance with all applicable state securities laws;” and

(b) If the Company so requires, the Company shall have received an opinion of its counsel that the Shares may be issued upon such particular exercise in compliance with the Securities Act without registration thereunder. Without limiting the generality of the foregoing, the Company may delay issuance of the Shares until completion of any action or obtaining of any consent, which the Company deems necessary under any applicable law (including without limitation state securities or “blue sky” laws).

12. RESTRICTIONS ON TRANSFER OF SHARES.

12.1 The Participant agrees that in the event the Company proposes to offer for sale to the public any of its equity securities and such Participant is requested by the Company and any underwriter engaged by the Company in connection with such offering to sign an agreement restricting the sale or other transfer of Shares, then it will promptly sign such agreement and will not transfer, whether in privately negotiated transactions or to the public in open market transactions or otherwise, any Shares or other securities of the Company held by him or her during such period as is determined by the Company and the underwriters, not to exceed 180 days following the closing of the offering, plus such additional period of time as may be required to comply with FINRA rules or similar rules thereto promulgated by another regulatory authority (such period, the “Lock-Up Period”). Such agreement shall be in writing and in form and substance reasonably satisfactory to the Company and such underwriter and pursuant to customary and prevailing terms and conditions. Notwithstanding whether the Participant has signed such an agreement, the Company may impose stop-transfer instructions with respect to the Shares or other securities of the Company subject to the foregoing restrictions until the end of the Lock-Up Period.

12.2 The Participant acknowledges and agrees that neither the Company, its stockholders nor its directors and officers, has any duty or obligation to disclose to the Participant any material information regarding the business of the Company or affecting the value of the Shares before, at the time of, or following a termination of the service of the Participant by the Company, including, without limitation, any information concerning plans for the Company to make a public offering of its securities or to be acquired by or merged with or into another firm or entity.

13. NO OBLIGATION TO MAINTAIN RELATIONSHIP.

The Participant acknowledges that: (i) the Company is not by the Plan or this Option Agreement obligated to continue the Participant as an employee, director or Consultant of the Company or an Affiliate; (ii) the Plan is discretionary in nature and may be suspended or terminated by the Company at any time; (iii) the grant of the Option is a one-time benefit which does not create any contractual or other right to receive future grants of options, or benefits in lieu of options; (iv) all determinations with respect to any such future grants, including, but not limited to, the times when options shall be granted, the number of shares subject to each option, the option price, and the time or times when each option shall be exercisable, will be at the sole discretion of the Company; (v) the Participant's participation in the Plan is voluntary; (vi) the value of the Option is an extraordinary item of compensation which is outside the scope of the Participant's employment or consulting contract, if any; and (vii) the Option is not part of normal or expected compensation for purposes of calculating any severance, resignation, redundancy, end of service payments, bonuses, long-service awards, pension or retirement benefits or similar payments.

14. IF OPTION IS INTENDED TO BE AN ISO.

If this Option is designated in the Stock Option Grant Notice as an ISO so that the Participant (or the Participant's Survivors) may qualify for the favorable tax treatment provided to holders of Options that meet the standards of Section 422 of the Code then any provision of this Agreement or the Plan which conflicts with the Code so that this Option would not be deemed an ISO is null and void and any ambiguities shall be resolved so that the Option qualifies as an ISO. The Participant should consult with the Participant's own tax advisors regarding the tax effects of the Option and the requirements necessary to obtain favorable tax treatment under Section 422 of the Code, including, but not limited to, holding period requirements.

Notwithstanding the foregoing, to the extent that the Option is designated in the Stock Option Grant Notice as an ISO and is not deemed to be an ISO pursuant to Section 422(d) of the Code because the aggregate Fair Market Value (determined as of the Date of Option Grant) of any of the Shares with respect to which this ISO is granted becomes exercisable for the first time during any calendar year in excess of \$100,000, the portion of the Option representing such excess value shall be treated as a Non-Qualified Option and the Participant shall be deemed to have taxable income measured by the difference between the then Fair Market Value of the Shares received upon exercise and the price paid for such Shares pursuant to this Agreement.

Neither the Company nor any Affiliate shall have any liability to the Participant, or any other party, if the Option (or any part thereof) that is intended to be an ISO is not an ISO or for any action taken by the Administrator, including without limitation the conversion of an ISO to a Non-Qualified Option.

15. NOTICE TO COMPANY OF DISQUALIFYING DISPOSITION OF AN ISO.

If this Option is designated in the Stock Option Grant Notice as an ISO then the Participant agrees to notify the Company in writing immediately after the Participant makes a Disqualifying Disposition of any of the Shares acquired pursuant to the exercise of the ISO. A Disqualifying Disposition is defined in Section 424(c) of the Code and includes any disposition

(including any sale) of such Shares before the later of (a) two years after the date the Participant was granted the ISO or (b) one year after the date the Participant acquired Shares by exercising the ISO, except as otherwise provided in Section 424(c) of the Code. If the Participant has died before the Shares are sold, these holding period requirements do not apply and no Disqualifying Disposition can occur thereafter.

