

## STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

OMB APPROVAL

OMB Number: 3235-0287

Estimated average burden

hours per response: 0.5

1. Name and Address of Reporting Person* <b>ORBIMED ADVISORS LLC</b>			2. Issuer Name and Ticker or Trading Symbol <b>PIERIS PHARMACEUTICALS, INC. [ PIRS ]</b>			5. Relationship of Reporting Person(s) to Issuer (Check all applicable) Director <input checked="" type="checkbox"/> 10% Owner Officer (give title below) Other (specify below)		
(Last)	(First)	(Middle)	3. Date of Earliest Transaction (Month/Day/Year) <b>12/18/2017</b>			6. Individual or Joint/Group Filing (Check Applicable Line) Form filed by One Reporting Person <input checked="" type="checkbox"/> Form filed by More than One Reporting Person		
<b>601 LEXINGTON AVENUE, 54TH FLOOR</b>			4. If Amendment, Date of Original Filed (Month/Day/Year)					
(Street)								
<b>NEW YORK</b>	<b>NY</b>	<b>10022</b>						
(City)	(State)	(Zip)						

Table I - Non-Derivative Securities Acquired, Disposed of, or Beneficially Owned

1. Title of Security (Instr. 3)	2. Transaction Date (Month/Day/Year)	2A. Deemed Execution Date, if any (Month/Day/Year)	3. Transaction Code (Instr. 8)		4. Securities Acquired (A) or Disposed Of (D) (Instr. 3, 4 and 5)			5. Amount of Securities Beneficially Owned Following Reported Transaction(s) (Instr. 3 and 4)	6. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	7. Nature of Indirect Beneficial Ownership (Instr. 4)
			Code	V	Amount	(A) or (D)	Price			
Common Stock	12/18/2017		M		27,241	A	\$2	7,221,463	I	See Footnotes <sup>(14)(16)</sup>
Common Stock	12/18/2017		M		259	A	\$2	65,657	I	See Footnotes <sup>(15)(16)</sup>
Common Stock	12/18/2017		M		5,227	A	\$3	7,226,690	I	See Footnotes <sup>(14)(16)</sup>
Common Stock	12/18/2017		M		50	A	\$3	65,707	I	See Footnotes <sup>(15)(16)</sup>
Common Stock	12/18/2017		M		6,654	A	\$2.62	7,233,344	I	See Footnotes <sup>(14)(16)</sup>
Common Stock	12/18/2017		M		63	A	\$2.62	65,770	I	See Footnotes <sup>(15)(16)</sup>
Common Stock	12/18/2017		M		8,717	A	\$1.94	7,242,061	I	See Footnotes <sup>(14)(16)</sup>
Common Stock	12/18/2017		M		83	A	\$1.94	65,853	I	See Footnotes <sup>(15)(16)</sup>
Common Stock	12/18/2017		M		10,180	A	\$1.62	7,252,241	I	See Footnotes <sup>(14)(16)</sup>
Common Stock	12/18/2017		M		97	A	\$1.62	65,950	I	See Footnotes <sup>(15)(16)</sup>
Common Stock	12/18/2017		M		19,811	A	\$1.59	7,272,052	I	See Footnotes <sup>(14)(16)</sup>
Common Stock	12/18/2017		M		189	A	\$1.59	66,139	I	See Footnotes <sup>(15)(16)</sup>
Common Stock	12/18/2017		M		8,097	A	\$2.05	7,280,149	I	See Footnotes <sup>(14)(16)</sup>
Common Stock	12/18/2017		M		77	A	\$2.05	66,216	I	See Footnotes <sup>(15)(16)</sup>
Common Stock	12/18/2017		M		9,642	A	\$1.73	7,289,791	I	See Footnotes <sup>(14)(16)</sup>
Common Stock	12/18/2017		M		92	A	\$1.73	66,308	I	See Footnotes <sup>(15)(16)</sup>
Common Stock	12/18/2017		M		10,182	A	\$1.64	7,299,973	I	See Footnotes <sup>(14)(16)</sup>
Common Stock	12/18/2017		M		97	A	\$1.64	66,405	I	See Footnotes <sup>(15)(16)</sup>
Common Stock	12/18/2017		M		14,858	A	\$2.01	7,314,831	I	See Footnotes <sup>(14)(16)</sup>

