

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

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

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

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)	2. Issuer Name and Ticker or Trading Symbol ALPINE IMMUNE SCIENCES, INC. [ALPN]	5. Relationship of Reporting Person(s) to Issuer (Check all applicable) <input checked="" type="checkbox"/> Director <input checked="" type="checkbox"/> 10% Owner Officer (give title below) Other (specify below)
	3. Date of Earliest Transaction (Month/Day/Year) 01/18/2019	
4. If Amendment, Date of Original Filed (Month/Day/Year)		

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	01/18/2019		P		372,439	A	\$5.37 ⁽¹⁾	3,670,955	I	See Footnotes ⁽²⁾⁽⁴⁾

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
Warrants to Purchase Common Stock ⁽³⁾	(3)	01/18/2019		P		145,251		(3)	01/18/2024	Common Stock	145,251	\$0	145,251	I	See Footnotes ⁽²⁾⁽⁴⁾

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 VI LLC		
(Last)	(First)	(Middle)
601 LEXINGTON AVENUE 54TH FLOOR		
(Street)		
NEW YORK	NY	10022
(City)	(State)	(Zip)

Explanation of Responses:

1. These shares of the Issuer's common stock ("Shares") were purchased in a block order at a price of \$5.37.
2. These securities are held of record by OrbiMed Private Investments VI, LP ("OPI VI"). OrbiMed Capital GP VI LLC ("GP VI") is the sole general partner of OPI VI, and OrbiMed Advisors LLC ("Advisors"), a registered adviser under the Investment Advisors Act of 1940, as amended, is the sole managing member of GP VI. By virtue of such relationships, GP VI and Advisors may be deemed to have voting and investment power with respect to the securities held by OPI VI 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"). Advisors exercised 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 VI.
3. Warrants ("Warrants") to purchase Shares. The Warrants are immediately exercisable for five years from the date of issuance and have an exercise price of \$12.74 per Share.
4. This report on Form 4 is jointly filed by GP VI and Advisors. 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 pecuniary interest therein, if any. The Reporting Persons have designated a representative, currently Peter A. Thompson, an employee of Advisors, to serve on the Issuer's board of directors. 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/ Jonathan T. Silverstein,
Member of OrbiMed Advisors 01/23/2019
LLC

** 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.