

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

SCHEDULE 13G
(Rule 13d-102)

INFORMATION TO BE INCLUDED IN STATEMENTS FILED PURSUANT
TO RULES 13d-1(b), (c), AND (d) AND AMENDMENTS THERETO FILED
PURSUANT TO RULE 13d-2(b)

(Amendment No. 1)¹

Spero Therapeutics, Inc.
(Name of Issuer)

Common Stock, \$0.001 par value
(Title of Class of Securities)

84833T103
(CUSIP Number)

December 31, 2018
(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)

¹ 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 disclosures provided in a prior cover page.

The information required on 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	NAME OF REPORTING PERSON Biotechnology Value Fund, L.P.	
2	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (a) <input checked="" type="checkbox"/> (b) <input type="checkbox"/>	
3	SEC USE ONLY	
4	CITIZENSHIP OR PLACE OF ORGANIZATION Delaware	
NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH	5	SOLE VOTING POWER 0 shares
	6	SHARED VOTING POWER 1,404,711*
	7	SOLE DISPOSITIVE POWER 0 shares
	8	SHARED DISPOSITIVE POWER 1,404,711*
9	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON 1,404,711*	
10	CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES <input type="checkbox"/>	
11	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (9) 7.7%*	
12	TYPE OF REPORTING PERSON PN	

* Includes 972,000 shares of Common Stock currently issuable upon the conversion of certain Series A Preferred (defined below). Excludes 44,000 shares of Common Stock underlying certain Series A Preferred held by BVF that may not be converted due to the Series A Blocker (defined below).

Excludes 493,000 shares of Common Stock underlying certain Series B Preferred (defined below) held by BVF that may not be converted due to the Series B Blocker (defined below).

The Reporting Persons may choose to convert the Series A Preferred or the Series B Preferred in other amounts among the Reporting Persons, while continuing to comply with the Beneficial Ownership Limitation (defined below). See Item 4(a) for a full description of the Reporting Person's beneficial ownership.

1	NAME OF REPORTING PERSON Biotechnology Value Fund II, L.P.	
2	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (a) <input checked="" type="checkbox"/> (b) <input type="checkbox"/>	
3	SEC USE ONLY	
4	CITIZENSHIP OR PLACE OF ORGANIZATION Delaware	
NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH	5	SOLE VOTING POWER 0 shares
	6	SHARED VOTING POWER 298,102*
	7	SOLE DISPOSITIVE POWER 0 shares
	8	SHARED DISPOSITIVE POWER 298,102*
9	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON 298,102*	
10	CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES <input type="checkbox"/>	
11	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (9) 1.7%*	
12	TYPE OF REPORTING PERSON PN	

* Excludes 823,000 shares of Common Stock underlying certain Series A Preferred (defined below) held by BVF2 that may not be converted due to the Series A Blocker (defined below).

Excludes 385,000 shares of Common Stock underlying certain Series B Preferred (defined below) held by BVF2 that may not be converted due to the Series B Blocker (defined below).

The Reporting Persons may choose to convert the Series A Preferred or the Series B Preferred in other amounts among the Reporting Persons, while continuing to comply with the Beneficial Ownership Limitation (defined below). See Item 4(a) for a full description of the Reporting Person's beneficial ownership.

1	NAME OF REPORTING PERSON Biotechnology Value Trading Fund OS LP	
2	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (a) <input checked="" type="checkbox"/> (b) <input type="checkbox"/>	
3	SEC USE ONLY	
4	CITIZENSHIP OR PLACE OF ORGANIZATION Cayman Islands	
NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH	5	SOLE VOTING POWER 0 shares
	6	SHARED VOTING POWER 60,345*
	7	SOLE DISPOSITIVE POWER 0 shares
	8	SHARED DISPOSITIVE POWER 60,345*
9	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON 60,345*	
10	CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES <input type="checkbox"/>	
11	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (9) Less than 1%*	
12	TYPE OF REPORTING PERSON PN	

* Excludes 168,000 shares of Common Stock underlying certain Series A Preferred (defined below) held by Trading Fund OS that may not be converted due to the Series A Blocker (defined below).