**Table I - Non-Derivative Securities Acquired, Disposed of, or Beneficially Owned**

1. Title of Security (Instr. 3)	2. Transaction Date (Month/Day/Year)	2A. Deemed Execution Date, if any (Month/Day/Year)	3. Transaction Code (Instr. 8)		4. Securities Acquired (A) or Disposed Of (D) (Instr. 3, 4 and 5)			5. Amount of Securities Beneficially Owned Following Reported Transaction(s) (Instr. 3 and 4)	6. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	7. Nature of Indirect Beneficial Ownership (Instr. 4)
			Code	V	Amount	(A) or (D)	Price			
Common Stock	12/18/2017		M		142	A	\$2.01	66,547	I	See Footnotes <sup>(15)(16)</sup>
Common Stock	12/18/2017		M		10,216	A	\$2.01	7,325,047	I	See Footnotes <sup>(14)(16)</sup>
Common Stock	12/18/2017		M		97	A	\$2.01	66,644	I	See Footnotes <sup>(15)(16)</sup>
Common Stock	12/18/2017		M		10,447	A	\$2.32	7,335,494	I	See Footnotes <sup>(14)(16)</sup>
Common Stock	12/18/2017		M		99	A	\$2.32	66,743	I	See Footnotes <sup>(15)(16)</sup>
Common Stock	12/18/2017		M		4,971	A	\$5.64	7,340,465	I	See Footnotes <sup>(14)(16)</sup>
Common Stock	12/18/2017		M		47	A	\$5.64	66,790	I	See Footnotes <sup>(15)(16)</sup>
Common Stock	12/18/2017		S		146,243	D	\$5.7	7,194,222	I	See Footnotes <sup>(14)(16)</sup>
Common Stock	12/18/2017		S		1,392	D	\$5.7	65,398	I	See Footnotes <sup>(15)(16)</sup>

**Table II - Derivative Securities Acquired, Disposed of, or Beneficially Owned (e.g., puts, calls, warrants, options, convertible securities)**

1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative Security	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transaction Code (Instr. 8)		5. Number of Derivative Securities Acquired (A) or Disposed of (D) (Instr. 3, 4 and 5)		6. Date Exercisable and Expiration Date (Month/Day/Year)		7. Title and Amount of Securities Underlying Derivative Security (Instr. 3 and 4)		8. Price of Derivative Security (Instr. 5)	9. Number of derivative Securities Beneficially Owned Following Reported Transaction(s) (Instr. 4)	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr. 4)
				Code	V	(A)	(D)	Date Exercisable	Expiration Date	Title	Amount or Number of Shares				
Stock Option (right to buy)	\$2	12/18/2017		M			27,241	(1)	02/15/2018	Common Stock	27,241	\$0	0	I	See Footnotes <sup>(14)(16)</sup>
Stock Option (right to buy)	\$2	12/18/2017		M			259	(1)	02/15/2018	Common Stock	259	\$0	0	I	See Footnotes <sup>(15)(16)</sup>
Stock Option (right to buy)	\$3	12/18/2017		M			5,227	(2)	02/15/2018	Common Stock	5,227	\$0	0	I	See Footnotes <sup>(14)(16)</sup>
Stock Option (right to buy)	\$3	12/18/2017		M			50	(2)	02/15/2018	Common Stock	50	\$0	0	I	See Footnotes <sup>(15)(16)</sup>
Stock Option (right to buy)	\$2.62	12/18/2017		M			6,654	(3)	02/15/2018	Common Stock	6,654	\$0	0	I	See Footnotes <sup>(14)(16)</sup>
Stock Option (right to buy)	\$2.62	12/18/2017		M			63	(3)	02/15/2018	Common Stock	63	\$0	0	I	See Footnotes <sup>(15)(16)</sup>
Stock Option (right to buy)	\$1.94	12/18/2017		M			8,717	(4)	02/15/2018	Common Stock	8,717	\$0	0	I	See Footnotes <sup>(14)(16)</sup>
Stock Option (right to buy)	\$1.94	12/18/2017		M			83	(4)	02/15/2018	Common Stock	83	\$0	0	I	See Footnotes <sup>(15)(16)</sup>
Stock Option (right to buy)	\$1.62	12/18/2017		M			10,180	(5)	02/15/2018	Common Stock	10,180	\$0	0	I	See Footnotes <sup>(14)(16)</sup>
Stock Option (right to buy)	\$1.62	12/18/2017		M			97	(5)	02/15/2018	Common Stock	97	\$0	0	I	See Footnotes <sup>(15)(16)</sup>