16. NOTICES.

Any notices required or permitted by the terms of this Agreement or the Plan shall be given by recognized courier service, facsimile, registered or certified mail, return receipt requested, addressed as follows:

If to the Company:

Spero Therapeutics, Inc.  
675 Massachusetts Avenue  
Cambridge, MA 02139  
Attention: Chief Financial Officer

If to the Participant, at the address set forth on the Stock Option Grant Notice

or to such other address or addresses of which notice in the same manner has previously been given. Any such notice shall be deemed to have been given upon the earlier of receipt, one business day following delivery to a recognized courier service or three business days following mailing by registered or certified mail.

17. GOVERNING LAW.

This Agreement shall be governed by and construed in accordance with the laws of the State of Delaware, without giving effect to its internal principles governing the conflict of law. For the purpose of litigating any dispute that arises under this Agreement, the parties hereby consent to exclusive jurisdiction in the Commonwealth of Massachusetts and agree that such litigation shall be conducted in the state courts of Suffolk County, Massachusetts or the federal courts of the United States for the District of Massachusetts.

18. BENEFIT OF AGREEMENT.

Subject to the provisions of the Plan and the other provisions hereof, this Agreement shall be for the benefit of and shall be binding upon the heirs, executors, administrators, successors and assigns of the parties hereto.

19. ENTIRE AGREEMENT.

This Agreement, together with the Plan, embodies the entire agreement and understanding between the parties hereto with respect to the subject matter hereof and supersedes all prior oral or written agreements and understandings relating to the subject matter hereof (with the exception of acceleration of vesting provisions contained in any other agreement with the Company). No statement, representation, warranty, covenant or agreement not expressly set forth in this Agreement shall affect or be used to interpret, change or restrict, the express terms and provisions of this Agreement. Notwithstanding the foregoing in all events, this Agreement shall be subject to and governed by the Plan.

20. MODIFICATIONS AND AMENDMENTS.

The terms and provisions of this Agreement may be modified or amended as provided in the Plan.

21. WAIVERS AND CONSENTS.

Except as provided in the Plan, the terms and provisions of this Agreement may be waived, or consent for the departure therefrom granted, only by written document executed by the party entitled to the benefits of such terms or provisions. No such waiver or consent shall be deemed to be or shall constitute a waiver or consent with respect to any other terms or provisions of this Agreement, whether or not similar. Each such waiver or consent shall be effective only in the specific instance and for the purpose for which it was given, and shall not constitute a continuing waiver or consent.

22. DATA PRIVACY.

By entering into this Agreement, the Participant: (i) authorizes the Company and each Affiliate, and any agent of the Company or any Affiliate administering the Plan or providing Plan recordkeeping services, to disclose to the Company or any of its Affiliates such information and data as the Company or any such Affiliate shall request in order to facilitate the grant of options and the administration of the Plan; and (ii) authorizes the Company and each Affiliate to store and transmit such information in electronic form for the purposes set forth in this Agreement.

[REMAINDER OF PAGE INTENTIONALLY LEFT BLANK]

NOTICE OF EXERCISE OF STOCK OPTION
[Form for Shares registered in the United States]

To: Spero Therapeutics, Inc.

IMPORTANT NOTICE: This form of Notice of Exercise may only be used at such time as the Company has filed a Registration Statement with the Securities and Exchange Commission under which the issuance of the Shares for which this exercise is being made is registered and such Registration Statement remains effective.

Ladies and Gentlemen:

I hereby exercise my Stock Option to purchase \_\_\_\_\_ shares (the "Shares") of the common stock, \$0.001 par value, of Spero Therapeutics, Inc. (the "Company"), at the exercise price of \$\_\_\_\_\_ per share, pursuant to and subject to the terms of that Stock Option Grant Notice dated \_\_\_\_\_, 201\_.

I understand the nature of the investment I am making and the financial risks thereof. I am aware that it is my responsibility to have consulted with competent tax and legal advisors about the relevant national, state and local income tax and securities laws affecting the exercise of the Option and the purchase and subsequent sale of the Shares.

I am paying the option exercise price for the Shares as follows:

\_\_\_\_\_

Please issue the Shares (check one):

[ ] to me; or

[ ] to me and \_\_\_\_\_, as joint tenants with right of survivorship,

at the following address:

\_\_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_

My mailing address for stockholder communications, if different from the address listed above,

is:

\_\_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_

---

Very truly yours,

\_\_\_\_\_  
Participant (signature)

\_\_\_\_\_  
Print Name

\_\_\_\_\_  
Date

Exhibit A-2



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

September 20, 2021

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 3,170,254 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, as amended (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, as amended, 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.

---

BOSTON      LONDON      LOS ANGELES      NEW YORK      SAN DIEGO      SAN FRANCISCO      WASHINGTON

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

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.

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 11, 2021 relating to the financial statements, which appears in Spero Therapeutics, Inc.'s Annual Report on Form 10-K for the year ended December 31, 2020.

/s/ PricewaterhouseCoopers LLP  
Boston, Massachusetts  
September 20, 2021