

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. 2)<sup>1</sup>

Protagonist Therapeutics, Inc.  
(Name of Issuer)

Common Stock, \$0.00001 par value  
(Title of Class of Securities)

74366E102  
(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)

<sup>1</sup> 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  1,247,629(1)
	7	SOLE DISPOSITIVE POWER  0 shares
	8	SHARED DISPOSITIVE POWER  1,247,629(1)
9	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON  1,247,629(1)	
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)  5.1%(1)	
12	TYPE OF REPORTING PERSON  PN	

(1) Includes 288,771 shares of Common Stock underlying certain A Warrants (defined in Item 4) owned by BVF. The A Warrants are subject to the A Warrants Blocker (defined in Item 4).

Includes 237,931 shares of Common Stock underlying certain B Warrants (defined in Item 4) owned by BVF. Excludes 50,839 shares of Common Stock underlying certain B Warrants owned by BVF, as a result of the B Warrants Blocker (defined in Item 4). As of the close of business on December 31, 2018, the B Warrants Blocker limits the aggregate exercise of B Warrants by the Reporting Persons to 237,931 out of the 624,999 shares of Common Stock underlying the B Warrants owned by the Reporting Persons in the aggregate.

Excludes 500,000 shares of Common Stock underlying certain New Warrants (defined in Item 4) owned by BVF, as a result of the New Warrants Blocker (defined in Item 4). As of the close of business on December 31, 2018, the New Warrants Blocker limits the aggregate exercise of New Warrants by the Reporting Persons to 0 out of the 1,000,000 shares of Common Stock underlying the New Warrants owned by the Reporting Persons in the aggregate.

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  785,039(1)
	7	SOLE DISPOSITIVE POWER  0 shares
	8	SHARED DISPOSITIVE POWER  785,039(1)
9	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON  785,039(1)	
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)  3.2%(1)	
12	TYPE OF REPORTING PERSON  PN	

(1) Includes 227,228 shares of Common Stock underlying certain A Warrants (defined in Item 4) owned by BVF2. The A Warrants are subject to the A Warrants Blocker (defined in Item 4).

Excludes 227,227 shares of Common Stock underlying certain B Warrants (defined in Item 4) owned by BVF2, as a result of the B Warrants Blocker (defined in Item 4). As of the close of business on December 31, 2018, the B Warrants Blocker limits the aggregate exercise of B Warrants by the Reporting Persons to 237,931 out of the 624,999 shares of Common Stock underlying the B Warrants owned by the Reporting Persons in the aggregate.

Excludes 410,000 shares of Common Stock underlying certain New Warrants (defined in Item 4) owned by BVF2, as a result of the New Warrants Blocker (defined in Item 4). As of the close of business on December 31, 2018, the New Warrants Blocker limits the aggregate exercise of New Warrants by the Reporting Persons to 0 out of the 1,000,000 shares of Common Stock underlying the Warrants owned by the Reporting Persons in the aggregate.

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  153,328(1)
	7	SOLE DISPOSITIVE POWER  0 shares
	8	SHARED DISPOSITIVE POWER  153,328(1)
9	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON  153,328(1)	
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%(1)	
12	TYPE OF REPORTING PERSON  PN	

(1) Includes 44,132 shares of Common Stock underlying certain A Warrants (defined in Item 4) owned by Trading Fund OS. The A Warrants are subject to the A Warrants Blocker (defined in Item 4).

Excludes 44,132 shares of Common Stock underlying certain B Warrants (defined in Item 4) owned by Trading Fund OS, as a result of the B Warrants Blocker (defined in Item 4). As of the close of business on December 31, 2018, the B Warrants Blocker limits the aggregate exercise of B Warrants by the Reporting Persons to 237,931 out of the 624,999 shares of Common Stock underlying the B Warrants owned by the Reporting Persons in the aggregate.