**Table II - Derivative Securities Acquired, Disposed of, or Beneficially Owned  
(e.g., puts, calls, warrants, options, convertible securities)**

1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative Security	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transaction Code (Instr. 8)		5. Number of Derivative Securities Acquired (A) or Disposed of (D) (Instr. 3, 4 and 5)		6. Date Exercisable and Expiration Date (Month/Day/Year)		7. Title and Amount of Securities Underlying Derivative Security (Instr. 3 and 4)		8. Price of Derivative Security (Instr. 5)	9. Number of derivative Securities Beneficially Owned Following Reported Transaction(s) (Instr. 4)	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr. 4)
				Code	V	(A)	(D)	Date Exercisable	Expiration Date	Title	Amount or Number of Shares				
Stock Option (right to buy)	\$1.59	12/18/2017		M			19,811	(6)	02/15/2018	Common Stock	19,811	\$0	0	I	See Footnotes <sup>(14)(16)</sup>
Stock Option (right to buy)	\$1.59	12/18/2017		M			189	(6)	02/15/2018	Common Stock	189	\$0	0	I	See Footnotes <sup>(15)(16)</sup>
Stock Option (right to buy)	\$2.05	12/18/2017		M			8,097	(7)	02/15/2018	Common Stock	8,097	\$0	0	I	See Footnotes <sup>(14)(16)</sup>
Stock Option (right to buy)	\$2.05	12/18/2017		M			77	(7)	02/15/2018	Common Stock	77	\$0	0	I	See Footnotes <sup>(15)(16)</sup>
Stock Option (right to buy)	\$1.73	12/18/2017		M			9,642	(8)	02/15/2018	Common Stock	9,642	\$0	0	I	See Footnotes <sup>(14)(16)</sup>
Stock Option (right to buy)	\$1.73	12/18/2017		M			92	(8)	02/15/2018	Common Stock	92	\$0	0	I	See Footnotes <sup>(15)(16)</sup>
Stock Option (right to buy)	\$1.64	12/18/2017		M			10,182	(9)	02/15/2018	Common Stock	10,182	\$0	0	I	See Footnotes <sup>(14)(16)</sup>
Stock Option (right to buy)	\$1.64	12/18/2017		M			97	(9)	02/15/2018	Common Stock	97	\$0	0	I	See Footnotes <sup>(15)(16)</sup>
Stock Option (right to buy)	\$2.01	12/18/2017		M			14,858	(10)	02/15/2018	Common Stock	14,858	\$0	0	I	See Footnotes <sup>(14)(16)</sup>
Stock Option (right to buy)	\$2.01	12/18/2017		M			142	(10)	02/15/2018	Common Stock	142	\$0	0	I	See Footnotes <sup>(15)(16)</sup>
Stock Option (right to buy)	\$2.01	12/18/2017		M			10,216	(11)	02/15/2018	Common Stock	10,216	\$0	0	I	See Footnotes <sup>(14)(16)</sup>
Stock Option (right to buy)	\$2.01	12/18/2017		M			97	(11)	02/15/2018	Common Stock	97	\$0	0	I	See Footnotes <sup>(15)(16)</sup>
Stock Option (right to buy)	\$2.32	12/18/2017		M			10,447	(12)	02/15/2018	Common Stock	10,447	\$0	0	I	See Footnotes <sup>(14)(16)</sup>
Stock Option (right to buy)	\$2.32	12/18/2017		M			99	(12)	02/15/2018	Common Stock	99	\$0	0	I	See Footnotes <sup>(15)(16)</sup>
Stock Option (right to buy)	\$5.64	12/18/2017		M			4,971	(13)	02/15/2018	Common Stock	4,971	\$0	0	I	See Footnotes <sup>(14)(16)</sup>
Stock Option (right to buy)	\$5.64	12/18/2017		M			47	(13)	02/15/2018	Common Stock	47	\$0	0	I	See Footnotes <sup>(15)(16)</sup>

