
**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549**

SCHEDULE 13D

**UNDER THE SECURITIES EXCHANGE ACT OF 1934
(Amendment No. 3)***

Alpine Immune Sciences, Inc.
(Name of Issuer)

Common Stock
(Title of Class of Securities)

02083G 100
(CUSIP Number)

Steve R. Bailey
Frazier Healthcare Partners
601 Union Street, Suite 3200
Seattle, WA 98101
Telephone: (206) 621-7200
(Name, Address and Telephone Number of Person Authorized to Receive Notices and Communications)

September 17, 2021
(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 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).

1.	Name of Reporting Persons. Frazier Life Sciences VIII, L.P.	
2.	Check the Appropriate Box if a Member of a Group (See Instructions) (a) <input type="checkbox"/> (b) <input checked="" type="checkbox"/>	
3.	SEC USE ONLY	
4.	Source of Funds (See Instructions) WC	
5.	Check 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 shares
	8.	Shared Voting Power 2,025,881 shares (1)
	9.	Sole Dispositive Power 0 shares
	10.	Shared Dispositive Power 2,025,881 shares (1)
11.	Aggregate Amount Beneficially Owned by Each Reporting Person 2,025,881 shares (1)	
12.	Check 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) 6.5% (2)	
14.	Type of Reporting Person (See Instructions) PN	

- (1) Consists of (i) 1,371,450 shares of Common Stock held directly by Frazier Life Sciences VIII, L.P. and (ii) 654,431 shares of Common Stock issuable to Frazier Life Sciences VIII, L.P. pursuant to warrants exercisable within 60 days of September 17, 2021. FHM Life Sciences VIII, L.P. is the general partner of Frazier Life Sciences VIII, L.P. and FHM Life Sciences VIII, L.L.C. is the general partner of FHM Life Sciences VIII, L.P. James N. Topper and Patrick J. Heron are the sole members of FHM Life Sciences VIII, L.L.C. and therefore share voting and investment power over the shares held by Frazier Life Sciences VIII, L.P.
- (2) Based on (i) 23,914,879 shares of Common Stock outstanding on July 30, 2021 as set forth in the Issuer's Form 10-Q filed with the SEC on August 10, 2021, (ii) 6,489,357 shares of Common Stock that were sold on September 17, 2021 as described in the Issuer's Current Form 8-K filed with the SEC on September 15, 2021 and (iii) 654,431 shares of Common Stock issuable to Frazier Life Sciences VIII, L.P. pursuant to warrants exercisable within 60 days of September 17, 2021.

1.	Name of Reporting Persons. FHM Life Sciences VIII, L.P.	
2.	Check the Appropriate Box if a Member of a Group (See Instructions) (a) <input type="checkbox"/> (b) <input checked="" type="checkbox"/>	
3.	SEC USE ONLY	
4.	Source of Funds (See Instructions) AF	
5.	Check 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 shares
	8.	Shared Voting Power 2,025,881 shares (1)
	9.	Sole Dispositive Power 0 shares
	10.	Shared Dispositive Power 2,025,881 shares (1)
11.	Aggregate Amount Beneficially Owned by Each Reporting Person 2,025,881 shares (1)	
12.	Check 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) 6.5% (2)	
14.	Type of Reporting Person (See Instructions) PN	