Excludes 90,000 shares of Common Stock underlying certain New Warrants (defined in Item 4) owned by Trading Fund OS, as a result of the New Warrants Blocker (defined in Item 4). As of the close of business on December 31, 2018, the New Warrants Blocker limits the aggregate exercise of New Warrants by the Reporting Persons to 0 out of the 1,000,000 shares of Common Stock underlying the New Warrants owned by the Reporting Persons in the aggregate.

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 153,328(1)
	7	SOLE DISPOSITIVE POWER 0 shares
	8	SHARED DISPOSITIVE POWER 153,328(1)
9	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON 153,328(1)	
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%(1)	
12	TYPE OF REPORTING PERSON CO	

(1) Includes 44,132 shares of Common Stock underlying certain A Warrants (defined in Item 4) owned by Trading Fund OS. The A Warrants are subject to the A Warrants Blocker (defined in Item 4).

Excludes 44,132 shares of Common Stock underlying certain B Warrants (defined in Item 4) owned by Trading Fund OS, as a result of the B Warrants Blocker (defined in Item 4). As of the close of business on December 31, 2018, the B Warrants Blocker limits the aggregate exercise of B Warrants by the Reporting Persons to 237,931 out of the 624,999 shares of Common Stock underlying the B Warrants owned by the Reporting Persons in the aggregate.

Excludes 90,000 shares of Common Stock underlying certain New Warrants (defined in Item 4) owned by Trading Fund OS, as a result of the New Warrants Blocker (defined in Item 4). As of the close of business on December 31, 2018, the New Warrants Blocker limits the aggregate exercise of New Warrants by the Reporting Persons to 0 out of the 1,000,000 shares of Common Stock underlying the New Warrants owned by the Reporting Persons in the aggregate.

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 2,502,390(1)
	7	SOLE DISPOSITIVE POWER 0 shares
	8	SHARED DISPOSITIVE POWER 2,502,390(1)
9	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON 2,502,390(1)	
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%(1)	
12	TYPE OF REPORTING PERSON PN, IA	

(1) Includes 625,001 shares of Common Stock underlying certain A Warrants (defined in Item 4) owned by the Reporting Persons. The A Warrants are subject to the A Warrants Blocker (defined in Item 4).

Includes 237,931 shares of Common Stock underlying certain B Warrants (defined in Item 4) owned by the Reporting Persons. Excludes 387,068 shares of Common Stock underlying certain B Warrants owned by the Reporting Persons, as a result of the B Warrants Blocker (defined in Item 4). As of the close of business on December 31, 2018, the B Warrants Blocker limits the aggregate exercise of B Warrants by the Reporting Persons to 237,931 out of the 624,999 shares of Common Stock underlying the B Warrants owned by the Reporting Persons in the aggregate.

Excludes 1,000,000 shares of Common Stock underlying certain New Warrants (defined in Item 4) owned by the Reporting Persons, as a result of the New Warrants Blocker (defined in Item 4). As of the close of business on December 31, 2018, the New Warrants Blocker limits the aggregate exercise of New Warrants by the Reporting Persons to 0 out of the 1,000,000 shares of Common Stock underlying the New Warrants owned by the Reporting Persons in the aggregate.

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 2,502,390(1)
	7	SOLE DISPOSITIVE POWER 0 shares
	8	SHARED DISPOSITIVE POWER 2,502,390(1)
9	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON 2,502,390(1)	
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%(1)	
12	TYPE OF REPORTING PERSON CO	

(1) Includes 625,001 shares of Common Stock underlying certain A Warrants (defined in Item 4) owned by the Reporting Persons. The A Warrants are subject to the A Warrants Blocker (defined in Item 4).

Includes 237,931 shares of Common Stock underlying certain B Warrants (defined in Item 4) owned by the Reporting Persons. Excludes 387,068 shares of Common Stock underlying certain B Warrants owned by the Reporting Persons, as a result of the B Warrants Blocker (defined in Item 4). As of the close of business on December 31, 2018, the B Warrants Blocker limits the aggregate exercise of B Warrants by the Reporting Persons to 237,931 out of the 624,999 shares of Common Stock underlying the B Warrants owned by the Reporting Persons in the aggregate.