Excludes 60,000 shares of Common Stock underlying certain Series B Preferred (defined below) held by Trading Fund OS that may not be converted due to the Series B Blocker (defined below).

The Reporting Persons may choose to convert the Series A Preferred or the Series B Preferred in other amounts among the Reporting Persons, while continuing to comply with the Beneficial Ownership Limitation (defined below). See Item 4(a) for a full description of the Reporting Person's beneficial ownership.

1	NAME OF REPORTING PERSON BVF Partners OS Ltd.	
2	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (a) <input checked="" type="checkbox"/> (b) <input type="checkbox"/>	
3	SEC USE ONLY	
4	CITIZENSHIP OR PLACE OF ORGANIZATION Cayman Islands	
NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH	5	SOLE VOTING POWER 0 shares
	6	SHARED VOTING POWER 60,345*
	7	SOLE DISPOSITIVE POWER 0 shares
	8	SHARED DISPOSITIVE POWER 60,345*
9	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON 60,345*	
10	CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES <input type="checkbox"/>	
11	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (9) Less than 1%*	
12	TYPE OF REPORTING PERSON CO	

* Excludes 168,000 shares of Common Stock underlying certain Series A Preferred (defined below) held by Trading Fund OS that may not be converted due to the Series A Blocker (defined below).

Excludes 60,000 shares of Common Stock underlying certain Series B Preferred (defined below) held by Trading Fund OS that may not be converted due to the Series B Blocker (defined below).

The Reporting Persons may choose to convert the Series A Preferred or the Series B Preferred in other amounts among the Reporting Persons, while continuing to comply with the Beneficial Ownership Limitation (defined below). See Item 4(a) for a full description of the Reporting Person's beneficial ownership..

1	NAME OF REPORTING PERSON BVF Partners L.P.	
2	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (a) <input checked="" type="checkbox"/> (b) <input type="checkbox"/>	
3	SEC USE ONLY	
4	CITIZENSHIP OR PLACE OF ORGANIZATION Delaware	
NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH	5	SOLE VOTING POWER 0 shares
	6	SHARED VOTING POWER 1,815,146*
	7	SOLE DISPOSITIVE POWER 0 shares
	8	SHARED DISPOSITIVE POWER 1,815,146*
9	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON 1,815,146*	
10	CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES <input type="checkbox"/>	
11	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (9) 9.99%*	
12	TYPE OF REPORTING PERSON PN, IA	

* Includes 972,000 shares of Common Stock currently issuable upon the conversion of certain Series A Preferred (defined below). Excludes 1,248,000 shares of Common Stock underlying certain Series A Preferred that may not be converted due to the Series A Blocker (defined below).

Excludes 1,000,000 shares of Common Stock underlying certain Series B Preferred (defined below) that may not be converted due to the Series B Blocker (defined below).

The Reporting Persons may choose to convert the Series A Preferred or the Series B Preferred in other amounts among the Reporting Persons, while continuing to comply with the Beneficial Ownership Limitation (defined below). See Item 4(a) for a full description of the Reporting Person's beneficial ownership.

1	NAME OF REPORTING PERSON BVF Inc.	
2	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (a) <input checked="" type="checkbox"/> (b) <input type="checkbox"/>	
3	SEC USE ONLY	
4	CITIZENSHIP OR PLACE OF ORGANIZATION Delaware	
NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH	5	SOLE VOTING POWER 0 shares
	6	SHARED VOTING POWER 1,815,146*
	7	SOLE DISPOSITIVE POWER 0 shares
	8	SHARED DISPOSITIVE POWER 1,815,146*
9	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON 1,815,146*	
10	CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES <input type="checkbox"/>	
11	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (9) 9.99%*	
12	TYPE OF REPORTING PERSON CO	

* Includes 972,000 shares of Common Stock currently issuable upon the conversion of certain Series A Preferred (defined below). Excludes 1,248,000 shares of Common Stock underlying certain Series A Preferred that may not be converted due to the Series A Blocker (defined below).

