

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

SCHEDULE 13G
Under the Securities Exchange Act of 1934

(Amendment No. ___)*

SPERO THERAPEUTICS, INC.

(Name of Issuer)

Common Stock, \$0.001 par value per share

(Title of Class of Securities)

84833T103

(CUSIP Number)

December 31, 2017

(Date of Event Which Requires Filing of this Statement)

Check the appropriate box to designate the rule pursuant to which this Schedule is filed:

- Rule 13d-1(b)
- Rule 13d-1(c)
- Rule 13d-1(d)

*The remainder of this cover page shall be filled out for a reporting person's initial filing on this form with respect to the subject class of securities, and for any subsequent amendment containing information which would alter the disclosures provided in a prior cover page.

The information required in the remainder of this cover page shall not be deemed to be "filed" for the purpose of Section 18 of the Securities Exchange Act of 1934 ("**Act**") or otherwise subject to the liabilities of that section of the Act but shall be subject to all other provisions of the Act (however, see the Notes).

1. Names of Reporting Persons.
I.R.S. Identification Nos. of above persons (entities only).
RA Capital Management, LLC
2. Check the Appropriate Box if a Member of a Group (See Instructions)
(a)
(b)
3. SEC Use Only
4. Citizenship or Place of Organization **Massachusetts**
- | | | |
|--|-----------------------------|-------------------------|
| Number of
Shares
Beneficially
Owned by
Each Reporting
Person With | 5. Sole Voting Power | 0 shares |
| | 6. Shared Voting Power | 1,225,647 shares |
| | 7. Sole Dispositive Power | 0 shares |
| | 8. Shared Dispositive Power | 1,225,647 shares |
9. Aggregate Amount Beneficially Owned by Each Reporting Person
1,225,647 shares
10. Check if the Aggregate Amount in Row (9) Excludes Certain Shares (See Instructions)
11. Percent of Class Represented by Amount in Row (9)
8.5%¹
12. Type of Reporting Person (See Instructions)
IA

¹ The percentage calculation assumes that there are currently 14,369,182 outstanding shares of Common Stock of the Issuer, based on the Issuer's Form 10-Q as filed with the Securities and Exchange Commission ("SEC") on December 14, 2017.

1. Names of Reporting Persons.
I.R.S. Identification Nos. of above persons (entities only).
Peter Kolchinsky

2. Check the Appropriate Box if a Member of a Group (See Instructions)
(a)
(b)

3. SEC Use Only

4. Citizenship or Place of Organization **United States**

Number of Shares Beneficially Owned by Each Reporting Person With	5. Sole Voting Power	0 shares
	6. Shared Voting Power	1,225,647 shares
	7. Sole Dispositive Power	0 shares
	8. Shared Dispositive Power	1,225,647 shares

9. Aggregate Amount Beneficially Owned by Each Reporting Person
1,225,647 shares

10. Check if the Aggregate Amount in Row (9) Excludes Certain Shares (See Instructions)

11. Percent of Class Represented by Amount in Row (9)
8.5%¹

12. Type of Reporting Person (See Instructions)
IN

¹ The percentage calculation assumes that there are currently 14,369,182 outstanding shares of Common Stock of the Issuer, based on the Issuer's Form 10-Q as filed with the Securities and Exchange Commission ("SEC") on December 14, 2017.

Item 1.

- (a) **Name of Issuer:** Spero Therapeutics, Inc. (the “Issuer”).
- (b) **Address of the Issuer’s Principal Executive Offices:** 675 Massachusetts Avenue, 14th Floor, Cambridge, Massachusetts 02139.

Item 2.

(a) **Name of Person Filing:** This joint statement on Schedule 13G is being filed by RA Capital Management, LLC (“Capital”) and Peter Kolchinsky. Capital and Mr. Kolchinsky are collectively referred to herein as the “Reporting Persons.” Capital is the general partner of the RA Capital Healthcare Fund, L.P. (the “Fund”), which owns 994,464 shares of the Issuer’s Common Stock, and serves as investment adviser for a separately managed account (the “Account”), which owns 231,183 shares of the Issuer’s Common Stock. Mr. Kolchinsky is the manager of Capital. As the investment adviser to the Fund and the Account, Capital may be deemed a beneficial owner, for purposes of Section 13(d) of the Securities Exchange Act of 1934 (the “Act”), of any securities of the Issuer owned by the Fund or the Account. As the manager of Capital, Mr. Kolchinsky may be deemed a beneficial owner, for purposes of Section 13(d) of the Act, of any securities of the Issuer beneficially owned by Capital. Capital and Mr. Kolchinsky disclaim beneficial ownership of the securities reported in this Schedule 13G Statement (the “Statement”) other than for the purpose of determining their obligations under Section 13(d) of the Act, and the filing of the Statement shall not be deemed an admission that either Capital or Mr. Kolchinsky is or was the beneficial owner of such securities for any other purpose.