Excludes 1,000,000 shares of Common Stock underlying certain New Warrants (defined in Item 4) owned by the Reporting Persons, as a result of the New Warrants Blocker (defined in Item 4). As of the close of business on December 31, 2018, the New Warrants Blocker limits the aggregate exercise of New Warrants by the Reporting Persons to 0 out of the 1,000,000 shares of Common Stock underlying the New Warrants owned by the Reporting Persons in the aggregate.

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  2,502,390(1)
	7	SOLE DISPOSITIVE POWER  0 shares
	8	SHARED DISPOSITIVE POWER  2,502,390(1)
9	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON  2,502,390(1)	
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%(1)	
12	TYPE OF REPORTING PERSON  IN	

(1) Includes 625,001 shares of Common Stock underlying certain A Warrants (defined in Item 4) owned by the Reporting Persons. The A Warrants are subject to the A Warrants Blocker (defined in Item 4).

Includes 237,931 shares of Common Stock underlying certain B Warrants (defined in Item 4) owned by the Reporting Persons. Excludes 387,068 shares of Common Stock underlying certain B Warrants owned by the Reporting Persons, as a result of the B Warrants Blocker (defined in Item 4). As of the close of business on December 31, 2018, the B Warrants Blocker limits the aggregate exercise of B Warrants by the Reporting Persons to 237,931 out of the 624,999 shares of Common Stock underlying the B Warrants owned by the Reporting Persons in the aggregate.

Excludes 1,000,000 shares of Common Stock underlying certain New Warrants (defined in Item 4) owned by the Reporting Persons, as a result of the New Warrants Blocker (defined in Item 4). As of the close of business on December 31, 2018, the New Warrants Blocker limits the aggregate exercise of New Warrants by the Reporting Persons to 0 out of the 1,000,000 shares of Common Stock underlying the New Warrants owned by the Reporting Persons in the aggregate.

See Item 4(a) for a full description of the Reporting Person's beneficial ownership.



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

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

7707 Gateway Boulevard, Suite 140  
Newark, California 94560

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., 40<sup>th</sup> Floor  
San Francisco, California 94104

Citizenship: Delaware

Biotechnology Value Fund II, L.P. ("BVF2")

44 Montgomery St., 40<sup>th</sup> 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., 40<sup>th</sup> Floor  
San Francisco, California 94104

Citizenship: Delaware

BVF Inc.

44 Montgomery St., 40<sup>th</sup> Floor  
San Francisco, California 94104

Citizenship: Delaware

Mark N. Lampert ("Mr. Lampert")

44 Montgomery St., 40<sup>th</sup> 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, \$0.00001 par value (the "Common Stock")

Item 2(e). CUSIP Number:  
74366E102

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:

The Reporting Persons hold 625,001 Class A Warrants (the "A Warrants") exercisable for an aggregate of 625,001 shares of Common Stock. The A Warrants have an exercise price of \$10 per share and expire on August 8, 2023. The A Warrants may not be exercised if, after such exercise, the Reporting Persons would beneficially own, as determined in accordance with Section 13(d) of the Exchange Act, more than 9.99% of the number of shares of Common Stock then issued and outstanding (the "A Warrants Blocker"). In providing beneficial ownership described herein, the Reporting Persons have assumed the A Warrants owned by each of BVF, BVF2 and Trading Fund OS and held in Partners managed accounts (the "Partners Managed Accounts") would be fully exercised.

