

OMB APPROVAL	
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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

1. Name and Address of Reporting Person* <u>ORBIMED ADVISORS LLC</u> _____ (Last) (First) (Middle) 601 LEXINGTON AVENUE 54TH FLOOR _____ (Street) NEW YORK NY 10022-4629 _____ (City) (State) (Zip)	2. Issuer Name and Ticker or Trading Symbol <u>ALPINE IMMUNE SCIENCES, INC.</u> [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) 09/17/2021	
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	09/17/2021		P		585,106	A	\$9.4 ⁽¹⁾	3,656,061	I	See Footnotes ⁽²⁾⁽⁴⁾
Common Stock	09/17/2021		P		425,531	A	\$9.4 ⁽¹⁾	425,531	I	See Footnotes ⁽³⁾⁽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)		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)					

1. Name and Address of Reporting Person*
ORBIMED ADVISORS LLC

 (Last) (First) (Middle)
 601 LEXINGTON AVENUE
 54TH FLOOR

 (Street)
 NEW YORK NY 10022-4629

 (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 10022-4629

 (City) (State) (Zip)

1. Name and Address of Reporting Person*
OrbiMed Genesis GP LLC

 (Last) (First) (Middle)

(Last) (First) (Middle)

601 LEXINGTON AVENUE

54TH FLOOR

(Street)

NEW YORK

NY

10022-4629

(City)

(State)

(Zip)

Explanation of Responses:

1. These shares of the Issuer's common stock were purchased in a block order at a price of \$9.40.
2. These shares of the Issuer's common stock are held of record by OrbiMed Private Investments VI, LP ("OPI VI"). OrbiMed Capital GP VI LLC ("GP VI") is the general partner of OPI VI, and OrbiMed Advisors LLC ("Advisors"), a registered investment adviser under the Investment Advisors Act of 1940, as amended, is the managing member of GP VI. Advisors and GP VI exercise investment and voting power through a management committee comprised of Carl L. Gordon, Sven H. Borho, and W. Carter Neild, each of whom disclaims beneficial ownership of the Shares held by OPI VI.
3. These shares of the Issuer's common stock are held of record by OrbiMed Genesis Master Fund, L.P. ("Genesis Master Fund"). OrbiMed Genesis GP LLC ("Genesis GP") is the general partner of Genesis Master Fund and Advisors is the managing member of Genesis GP. Advisors and Genesis GP exercise investment and voting power through a management committee comprised of Carl L. Gordon, Sven H. Borho, and W. Carter Neild, each of whom disclaims beneficial ownership of the securities held by Genesis Master Fund.
4. This report on Form 4 is jointly filed by GP VI, Advisors, and Genesis GP. 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 pecuniary interest therein, if any. Advisors and GP VI have designated Peter A. Thompson ("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, or Thompson, is a beneficial owner of such securities for the purpose of Section 16 of the Exchange Act, or for any other purpose.

/s/ Carl Gordon Member of
OrbiMed Advisors LLC 09/21/2021

/s/ Carl Gordon Member of
the Managing Member of
OrbiMed Capital GP VI LLC 09/21/2021

/s/ Carl Gordon Member of
the Managing Member of
OrbiMed Genesis GP LLC 09/21/2021

** 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.