1. Name and Address of Reporting Person\*

[ORBIMED ADVISORS LLC](#)

(Last) (First) (Middle)

601 LEXINGTON AVENUE, 54TH FLOOR

(Street)

NEW YORK NY 10022

(City)

(State)

(Zip)

1. Name and Address of Reporting Person\*

OrbiMed Capital GP III LLC

(Last) (First) (Middle)

601 LEXINGTON AVENUE, 54TH FLOOR

(Street)

NEW YORK NY 10022

(City) (State) (Zip)

1. Name and Address of Reporting Person\*

ISALY SAMUEL D

(Last) (First) (Middle)

601 LEXINGTON AVENUE, 54TH FLOOR

(Street)

NEW YORK NY 10022

(City) (State) (Zip)

**Explanation of Responses:**

1. The stock options were included in an award to Chau Khuong, an employee of the Reporting Persons, made on December 17, 2014 for services as a director of the Issuer. The award included stock options relating to a total of 30,000 shares of the Issuer's Common Stock and was scheduled to vest quarterly over three years beginning March 31, 2015, with 100% of the total shares vested and exercisable on March 31, 2018, subject to the director's provision of service to the issuer on each vesting date. Mr. Khuong is no longer a director of the Issuer.
2. The stock options were included in an award to Chau Khuong, an employee of the Reporting Persons, made on April 30, 2015 for services as a director of the Issuer. The award included stock options relating to a total of 5,277 shares of the Issuer's Common Stock and was vested and exercisable on April 30, 2015. Mr. Khuong is no longer a director of the Issuer.
3. The stock options were included in an award to Chau Khuong, an employee of the Reporting Persons, made on July 15, 2015 for services as a director of the Issuer. The award included stock options relating to a total of 6,717 shares of the Issuer's Common Stock and was vested and exercisable on July 15, 2015. Mr. Khuong is no longer a director of the Issuer.
4. The stock options were included in an award to Chau Khuong, an employee of the Reporting Persons, made on October 15, 2015 for services as a director of the Issuer. The award included stock options relating to a total of 8,800 shares of the Issuer's Common Stock and was vested and exercisable on October 15, 2015. Mr. Khuong is no longer a director of the Issuer.
5. The stock options were included in an award to Chau Khuong, an employee of the Reporting Persons, made on January 15, 2016 for services as a director of the Issuer. The award included stock options relating to a total of 10,277 shares of the Issuer's Common Stock and was vested and exercisable on January 15, 2016. Mr. Khuong is no longer a director of the Issuer.
6. The stock options were included in an award to Chau Khuong, an employee of the Reporting Persons, made on February 16, 2016 for services as a director of the Issuer. The award included stock options relating to a total of 20,000 shares of the Issuer's Common Stock and was scheduled to vest in four equal installments on each of March 31, 2016, June 30, 2016, September 30, 2016 and December 31, 2016 with 100% of the total shares vested and exercisable on December 31, 2016, subject to the director's provision of service to the issuer on each vesting date. Mr. Khuong is no longer a director of the Issuer.
7. The stock options were included in an award to Chau Khuong, an employee of the Reporting Persons, made on April 27, 2016 for services as a director of the Issuer. The award included stock options relating to a total of 8,174 shares of the Issuer's Common Stock and was vested and exercisable on April 27, 2016. Mr. Khuong is no longer a director of the Issuer.
8. The stock options were included in an award to Chau Khuong, an employee of the Reporting Persons, made on July 25, 2016 for services as a director of the Issuer. The award included stock options relating to a total of 9,734 shares of the Issuer's Common Stock and was vested and exercisable on July 25, 2016. Mr. Khuong is no longer a director of the Issuer.