Excludes 1,000,000 shares of Common Stock underlying certain Series B Preferred (defined below) that may not be converted due to the Series B Blocker (defined below).

The Reporting Persons may choose to convert the Series A Preferred or the Series B Preferred in other amounts among the Reporting Persons, while continuing to comply with the Beneficial Ownership Limitation (defined below). See Item 4(a) for a full description of the Reporting Person's beneficial ownership.

1	NAME OF REPORTING PERSON Mark N. Lampert	
2	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (a) <input checked="" type="checkbox"/> (b) <input type="checkbox"/>	
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 1,815,146*
	7	SOLE DISPOSITIVE POWER 0 shares
	8	SHARED DISPOSITIVE POWER 1,815,146*
9	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON 1,815,146*	
10	CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES <input type="checkbox"/>	
11	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (9) 9.99%*	
12	TYPE OF REPORTING PERSON IN	

* Includes 972,000 shares of Common Stock currently issuable upon the conversion of certain Series A Preferred (defined below). Excludes 1,248,000 shares of Common Stock underlying certain Series A Preferred that may not be converted due to the Series A Blocker (defined below).

Excludes 1,000,000 shares of Common Stock underlying certain Series B Preferred (defined below) that may not be converted due to the Series B Blocker (defined below).

The Reporting Persons may choose to convert the Series A Preferred or the Series B Preferred in other amounts among the Reporting Persons, while continuing to comply with the Beneficial Ownership Limitation (defined below). See Item 4(a) for a full description of the Reporting Person's beneficial ownership.

Item 1(a). Name of Issuer:
Spero Therapeutics, Inc., a Delaware corporation (the "Issuer").

Item 1(b). Address of Issuer's Principal Executive Offices:

675 Massachusetts Avenue, 14th Floor
Cambridge, Massachusetts 02139

Item 2(a). Name of Person Filing

Item 2(b). Address of Principal Business Office or, if None, Residence

Item 2(c). Citizenship

Biotechnology Value Fund, L.P. ("BVF")
44 Montgomery St., 40th Floor
San Francisco, California 94104
Citizenship: Delaware

Biotechnology Value Fund II, L.P. ("BVF2")
44 Montgomery St., 40th Floor
San Francisco, California 94104
Citizenship: Delaware

Biotechnology Value Trading Fund OS LP ("Trading Fund OS")
PO Box 309 Uglan House
Grand Cayman, KY1-1104
Cayman Islands
Citizenship: Cayman Islands

BVF Partners OS Ltd. ("Partners OS")
PO Box 309 Uglan House
Grand Cayman, KY1-1104
Cayman Islands
Citizenship: Cayman Islands

BVF Partners L.P. ("Partners")
44 Montgomery St., 40th Floor
San Francisco, California 94104
Citizenship: Delaware

BVF Inc.
44 Montgomery St., 40th Floor
San Francisco, California 94104
Citizenship: Delaware

Mark N. Lampert ("Mr. Lampert")
44 Montgomery St., 40th Floor
San Francisco, California 94104
Citizenship: United States

Each of the foregoing is referred to as a "Reporting Person" and collectively as the "Reporting Persons."

Item 2(d). Title of Class of Securities:
Common Stock, \$0.001 par value (the "Common Stock")

Item 2(e). CUSIP Number:
84833T103

Item 3. If This Statement is Filed Pursuant to Rule 13d-1(b), or 13d-2(b) or (c), Check Whether the Person Filing is a:

- /x/ Not applicable.
- (a) // Broker or dealer registered under Section 15 of the Exchange Act.
- (b) // Bank as defined in Section 3(a)(6) of the Exchange Act.
- (c) // Insurance company as defined in Section 3(a)(19) of the Exchange Act.
- (d) // Investment company registered under Section 8 of the Investment Company Act.
- (e) // An investment adviser in accordance with Rule 13d-1(b)(1)(ii)(E).
- (f) // An employee benefit plan or endowment fund in accordance with Rule 13d-1(b)(1)(ii)(F).
- (g) // A parent holding company or control person in accordance with Rule 13d-1(b)(1)(ii)(G).
- (h) // A savings association as defined in Section 3(b) of the Federal Deposit Insurance Act.
- (i) // A church plan that is excluded from the definition of an investment company under Section 3(c)(14) of the Investment Company Act.
- (j) // Group, in accordance with Rule 13d-1(b)(1)(ii)(J).
- (k) // Group, in accordance with Rule 240.13d-1(b)(1)(ii)(K). If filing as a non-U.S. institution in accordance with Rule 240.13d-1(b)(1)(ii)(J), please specify the type of institution: _____

Item 4. Ownership

(a) Amount beneficially owned:

As of the close of business on December 31, 2018, the Reporting Persons held 2,220 shares of Series A Convertible Preferred Stock (the "Series A Preferred"), convertible for an aggregate of 2,220,000 shares of Common Stock. The Series A Preferred may not be converted if, after such conversion, the Reporting Persons would beneficially own, as determined in accordance with Section 13(d) of the Securities Exchange Act of 1934 (the "Exchange Act"), more than 9.99% of the number of shares of Common Stock then issued and outstanding (the "Series A Blocker"). As of the close of business on December 31, 2018, the Series A Blocker limits the aggregate conversion of Series A Preferred by the Reporting Persons to 972,000 out of the 2,220,000 shares of Common Stock underlying the Series A Preferred owned by the Reporting Persons in the aggregate. In providing beneficial ownership described herein, the Reporting Persons have assumed that certain Series A Preferred held by BVF to acquire 972,000 shares of Common Stock would be converted, which would bring the Reporting Persons to the aggregate 9.99% limitation, and the remaining Series A Preferred convertible into 1,248,000 shares of Common Stock owned by the Reporting Persons in the aggregate would not be converted due to the Series A Blocker.

As of the close of business on December 31, 2018, the Reporting Persons held 1,000 shares of Series B Convertible Preferred Stock (the "Series B Preferred") convertible for an aggregate of 1,000,000 shares of Common Stock. The Series B Preferred may not be converted if, after such conversion, the Reporting Persons would beneficially own, as determined in accordance with Section 13(d) Exchange Act, more than 9.99% of the number of shares of Common Stock then issued and outstanding (the "Series B Blocker" and together with the "Series A Blocker", the "Beneficial Ownership Limitation"). As of the close of business on December 31, 2018, the Series B Blocker limits the aggregate conversion of Series B Preferred by the Reporting Persons to 0 out of the 1,000,000 shares of Common Stock underlying the Series B Preferred owned by the Reporting Persons in the aggregate.

The Reporting Persons may choose to convert the Series A Preferred or the Series B in other amounts among the Reporting Persons, while continuing to comply with the Beneficial Ownership Limitation.

As of the close of business on December 31, 2018 (i) BVF beneficially owned 1,404,711 shares of Common Stock, (ii) BVF2 beneficially owned 298,102 shares of Common Stock, and (iii) Trading Fund OS beneficially owned 60,345 shares of Common Stock.

Partners OS, as the general partner of Trading Fund OS, may be deemed to beneficially own the 60,345 shares of Common Stock beneficially owned by Trading Fund OS.

Partners, as the general partner of BVF, BVF2, the investment manager of Trading Fund OS, and the sole member of Partners OS, may be deemed to beneficially own the 1,815,146 shares of Common Stock beneficially owned in the aggregate by BVF, BVF2, Trading Fund OS, and certain Partners managed accounts (the "Partners Managed Accounts"), including 51,988 shares of Common Stock, which excludes 213,000 shares of Common Stock underlying the Series A Preferred and 62,000 shares of Common Stock underlying the Series B Preferred, held in the Partners Managed Accounts.

