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

SCHEDULE 13D
Under the Securities Exchange Act of 1934
(Amendment No. 2)*

Alpine Immune Sciences, Inc.
(Name of Issuer)

Common Stock, par value \$0.001 per share

(Title of Class of Securities)

02083G100
(CUSIP Number)

OrbiMed Advisors LLC
OrbiMed Capital GP VI 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)

January 18, 2019

(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).

SCHEDULE 13D

CUSIP No. 02083G100		
1	NAME OF REPORTING PERSONS OrbiMed Advisors LLC	
2	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (See Instructions) (a) <input type="checkbox"/> (b) <input type="checkbox"/>	
3	SEC USE ONLY	
4	SOURCE OF FUNDS (See Instructions) 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 3,816,206 (1)
	9	SOLE DISPOSITIVE POWER 0
	10	SHARED DISPOSITIVE POWER 3,816,206 (1)
11	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON 3,816,206 (1)	
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) 20.40% (2)	
14	TYPE OF REPORTING PERSON (See Instructions) IA	

(1) Evidenced by (i) 3,670,955 shares of common stock (“Shares”) outstanding of Alpine Immune Sciences, Inc. (the “Issuer”) and (ii) 145,251 Shares issuable upon the exercise of warrants to purchase Shares (the “Warrants”).

(2) This percentage is calculated based on (i) 13,852,464 Shares outstanding on November 1, 2018 as set forth in the Issuer’s Form 10-Q filed with the SEC on November 8, 2018, (ii) 4,706,700 Shares that were sold on January 18, 2019, as described in the Issuer’s Form 8-K filed with the SEC on January 16, 2019, and (iii) 145,251 Shares subject to currently exercisable Warrants.

SCHEDULE 13D

CUSIP No. 02083G100		
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2	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (See Instructions) (a) <input type="checkbox"/> (b) <input type="checkbox"/>	
3	SEC USE ONLY	
4	SOURCE OF FUNDS (See Instructions) 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
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Item 1. Security and Issuer

This Amendment No. 2 (“Amendment No. 2”) to Schedule 13D supplements and amends the Statement on Schedule 13D of OrbiMed Advisors LLC and OrbiMed Capital GP VI LLC (the “Statement”) originally filed with the Securities and Exchange Commission (the “SEC”) on August 3, 2017 with Samuel D. Isaly as an additional reporting person, and amended by Amendment No. 1 thereto filed with the SEC on January 25, 2018. The Statement relates to the common stock, par value \$0.001 per share (the “Shares”), of Alpine Immune Sciences, Inc., a Delaware corporation (the “Issuer”), with its principal offices located at 201 Elliott Avenue West, Suite 230, Seattle, WA 98119. The Shares are listed on the NASDAQ Global Market under the ticker symbol “ALPN”. Information given in response to each item shall be deemed incorporated by reference in all other items, as applicable.

On January 15, 2019, the Issuer entered into a Securities Purchase Agreement (the “Purchase Agreement”) with certain investors, including OPI VI (as defined below in Item 2) (the “Investors”), pursuant to which the Issuer agreed to issue and sell to the Investors the following securities (the “Private Placement”): (i) an aggregate of 4,706,700 Shares; and (ii) warrants (“Warrants”) to purchase up to 1,835,610 additional Shares, for an aggregate purchase price of approximately \$25.3 million. As a result of the Private Placement, 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. 1 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 VI LLC (“GP VI”), 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 managing member of GP VI, which is the sole general partner of OrbiMed Private Investments VI, LP (“OPI VI”), which holds Shares, as described herein. Advisors has its principal offices at 601 Lexington Avenue, 54th Floor, New York, New York 10022.

GP VI has its principal offices at 601 Lexington Avenue, 54th Floor, New York, New York 10022.

The directors and executive officers of Advisors and GP VI 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; and
- (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

Pursuant to its authority under the limited partnership agreement of OPI VI, GP VI, as general partner of OPI VI, caused OPI VI to purchase 372,439 Shares and received 145,251 Warrants in the Private Placement, which closed on January 18, 2019, at an aggregate price of \$1,999,997.43 using OPI VI's working capital.

As a result of the transactions described in this Item 3, the Reporting Persons may be deemed to be the beneficial owners of approximately 20.40% of the outstanding Shares. GP VI, as the general partner of OPI VI, may be deemed to be the beneficial owner of approximately 20.40% of the outstanding Shares. Advisors, as the managing member of GP VI, may be deemed to be the beneficial owner of approximately 20.40% of the outstanding Shares.

Item 4. Purpose of Transaction

This Amendment No. 2 to the Statement relates to the transactions by the Reporting Persons more fully described in Item 3 above. The Reporting Persons caused OPI VI to acquire Shares and Warrants for the purpose of making an investment in the Issuer and not with the intention of acquiring control of the Issuer's business on behalf of OPI VI.

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 Shares 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 Shares 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 Amendment No. 2, 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 Exchange Act, directly or indirectly, including by reason of their mutual affiliation, to be the beneficial owners of the Shares described in Item 6 below. Based upon information contained in the Issuer's Form 8-K, filed with the SEC on January 16, 2019 (and the Issuer's Form 10-Q, filed with the SEC on November 8, 2018), such Shares deemed to be indirectly beneficially owned by the Reporting Persons constitutes approximately 20.40% of the issued and outstanding Shares. Advisors, pursuant to its authority as the sole managing member of GP VI, the sole general partner of OPI VI, may be deemed to indirectly beneficially own the Shares held by OPI VI. GP VI, pursuant to its authority as the general partner of OPI VI, may be deemed to indirectly beneficially own the Shares held by OPI VI.

As a result, Advisors and GP VI share the power to direct the vote and to direct the disposition of the Shares held by OPI VI. 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 VI.