(b) **Address of Principal Business Office:** The principal business office of the Reporting Persons is c/o RA Capital Management, LLC, 20 Park Plaza, Suite 1200, Boston, MA 02116.

(c) **Citizenship:** Capital is a Massachusetts limited liability company. Mr. Kolchinsky is a United States citizen.

(d) **Title and Class of Securities:** Common stock (“Common Stock”)

(e) **CUSIP Number:** 84833T103

Item 3. If this statement is filed pursuant to §§240.13d-1(b) or 240.13d-2(b) or (c), check whether the person filing is a:

- (e) RA Capital Management LLC is a registered investment adviser and is filing this statement in accordance with §240.13d-1(b)(1)(ii)(E);
- (g) Peter Kolchinsky is a control person and is filing this statement in accordance with §240.13d-1(b)(1)(ii)(G).

Item 4. Ownership:

Provide the following information regarding the aggregate number and percentage of the class of securities of the issuer identified in Item 1.

- (a) Amount Beneficially Owned:
See the response(s) to Item 9 on the attached cover page(s).
- (b) Percent of Class:
See the response(s) to Item 11 on the attached cover page(s).
- (c) Number of shares as to which such person has:
 - (i) sole power to vote or to direct the vote:
See the response(s) to Item 5 on the attached cover page(s).
 - (ii) shared power to vote or to direct the vote
See the response(s) to Item 6 on the attached cover page(s).
 - (iii) sole power to dispose or to direct the disposition of
See the response(s) to Item 7 on the attached cover page(s).
 - (iv) shared power to dispose or to direct the disposition of
See the response(s) to Item 8 on the attached cover page(s).

Item 5. Ownership of Five Percent or Less of a Class:

Not applicable.

Item 6. Ownership of More than Five Percent on Behalf of Another Person:

Not applicable.

Item 7. Identification and Classification of the Subsidiary Which Acquired the Security Being Reported on By the Parent Holding Company or Control Person:

Not applicable.

Item 8. Identification and Classification of Members of the Group:

Not applicable.

Item 9. Notice of Dissolution of Group:

Not applicable.

Item 10. Certification:

By signing below I hereby certify that, to the best of my knowledge and belief, the securities referred to above were not acquired and are not held for the purpose of or with the effect of changing or influencing the control of the issuer of the securities and were not acquired and are not held in connection with or as a participant in any transaction having that purpose or effect.

SIGNATURE

After reasonable inquiry and to the best of my knowledge and belief, I certify that the information set forth in this statement is true, complete and correct.

DATE: February 14, 2018

RA CAPITAL MANAGEMENT, LLC

By: /s/ Peter Kolchinsky
Peter Kolchinsky
Authorized Signatory

PETER KOLCHINSKY

/s/ Peter Kolchinsky

Exhibit 1JOINT FILING AGREEMENT

This Joint Filing Agreement, dated as of February 14, 2018, is by and among RA Capital Management, LLC and Peter Kolchinsky (the foregoing are collectively referred to herein as the "Filers").

Each of the Filers may be required to file with the United States Securities and Exchange Commission a statement on Schedule 13G and/or 13D with respect to Common Stock, par value \$0.001 per share, of Spero Therapeutics, Inc. beneficially owned by them from time to time.

Pursuant to and in accordance with Rule 13(d)(1)(k) promulgated under the Securities Exchange Act of 1934, as amended, the Filers hereby agree to file a single statement on Schedule 13G and/or 13D (and any amendments thereto) on behalf of each of such parties, and hereby further agree to file this Joint Filing Agreement as an exhibit to such statement, as required by such rule.

This Joint Filing Agreement may be terminated by any of the Filers upon one week's prior written notice or such lesser period of notice as the Filers may mutually agree.

Executed and delivered as of the date first above written.

RA CAPITAL MANAGEMENT, LLC

By: /s/ Peter Kolchinsky

Peter Kolchinsky
Authorized Signatory

PETER KOLCHINSKY

/s/ Peter Kolchinsky