- (1) Consists of (i) 1,371,450 shares of Common Stock held directly by Frazier Life Sciences VIII, L.P. and (ii) 654,431 shares of Common Stock issuable to Frazier Life Sciences VIII, L.P. pursuant to warrants exercisable within 60 days of September 17, 2021. FHM Life Sciences VIII, L.P. is the general partner of Frazier Life Sciences VIII, L.P. and FHM Life Sciences VIII, L.L.C. is the general partner of FHM Life Sciences VIII, L.P. James N. Topper and Patrick J. Heron are the sole members of FHM Life Sciences VIII, L.L.C. and therefore share voting and investment power over the shares held by Frazier Life Sciences VIII, L.P.
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1.	Name of Reporting Persons. FHM Life Sciences VIII, L.L.C.	
2.	Check the Appropriate Box if a Member of a Group (See Instructions) (a) <input type="checkbox"/> (b) <input checked="" type="checkbox"/>	
3.	SEC USE ONLY	
4.	Source of Funds (See Instructions) AF	
5.	Check 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 shares
	8.	Shared Voting Power 2,025,881 shares (1)
	9.	Sole Dispositive Power 0
	10.	Shared Dispositive Power 2,025,881 shares (1)
11.	Aggregate Amount Beneficially Owned by Each Reporting Person 2,025,881 shares (1)	
12.	Check 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) 6.5% (2)	
14.	Type of Reporting Person (See Instructions) OO	

- (1) Consists of (i) 1,371,450 shares of Common Stock held directly by Frazier Life Sciences VIII, L.P. and (ii) 654,431 shares of Common Stock issuable to Frazier Life Sciences VIII, L.P. pursuant to warrants exercisable within 60 days of September 17, 2021. FHM Life Sciences VIII, L.P. is the general partner of Frazier Life Sciences VIII, L.P. and FHM Life Sciences VIII, L.L.C. is the general partner of FHM Life Sciences VIII, L.P. James N. Topper and Patrick J. Heron are the sole members of FHM Life Sciences VIII, L.L.C. and therefore share voting and investment power over the shares held by Frazier Life Sciences VIII, L.P.
- (2) Based on (i) 23,914,879 shares of Common Stock outstanding on July 30, 2021 as set forth in the Issuer's Form 10-Q filed with the SEC on August 10, 2021, (ii) 6,489,357 shares of Common Stock that were sold on September 17, 2021 as described in the Issuer's Current Form 8-K filed with the SEC on September 15, 2021 and (iii) 654,431 shares of Common Stock issuable to Frazier Life Sciences VIII, L.P. pursuant to warrants exercisable within 60 days of September 17, 2021.

1.	Name of Reporting Persons. Frazier Life Sciences Public Fund L.P.	
2.	Check the Appropriate Box if a Member of a Group (See Instructions) (a) <input type="checkbox"/> (b) <input checked="" type="checkbox"/>	
3.	SEC USE ONLY	
4.	Source of Funds (See Instructions) AF	
5.	Check 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 shares
	8.	Shared Voting Power 1,122,636 shares (1)
	9.	Sole Dispositive Power 0
	10.	Shared Dispositive Power 1,122,636 shares (1)
11.	Aggregate Amount Beneficially Owned by Each Reporting Person 1,122,636 shares (1)	
12.	Check 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) 3.6% (2)	
14.	Type of Reporting Person (See Instructions) PN	

- (1) Consists of (i) 400,394 shares of Common Stock held directly by Frazier Life Sciences Public Fund L.P. and (ii) 722,242 shares of Common Stock issuable to Frazier Life Sciences Public Fund L.P. pursuant to warrants exercisable within 60 days of September 17, 2021. FHM Life Sciences VIII, L.P. is the general partner of Frazier Life Sciences Public Fund L.P. and FHM Life Sciences VIII, L.L.C. is the general partner of FHM Life Sciences VIII, L.P. James N. Topper and Patrick J. Heron are the sole members of FHM Life Sciences VIII, L.L.C. and therefore share voting and investment power over the shares held by Frazier Life Sciences Public Fund L.P.
- (2) Based on (i) 23,914,879 shares of Common Stock outstanding on July 30, 2021 as set forth in the Issuer's Form 10-Q filed with the SEC on August 10, 2021, (ii) 6,489,357 shares of Common Stock that were sold on September 17, 2021 as described in the Issuer's Current Form 8-K filed with the SEC on September 15, 2021 and (iii) 722,242 shares of Common Stock issuable to Frazier Life Sciences Public Fund L.P. pursuant to warrants exercisable within 60 days of September 17, 2021.

