

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* <u>ORBIMED ADVISORS LLC</u> (Last) (First) (Middle) <u>601 LEXINGTON AVENUE</u> <u>54TH FLOOR</u> (Street) <u>NEW YORK</u> <u>NY</u> <u>10022</u> (City) (State) (Zip)	2. Issuer Name and Ticker or Trading Symbol <u>Aeglea BioTherapeutics, Inc. [AGLE]</u> 3. Date of Earliest Transaction (Month/Day/Year) <u>02/16/2017</u> 4. If Amendment, Date of Original Filed (Month/Day/Year)	5. Relationship of Reporting Person(s) to Issuer (Check all applicable) Director ☒ 10% Owner Officer (give title below) Other (specify below) 6. Individual or Joint/Group Filing (Check Applicable Line) ☒ Form filed by One Reporting Person ☐ Form filed by More than One Reporting Person
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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	02/16/2017		P		30,500	A	\$5.04 ⁽¹⁾	1,390,724	I	See Footnotes ⁽⁴⁾⁽⁵⁾
Common Stock	02/17/2017		P		71,800	A	\$5.19 ⁽²⁾	1,462,524	I	See Footnotes ⁽⁴⁾⁽⁵⁾
Common Stock	02/21/2017		P		7,000	A	\$5.36 ⁽³⁾	1,469,524	I	See Footnotes ⁽⁴⁾⁽⁵⁾

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				

1. Name and Address of Reporting Person* <u>ORBIMED ADVISORS LLC</u> (Last) (First) (Middle) <u>601 LEXINGTON AVENUE</u> <u>54TH FLOOR</u> (Street) <u>NEW YORK</u> <u>NY</u> <u>10022</u> (City) (State) (Zip)	1. Name and Address of Reporting Person* <u>OrbiMed Capital GP V LLC</u> (Last) (First) (Middle) <u>601 LEXINGTON AVENUE</u> <u>54TH FLOOR</u> (Street) <u>NEW YORK</u> <u>NY</u> <u>10022</u> (City) (State) (Zip)
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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 price reported in Column 4 is a weighted average price. These shares of the Issuer's common stock ("Shares") were purchased in multiple transactions at prices ranging from \$4.97 to \$5.10 inclusive. Upon request, the Reporting Persons undertakes to provide the Issuer, any security holder of the Issuer, or the Securities and Exchange Commission (the "SEC") full information regarding the Shares purchased at each separate price within the range set forth in this footnote.
2. The price reported in Column 4 is a weighted average price. These Shares were purchased in multiple transactions at prices ranging from \$5.10 to \$5.25 inclusive. Upon request, the Reporting Persons undertake to provide the Issuer, any security holder of the Issuer, or the SEC full information regarding the Shares purchased at each separate price within the range set forth in this footnote.
3. The price reported in Column 4 is a weighted average price. These Shares were purchased in multiple transactions at prices ranging from \$5.25 to \$5.50 inclusive. Upon request, the Reporting Persons undertake to provide the Issuer, any security holder of the Issuer, or the SEC full information regarding the Shares purchased at each separate price within the range set forth in this footnote.
4. These securities are held of record by OrbiMed Private Investments V, LP ("OPI V"). OrbiMed Capital GP V LLC ("GP V") is the sole general partner of OPI V, and OrbiMed Advisors LLC ("Advisors"), a registered adviser under the Investment Advisors Act of 1940, as amended, is the sole managing member of GP V. Samuel D. Isaly ("Isaly"), a natural person, is the managing member of, and holder of a controlling interest in, Advisors. By virtue of such relationships, GP V, Advisors and Isaly may be deemed to have voting and investment power with respect to the securities held by OPI V noted above and as a result may be deemed to beneficially own such securities for purposes of Rule 13d-3 under the Securities Exchange Act of 1934, as amended (the "Exchange Act").
5. This report on Form 4 is jointly filed by GP V, 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 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 of such securities for the purpose of Section 16 of the Exchange Act, or for any other purpose.

/s/ Samuel D. Isaly

02/21/2017

** 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.