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

SCHEDULE 13D
Under the Securities Exchange Act of 1934
(Amendment No. 4)*

PIERIS PHARMACEUTICALS, INC.

(Name of Issuer)

COMMON STOCK

(Title of Class of Securities)

720795103

(CUSIP Number)

**OrbiMed Advisors LLC
OrbiMed Capital GP III LLC**

**601 Lexington Avenue, 54th Floor
New York, NY 10022
Telephone: (212) 739-6400**

(Name, Address and Telephone Number of Person
Authorized to Receive Notices and Communications)

(Name, Address and Telephone Number of Person Authorized
to Receive Notices and Communications)

February 16, 2018

(Date of Event Which Requires Filing of this Statement)

If the filing person has previously filed a statement on Schedule 13G to report the acquisition that is the subject of this Schedule 13D, and is filing this schedule because of § 240.13d-1(e), 240.13d-1(f) or 240.13d-1(g), check the following box .

Note: Schedules filed in paper format shall include a signed original and five copies of the schedule, including all exhibits. See § 240.13d-7(b) for other parties to whom copies are to be sent.

*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).

CUSIP No. 720795103

1	NAME OF REPORTING PERSONS OrbiMed Advisors LLC	
2	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (a) <input type="checkbox"/> (b) <input checked="" type="checkbox"/>	
3	SEC USE ONLY	
4	SOURCE OF FUNDS AF	
5	CHECK BOX IF DISCLOSURE OF LEGAL PROCEEDINGS IS REQUIRED PURSUANT TO ITEMS 2(d) or 2(e) <input type="checkbox"/>	
6	CITIZENSHIP OR PLACE OF ORGANIZATION Delaware	
NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH	7	SOLE VOTING POWER 0
	8	SHARED VOTING POWER 5,550,000*
	9	SOLE DISPOSITIVE POWER 0
	10	SHARED DISPOSITIVE POWER 5,550,000*
11	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON 5,550,000*	
12	CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (11) EXCLUDES CERTAIN SHARES (See Instructions) <input type="checkbox"/>	
13	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (11) 10.88%*	
14	TYPE OF REPORTING PERSON (See Instructions) IA	

* This percentage is calculated based upon 51,029,849 shares of common stock, par value \$0.001 per share (the "Shares"), outstanding of Pieris Pharmaceuticals, Inc., a Nevada corporation (the "Issuer"), as set forth in the Issuer's Form 8-K filed with the Securities and Exchange Commission (the "SEC") on February 20, 2018.

CUSIP No. 720795103	
1	NAME OF REPORTING PERSONS OrbiMed Capital GP III LLC
2	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (a) <input type="checkbox"/> (b) <input checked="" type="checkbox"/>
3	SEC USE ONLY
4	SOURCE OF FUNDS AF
5	CHECK BOX IF DISCLOSURE OF LEGAL PROCEEDINGS IS REQUIRED PURSUANT TO ITEMS 2(d) or 2(e) <input checked="" type="checkbox"/>
6	CITIZENSHIP OR PLACE OF ORGANIZATION Delaware
NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH	7 SOLE VOTING POWER 0
	8 SHARED VOTING POWER 5,500,730*
	9 SOLE DISPOSITIVE POWER 0
	10 SHARED DISPOSITIVE POWER 5,500,730*
11	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON 5,500,730*
12	CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (11) EXCLUDES CERTAIN SHARES (See Instructions) <input checked="" type="checkbox"/>
13	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (11) 10.78%*
14	TYPE OF REPORTING PERSON (See Instructions) OO

* This percentage is calculated based upon 51,029,849 shares of common stock, par value \$0.001 per share (the “Shares”), outstanding of Pieris Pharmaceuticals, Inc., a Nevada corporation (the “Issuer”), as set forth in the Issuer’s Form 8-K filed with the Securities and Exchange Commission (the “SEC”) on February 20, 2018.