- (c) Except as disclosed in Item 3 above, 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 of the Statement, GP VI is the sole general partner of OPI VI, pursuant to the terms of the limited partnership agreement of OPI VI. Advisors is the sole managing member of GP VI, pursuant to the terms of the limited liability company agreement of GP VI. Pursuant to these agreements and relationships, Advisors and GP VI have discretionary investment management authority with respect to the assets of OPI VI. Such authority includes the power of GP VI to vote and otherwise dispose of securities purchased by OPI VI. The number of Shares attributable to OPI VI is 3,816,206, which includes Warrants to purchase 145,251 Shares. Advisors and GP VI may each be considered to hold indirectly 3,816,206 Shares.

Peter Thompson ("Thompson"), an employee of Advisors, has been a member of the Board of Directors of the Issuer since June 2016 and, accordingly, the Reporting Persons may have the ability to affect and influence control of the Issuer. From time to time, Thompson may receive stock options or other awards of equity-based compensation pursuant to the Issuer's compensation arrangements for non-employee directors. Thompson is obligated to transfer any securities issued under any such stock options or other awards, or the economic benefit thereof, to the Reporting Persons, which will in turn ensure that such securities or economic benefits are provided to OPI VI.

Private Placement

Purchase Agreement

In connection with the Private Placement, on January 15, 2019, the Issuer entered into the Purchase Agreement with OPI VI and certain other parties, pursuant to which on January 18, 2019 OPI VI (i) purchased 372,439 Shares, and (ii) received Warrants to purchase 145,251 Shares, for an aggregate purchase price of \$1,999,997.43. The closing of the Private Placement occurred on January 18, 2019. The foregoing description of the Purchase Agreement does not purport to be complete and is qualified in its entirety by reference to the full text of the Purchase Agreement, a form of which is included in this Statement as Exhibit 4 and incorporated herein by reference.

Lock-up Agreement

In connection with the Private Placement, holders of substantially all of the Issuer's outstanding Shares, including OPI IV, and each executive officer and director of the Issuer, have entered into an agreement (the "Lock-Up Agreement"), pursuant to which such parties have agreed not to, except in limited circumstances, offer, sell, pledge or otherwise dispose of any Shares, including, as applicable, Shares received in the Private Placement, from the closing of the Private Placement until 90 days from the closing date of the Private Placement.

The foregoing description of the Lock-Up Agreement does not purport to be complete and is qualified in its entirety by reference to the full text of the Lock-Up Agreement, a form of which is included in this Statement as Exhibit 2 and incorporated herein by reference.

Registration Rights Agreement.

In connection with the Private Placement, on January 15, 2019, the Issuer, OPI VI and certain other parties also entered into a registration rights agreement (the "Registration Rights Agreement"). Pursuant to the Registration Rights Agreement, the Issuer is required to prepare and file a registration statement with the SEC on the date on which the Issuer files its Annual Report on Form 10-K for the year ended December 31, 2018, and in any event no later than March 18, 2019 (the "Filing Deadline"), and to use commercially reasonable efforts to have the registration statement declared effective within 25 days of the Filing Deadline if there is no review by the SEC, and within 90 days of the Filing Deadline in the event of such review.

The foregoing description of the Registration Rights Agreement does not purport to be complete and is qualified in its entirety by reference to the full text of the Registration Rights Agreement, a form of which is included in this Statement as Exhibit 3 and incorporated herein by reference.

Other than as described in this Amendment No. 2, to the best of the Reporting Persons' knowledge, there are no other contracts, arrangements, understandings or relationships (legal or otherwise) among the persons named in Item 2 and between such persons and any person with respect to any securities of the Issuer.

Item 7. Materials to Be Filed as Exhibits

Exhibit	Description
1.	Joint Filing Agreement among OrbiMed Advisors LLC and OrbiMed Capital GP VI LLC.
2.	Form of Lock-Up Agreement (incorporated by reference to Exhibit I of Exhibit 10.1 to Securities Purchase Agreement on the Issuer's Current Report on Form 8-K (SEC 001-37449), filed with the SEC on January 16, 2019).
3.	Registration Rights Agreement by and among the Issuer and the Purchasers, dated January 15, 2019 (incorporated by reference to Exhibit 10.2 to the Issuer's Current Report on Form 8-K (SEC 001-37449), filed with the SEC on January 16, 2019).
4.	Securities Purchase Agreement by and among the Issuer and the Purchasers set forth therein dated January 15, 2019 (incorporated by reference to Exhibit 10.1 to the Issuer's Current Report on Form 8-K (SEC 001-37449), filed on January 16, 2019).

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: January 23, 2019

OrbiMed Advisors LLC

By: /s/ Jonathan T. Silverstein

Name: Jonathan T. Silverstein

Title: Member of OrbiMed Advisors LLC

OrbiMed Capital GP VI LLC

By: OrbiMed Advisors LLC
its Managing Member

By: /s/ Jonathan T. Silverstein

Name: Jonathan T. Silverstein

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
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 VI LLC are managed by the executive officers and directors of its managing member, OrbiMed Advisors LLC, set forth on Schedule I attached hereto.

EXHIBIT INDEX

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JOINT FILING AGREEMENT

The undersigned hereby agree that the Statement on this Schedule 13D, dated January 23, 2019 (the "Schedule 13D"), with respect to the Shares of Alpine Immune Sciences, Inc. is filed, and all amendments thereto will be filed, on behalf of each of us pursuant to and in accordance with the provisions of Rule 13d-1(k) under the Securities and 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 23rd day of January, 2019.

OrbiMed Advisors LLC

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

OrbiMed Capital GP VI LLC

By: OrbiMed Advisors LLC
its Managing Member

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