BVF Inc., as the general partner of Partners, may be deemed to beneficially own the 1,815,146 shares of Common Stock beneficially owned by Partners.

Mr. Lampert, as a director and officer of BVF Inc., may be deemed to beneficially own the 1,815,146 shares of Common Stock beneficially owned by BVF Inc.

The foregoing should not be construed in and of itself as an admission by any Reporting Person as to beneficial ownership of any shares of Common Stock owned by another Reporting Person. Partners OS disclaims beneficial ownership of the shares of Common Stock beneficially owned by Trading Fund OS. Each of Partners, BVF Inc. and Mr. Lampert disclaims beneficial ownership of the shares of Common Stock beneficially owned by BVF, BVF2, Trading Fund OS, and the Partners Managed Accounts, and the filing of this statement shall not be construed as an admission that any such person or entity is the beneficial owner of any such securities.

(b) Percent of class:

The following percentages are based on a denominator that is the sum of (i) 17,205,962 shares of Common Stock outstanding as disclosed in the Issuer's Form S-3 filed with the SEC on December 3, 2018 and (ii) 972,000 shares of Common Stock issuable upon the conversion of certain Series A Preferred, as applicable.

As of the close of business on December 31, 2018 (i) BVF beneficially owned approximately 7.7% of the outstanding shares of Common Stock, (ii) BVF2 beneficially owned approximately 1.7% of the outstanding shares of Common Stock, (iii) Trading Fund OS beneficially owned less than 1% of the outstanding shares of Common Stock, (iv) Partners OS may be deemed to beneficially own less than 1% of the outstanding shares of Common Stock, and (v) each of Partners, BVF Inc. and Mr. Lampert may be deemed to beneficially own approximately 9.99% of the outstanding shares of Common Stock (less than 1% of which is held in the Partners Managed Accounts).

(c) Number of shares as to which such person has:

(i) Sole power to vote or to direct the vote

See Cover Pages Items 5-9.

(ii) Shared power to vote or to direct the vote

See Cover Pages Items 5-9.

(iii) Sole power to dispose or to direct the disposition of

See Cover Pages Items 5-9.

(iv) Shared power to dispose or to direct the disposition of

See Cover Pages Items 5-9.

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.

Partners, BVF Inc. and Mr. Lampert share voting and dispositive power over the shares of Common Stock beneficially owned by BVF, BVF2, Trading Fund OS, and the Partners Managed Accounts.

Item 7. Identification and Classification of the Subsidiary That 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.

See Exhibit 99.1 to the Schedule 13G filed by the Reporting Persons with the Securities and Exchange Commission on November 9, 2017.

Item 9. Notice of Dissolution of Group.

Not Applicable.

Item 10. Certifications.

By signing below each of the undersigned certifies that, to the best of its 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 his knowledge and belief, each of the undersigned certifies that the information set forth in this statement is true, complete and correct.

Dated: February 14, 2019

BIOTECHNOLOGY VALUE FUND, L.P.

By: BVF Partners L.P., its general partner
By: BVF Inc., its general partner

By: /s/ Mark N. Lampert
Mark N. Lampert
President

BVF INC.

By: /s/ Mark N. Lampert
Mark N. Lampert
President

/s/ Mark N. Lampert
MARK N. LAMPERT

BIOTECHNOLOGY VALUE FUND II, L.P.

By: BVF Partners L.P., its general partner
By: BVF Inc., its general partner

By: /s/ Mark N. Lampert
Mark N. Lampert
President

BVF PARTNERS L.P.

By: BVF Inc., its general partner

By: /s/ Mark N. Lampert
Mark N. Lampert
President

BVF PARTNERS OS LTD.

By: BVF Partners L.P., its sole member
By: BVF Inc., its general partner

By: /s/ Mark N. Lampert
Mark N. Lampert
President

BIOTECHNOLOGY VALUE TRADING FUND OS LP

By: BVF Partners L.P., its investment manager
By: BVF Inc., its general partner

By: /s/ Mark N. Lampert
Mark N. Lampert
President