Item 1. Security and Issuer

This Amendment No. 4 (“Amendment No. 4”) to Schedule 13D supplements and amends the Statement on Schedule 13D of OrbiMed Advisors LLC and OrbiMed Capital GP III LLC (the “Statement”) originally filed with the Securities and Exchange Commission (the “SEC”) on July 9, 2015 with Samuel D. Isaly as an additional reporting person, and amended by Amendment No. 1 thereto filed with the SEC on July 12, 2016, Amendment No. 2 thereto filed with the SEC on January 5, 2018 and Amendment No. 3 on January 25, 2018. The Statement relates to the common stock, par value \$0.001 per share (the “Shares”), of Pieris Pharmaceuticals, Inc., a corporation organized under the laws of Nevada (the “Issuer”), with its principal executive offices located at 255 State Street, 9th Floor, Boston, MA 02109. The Shares are listed on the NASDAQ Global Market under the ticker symbol “PIRS”. Information given in response to each item shall be deemed incorporated by reference in all other items, as applicable.

On February 16, 2018, the Issuer closed a direct registered offering announced on February 13, 2018. The Issuer issued in the offering a total of 5,500,000 Shares at a purchase price of \$8.00 per share with gross proceeds of \$44,000,000 (the “Share Issuance”). None of the Reporting Persons participated in the offering. As a result of the Share Issuance, the percentage of outstanding Shares that the Reporting Persons may be deemed to beneficially own was reduced by more than one percent of the Issuer’s Shares outstanding since the filing of Amendment No. 3 to the Statement.

Item 2. Identity and Background

(a) This Statement is being filed by OrbiMed Advisors LLC (“Advisors”), a limited liability company organized under the laws of Delaware, and OrbiMed Capital GP III LLC (“GP III”), a limited liability company organized under the laws of Delaware (collectively, the “Reporting Persons”).

(b) – (c), (f) Advisors, a registered investment adviser under the Investment Advisers Act of 1940, as amended, is the sole general partner of OrbiMed Associates III, LP (“Associates III”) and the sole managing member of GP III, which is the sole general partner of OrbiMed Private Investments III, LP (“OPI III”). OPI III and Associates III hold Shares as described herein. Advisors, GP III has its principal offices at 601 Lexington Avenue, 54th Floor, New York, New York 10022.

The directors and executive officers of Advisors and GP III are set forth on Schedules I and II, attached hereto. Schedules I and II set forth the following information with respect to each such person:

- (i) name;
- (ii) business address;
- (iii) present principal occupation or employment and the name, principal business and address of any corporation or other organization in which such employment is conducted;
- (iv) citizenship.

(d) – (e) During the last five years, neither the Reporting Persons nor any Person named in Schedule I or II have been (i) convicted in a criminal proceeding (excluding traffic violations or similar misdemeanors) or (ii) a party to a civil proceeding of a judicial or administrative body of competent jurisdiction and as a result of such proceeding was or is subject to a judgment, decree or final order enjoining future violations of, or prohibiting or mandating activities subject to, federal or state securities laws or finding any violation with respect to such laws.

Item 3. Source and Amount of Funds or Other Consideration

Not applicable.

Item 4. Purpose of Transaction

The Shares initially had been acquired by the Reporting Persons for the purpose of making an investment in the Issuer and not with the intention of acquiring control of the Issuer's business.

The Reporting Persons from time to time intend to review their investment in the Issuer on the basis of various factors, including the Issuer's business, financial condition, results of operations and prospects, general economic and industry conditions, the securities markets in general and those for the Issuer's common stock in particular, as well as other developments and other investment opportunities. Based upon such review, the Reporting Persons will take such actions in the future as the Reporting Persons may deem appropriate in light of the circumstances existing from time to time. If the Reporting Persons believe that further investment in the Issuer is attractive, whether because of the market price of the common stock or otherwise, they may acquire Shares or other securities of the Issuer either in the open market or in privately negotiated transactions. Similarly, depending on market and other factors, the Reporting Persons may determine to dispose of some or all of the Shares currently owned by the Reporting Persons or otherwise acquired by the Reporting Persons either in the open market or in privately negotiated transactions.