In addition to the A Warrants, the Reporting Persons hold 624,999 Class B Warrants (the “B Warrants”) exercisable for an aggregate of 624,999 shares of Common Stock. The B Warrants have an exercise price of \$15 per share and expire on August 8, 2023. The B Warrants may not be exercised if, after such exercise, the Reporting Persons would beneficially own, as determined in accordance with Section 13(d) of the Exchange Act, more than 9.99% of the number of shares of Common Stock then issued and outstanding (the “B Warrants Blocker”). As of the close of business on December 31, 2018, the B Warrants Blocker limits the aggregate exercise of B Warrants by the Reporting Persons to 237,931 out of the 624,999 shares of Common Stock underlying the B Warrants owned by the Reporting Persons in the aggregate. In providing beneficial ownership described herein, the Reporting Persons have assumed that 237,931 of certain B Warrants owned by BVF have been exercised and the remaining B Warrants owned by BVF, BVF2 and Trading Fund OS and held in the Partners Managed Accounts would not be exercised due to the B Warrants Blocker.

In addition to the A and B Warrants, the Reporting Persons hold 1,000,000 Warrants (the “New Warrants”) exercisable for an aggregate of 1,000,000 shares of Common Stock. The New Warrants are pre-funded warrants and have an exercise price of \$0.00001 per share and expire on December 21, 2028. The New Warrants may not be exercised if, after such exercise, the Reporting Persons would beneficially own, as determined in accordance with Section 13(d) of the Exchange Act, more than 9.99% of the number of shares of Common Stock then issued and outstanding (the “New Warrants Blocker”). As of the close of business on December 31, 2018, the New Warrants Blocker limits the aggregate exercise of New Warrants by the Reporting Persons to 0 out of the 1,000,000 shares of Common Stock underlying the New Warrants owned by the Reporting Persons in the aggregate. In providing beneficial ownership described herein, the Reporting Persons have assumed the New Warrants owned by each of BVF, BVF2 and Trading Fund OS and held in the Partners Managed Accounts would not be exercised due to the New Warrants Blocker.

As of the close of business on December 31, 2018 (i) BVF beneficially owned 1,247,629 shares of Common Stock, including (a) 288,771 shares of Common Stock underlying certain A Warrants held by it and (b) 237,931 shares of Common Stock underlying certain B Warrants held by it, and excluding (a) 50,839 shares of Common Stock underlying certain B Warrants held by it and (b) 500,000 shares of Common Stock underlying certain New Warrants held by it; (ii) BVF2 beneficially owned 785,039 shares of Common Stock, including 227,228 shares of Common Stock underlying certain A Warrants held by it, and excluding (a) 227,227 shares of Common Stock underlying certain B Warrants held by it and (b) 410,000 shares of Common Stock underlying certain New Warrants held by it; and (iii) Trading Fund OS beneficially owned 153,328 shares of Common Stock, including 44,132 shares of Common Stock underlying certain A Warrants held by it, and excluding (a) 44,132 shares of Common Stock underlying certain B Warrants held by it and (b) 90,000 shares of Common Stock underlying certain New Warrants held by it.

Partners OS, as the general partner of Trading Fund OS, may be deemed to beneficially own the 153,328 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 2,502,390 shares of Common Stock beneficially owned in the aggregate by BVF, BVF2, Trading Fund OS, including 316,394 shares of Common Stock held in the Partners Managed Accounts, which includes 64,870 shares of Common Stock underlying certain A Warrants and excludes 64,870 shares of Common Stock underlying certain B Warrants.

BVF Inc., as the general partner of Partners, may be deemed to beneficially own the 2,502,390 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 2,502,390 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 held in 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 which is the sum of: (i) 24,186,019 shares of Common Stock outstanding, as of October 31, 2018, which is the total number of shares of Common Stock outstanding as disclosed in the Issuer's Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission on November 6, 2018, (ii) certain or all of the 625,001 shares of Common Stock underlying the A Warrants, as applicable, and (iii) 237,931 shares of Common Stock underlying the B Warrants, as applicable.

As of the close of business on December 31, 2018 (i) BVF beneficially owned approximately 5.1% of the outstanding shares of Common Stock, (ii) BVF2 beneficially owned approximately 3.2% 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 (1.3% of the outstanding shares of Common Stock are 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 with the Securities and Exchange Commission on May 24, 2018.

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