9. The stock options were included in an award to Chau Khuong, an employee of the Reporting Persons, made on October 25, 2016 for services as a director of the Issuer. The award included stock options relating to a total of 10,279 shares of the Issuer's Common Stock and was vested and exercisable on October 25, 2016. Mr. Khuong is no longer a director of the Issuer.
10. The stock options were included in an award to Chau Khuong, an employee of the Reporting Persons, made on January 25, 2017 for services as a director of the Issuer. The award included stock options relating to a total of 20,000 shares of the Issuer's Common Stock and was scheduled to vest in four equal installments on each of March 31, 2017, June 30, 2017, September 30, 2017 and December 31, 2017 with 100% of the total shares vested and exercisable on December 31, 2017, subject to the director's provision of service to the issuer on each vesting date. Mr. Khuong is no longer a director of the Issuer.
11. The stock options were included in an award to Chau Khuong, an employee of the Reporting Persons, made on January 25, 2017 for services as a director of the Issuer. The award included stock options relating to a total of 10,313 shares of the Issuer's Common Stock and was vested and exercisable on January 25, 2017. Mr. Khuong is no longer a director of the Issuer.
12. The stock options were included in an award to Chau Khuong, an employee of the Reporting Persons, made on April 25, 2017 for services as a director of the Issuer. The award included stock options relating to a total of 10,546 shares of the Issuer's Common Stock and was vested and exercisable on April 25, 2017. Mr. Khuong is no longer a director of the Issuer.
13. The stock options were included in an award to Chau Khuong, an employee of the Reporting Persons, made on July 25, 2017 for services as a director of the Issuer. The award included stock options relating to a total of 5,018 shares of the Issuer's Common Stock and was vested and exercisable on July 25, 2017. Mr. Khuong is no longer a director of the Issuer.
14. These Shares are held of record by OrbiMed Private Investments III, LP ("OPI III"). OrbiMed Capital GP III LLC ("GP III") is the general partner of OPI III, and OrbiMed Advisors LLC ("Advisors") is the managing member of GP III. Samuel D. Isaly ("Isaly"), a natural person, is the managing member of and owner of a controlling interest in Advisors. By virtue of such relationships, GP III, Advisors and Isaly may be deemed to have voting and investment power over the securities held by OPI III and as a result may be deemed to have beneficial ownership over such securities.
15. These Shares are held of record by OrbiMed Associates III, LP ("Associates III"). Advisors is the general partner of Associates III. Isaly is the managing member of and owner of a controlling interest in Advisors. By virtue of such relationships, Advisors and Isaly may be deemed to have voting and investment power over the securities held by Associates III and as a result may be deemed to have beneficial ownership over such securities.
16. This report on Form 4 is jointly filed by GP III, Advisors, and Isaly. Each of the Reporting Persons disclaims beneficial ownership of the securities reported herein for purposes of Rule 16a-1(a) under the Securities Exchange Act of 1934, as amended (the "Exchange Act"), except to the extent of its or his pecuniary interest therein, if any. This report shall not be deemed an admission that any of the Reporting Persons is a beneficial owner for the purpose of Section 16 of the Exchange Act, or for any other purpose.

/s/ Samuel D. Isaly

12/20/2017

\*\* Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

\* If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

\*\* Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

**Persons who respond to the collection of information contained in this form are not required to respond unless the form displays a currently valid OMB Number.**