Except as set forth in this Statement, the Reporting Persons have not formulated any plans or proposals which relate to or would result in: (a) the acquisition by any person of additional securities of the Issuer or the disposition of securities of the Issuer, (b) an extraordinary corporate transaction, such as a merger, reorganization or liquidation, involving the Issuer or any of its subsidiaries, (c) a sale or transfer of a material amount of the assets of the Issuer or any of its subsidiaries, (d) any change in the present Board of Directors or management of the Issuer, including any plans or proposals to change the number or term of directors or to fill any existing vacancies on the board, (e) any material change in the Issuer's capitalization or dividend policy of the Issuer, (f) any other material change in the Issuer's business or corporate structure, (g) any change in the Issuer's charter or bylaws or other instrument corresponding thereto or other action which may impede the acquisition of control of the Issuer by any person, (h) causing a class of the Issuer's securities to be deregistered or delisted from a national securities exchange or to cease to be authorized to be quoted in an inter-dealer quotation system of a registered national securities association, (i) a class of equity securities of the Issuer becoming eligible for termination of registration pursuant to Section 12(g)(4) of the Act or (j) any action similar to any of those enumerated above.

Item 5. Interest in Securities of the Issuer

(a) – (b) As of the date of this filing, the Reporting Persons may be deemed, for purposes of Rule 13d-3 of the Act, directly or indirectly, including by reason of their mutual affiliation, to be the beneficial owners of the Shares. Based upon information contained in the Issuer's Form 8-K filed with the SEC on February 20, 2018, such Shares deemed to be indirectly beneficially owned by GP III constitutes approximately 10.78% of the issued and outstanding Shares, and such Shares deemed to be indirectly beneficially owned by Advisors constitutes approximately 10.88% of the issued and outstanding Shares. Advisors, pursuant to its authority as the sole managing member of GP III, which is the sole general partner of OPI III, and as the sole general partner of Associates III, may be deemed to indirectly beneficially own the Shares held by OPI III and Associates III. GP III, pursuant to its authority as the general partner of OPI III, may be deemed to indirectly beneficially own the Shares held by OPI III. As a result, Advisors and GP III share the power to direct the vote and the disposition of the Shares held by OPI III described in Item 6 below, and Advisors has the power to direct the vote and the disposition of the Shares held by Associates III. Advisors exercises this investment and voting power through a management committee comprised of Carl L. Gordon, Sven H. Borho and Jonathan T. Silverstein, each of whom disclaims beneficial ownership of the Shares held by OPI III and Associates III.

(c)

Seller	Date of Transaction	Transaction	Number of Shares	Price Per Share*
OPI III	February 13, 2018	Acquired upon the exercise of stock options	6,057	\$4.68
Associates III	February 13, 2018	Acquired upon the exercise of stock options	58	\$4.68
OPI III	February 13, 2018	Acquired upon the exercise of stock options	1,765	\$5.08
Associates III	February 13, 2018	Acquired upon the exercise of stock options	17	\$5.08
OPI III	February 13, 2018	Sold	7,822	\$8.98
Associates III	February 13, 2018	Sold	75	\$8.98

* The Shares were sold in a block order at a price of \$8.98 (February 13, 2018).

Except as disclosed above and in Amendment No. 2, the Reporting Persons have not effected any transactions in the Shares during the past sixty (60) days.

(d) Not applicable.

(e) Not applicable.

Item 6. Contracts, Arrangements, Understandings or Relationship with Respect to Securities of the Issuer

In addition to the relationships between the Reporting Persons described in Items 2 and 5 above, GP III is the sole general partner of OPI III, pursuant to the terms of the limited partnership agreement of OPI III. Advisors is the sole managing member of GP III, pursuant to the terms of the limited liability company agreement of GP III, and the sole general partner of Associates III, pursuant to the terms of the limited partnership agreement of Associates III. Pursuant to these agreements and relationships, Advisors and GP III have discretionary investment management authority with respect to the assets of OPI III, and Advisors has discretionary investment management authority with respect to the assets of Associates III. Such authority includes the power of GP III and Advisors to vote and otherwise dispose of securities purchased by OPI III, and the power of Advisors to vote and otherwise dispose of securities purchased by Associates III. The number of outstanding Shares held of record by OPI III is 5,500,730, and the number of outstanding Shares held of record by Associates III is 49,270. Advisors may be considered to hold indirectly 5,550,000 Shares, and GP III may be considered to hold indirectly 5,500,730 Shares.

Item 7. Materials to Be Filed as Exhibits

Exhibit 1 - Joint Filing Agreement among OrbiMed Advisors LLC and OrbiMed Capital GP III LLC.

SIGNATURE

After reasonable inquiry and to the best of each of the undersigned's knowledge and belief, each of the undersigned certifies that the information set forth in this statement is true, complete and correct.

Dated: February 21, 2018

OrbiMed Advisors LLC

By: /s/ Jonathan T. Silverstein
Name: Jonathan T. Silverstein
Title: Member of OrbiMed Advisors LLC

By: /s/ Sven H. Borho
Name: Sven H. Borho
Title: Member of OrbiMed Advisors LLC

By: /s/ Carl L. Gordon
Name: Carl L. Gordon
Title: Member of OrbiMed Advisors LLC

OrbiMed Capital GP III LLC

By: OrbiMed Advisors LLC
its Managing Member

By: /s/ Jonathan T. Silverstein
Name: Jonathan T. Silverstein
Title: Member of OrbiMed Advisors LLC

By: /s/ Sven H. Borho
Name: Sven H. Borho
Title: Member of OrbiMed Advisors LLC

By: /s/ Carl L. Gordon
Name: Carl L. Gordon
Title: Member of OrbiMed Advisors LLC

Schedule I

The name and present principal occupation of each of the executive officers and directors of OrbiMed Advisors LLC are set forth below. Unless otherwise noted, each of these persons are United States citizens and have as their business address 601 Lexington Avenue, 54th Floor, New York, NY 10022.

Name	Position with Reporting Person	Principal Occupation
Samuel D. Isaly	Managing Member	Managing Member OrbiMed Advisors LLC
Carl L. Gordon	Member	Member OrbiMed Advisors LLC
Sven H. Borho German and Swedish Citizen	Member	Member OrbiMed Advisors LLC
Jonathan T. Silverstein	Member	Member OrbiMed Advisors LLC
W. Carter Neild	Member	Member OrbiMed Advisors LLC
Geoffrey C. Hsu	Member	Member OrbiMed Advisors LLC
Evan D. Sotiriou	Chief Financial Officer	Chief Financial Officer OrbiMed Advisors LLC

Schedule II

The business and operations of OrbiMed Capital GP III LLC are managed by the executive officers and directors of its managing member, OrbiMed Advisors LLC, set forth on Schedule I.

JOINT FILING AGREEMENT

The undersigned hereby agree that the Statement on this Schedule 13D, dated February 21, 2018 (the "Schedule 13D"), with respect to the Common Stock, of Pieris Pharmaceuticals, Inc. is filed on behalf of each of us pursuant to and in accordance with the provisions of Rule 13d-1(k) under the Securities Exchange Act of 1934, as amended, and that this Agreement shall be included as an Exhibit to this Schedule 13D. Each of the undersigned agrees to be responsible for the timely filing of the Schedule 13D, and for the completeness and accuracy of the information concerning itself contained therein. This Agreement may be executed in any number of counterparts, all of which taken together shall constitute one and the same instrument.

IN WITNESS WHEREOF, the undersigned have executed this Agreement as of the 21st day of February 2018.

OrbiMed Advisors LLC

By: /s/ Jonathan T. Silverstein
Name: Jonathan T. Silverstein
Title: Member of OrbiMed Advisors LLC

By: /s/ Sven H. Borho
Name: Sven H. Borho
Title: Member of OrbiMed Advisors LLC

By: /s/ Carl L. Gordon
Name: Carl L. Gordon
Title: Member of OrbiMed Advisors LLC

OrbiMed Capital GP III LLC

By: OrbiMed Advisors LLC
its Managing Member

By: /s/ Jonathan T. Silverstein
Name: Jonathan T. Silverstein
Title: Member of OrbiMed Advisors LLC

By: /s/ Sven H. Borho
Name: Sven H. Borho
Title: Member of OrbiMed Advisors LLC

By: /s/ Carl L. Gordon
Name: Carl L. Gordon
Title: Member of OrbiMed Advisors LLC