1.	Name of Reporting Persons. FHMLSP, L.P.	
2.	Check the Appropriate Box if a Member of a Group (See Instructions) (a) <input type="checkbox"/> (b) <input checked="" type="checkbox"/>	
3.	SEC USE ONLY	
4.	Source of Funds (See Instructions) AF	
5.	Check 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 shares
	8.	Shared Voting Power 1,122,636 shares (1)
	9.	Sole Dispositive Power 0
	10.	Shared Dispositive Power 1,122,636 shares (1)
11.	Aggregate Amount Beneficially Owned by Each Reporting Person 1,122,636 shares (1)	
12.	Check 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) 3.6% (2)	
14.	Type of Reporting Person (See Instructions) PN	

- (1) Consists of (i) 400,394 shares of Common Stock held directly by Frazier Life Sciences Public Fund L.P. and (ii) 722,242 shares of Common Stock issuable to Frazier Life Sciences Public Fund L.P. pursuant to warrants exercisable within 60 days of September 17, 2021. FHM Life Sciences VIII, L.P. is the general partner of Frazier Life Sciences Public Fund L.P. and FHM Life Sciences VIII, L.L.C. is the general partner of FHM Life Sciences VIII, L.P. James N. Topper and Patrick J. Heron are the sole members of FHM Life Sciences VIII, L.L.C. and therefore share voting and investment power over the shares held by Frazier Life Sciences Public Fund L.P.
- (2) Based on (i) 23,914,879 shares of Common Stock outstanding on July 30, 2021 as set forth in the Issuer's Form 10-Q filed with the SEC on August 10, 2021, (ii) 6,489,357 shares of Common Stock that were sold on September 17, 2021 as described in the Issuer's Current Form 8-K filed with the SEC on September 15, 2021 and (iii) 722,242 shares of Common Stock issuable to Frazier Life Sciences Public Fund L.P. pursuant to warrants exercisable within 60 days of September 17, 2021.

1.	Name of Reporting Persons. FHMLSP, L.L.C.	
2.	Check the Appropriate Box if a Member of a Group (See Instructions) (a) <input type="checkbox"/> (b) <input checked="" type="checkbox"/>	
3.	SEC USE ONLY	
4.	Source of Funds (See Instructions) AF	
5.	Check 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 shares
	8.	Shared Voting Power 1,122,636 shares (1)
	9.	Sole Dispositive Power 0
	10.	Shared Dispositive Power 1,122,636 shares (1)
11.	Aggregate Amount Beneficially Owned by Each Reporting Person 1,122,636 shares (1)	
12.	Check 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) 3.6% (2)	
14.	Type of Reporting Person (See Instructions) OO	

- (1) Consists of (i) 400,394 shares of Common Stock held directly by Frazier Life Sciences Public Fund L.P. and (ii) 722,242 shares of Common Stock issuable to Frazier Life Sciences Public Fund L.P. pursuant to warrants exercisable within 60 days of September 17, 2021. FHM Life Sciences VIII, L.P. is the general partner of Frazier Life Sciences Public Fund L.P. and FHM Life Sciences VIII, L.L.C. is the general partner of FHM Life Sciences VIII, L.P. James N. Topper and Patrick J. Heron are the sole members of FHM Life Sciences VIII, L.L.C. and therefore share voting and investment power over the shares held by Frazier Life Sciences Public Fund L.P.
- (2) Based on (i) 23,914,879 shares of Common Stock outstanding on July 30, 2021 as set forth in the Issuer's Form 10-Q filed with the SEC on August 10, 2021, (ii) 6,489,357 shares of Common Stock that were sold on September 17, 2021 as described in the Issuer's Current Form 8-K filed with the SEC on September 15, 2021 and (iii) 722,242 shares of Common Stock issuable to Frazier Life Sciences Public Fund L.P. pursuant to warrants exercisable within 60 days of September 17, 2021.

1.	Name of Reporting Persons. James N. Topper	
2.	Check the Appropriate Box if a Member of a Group (See Instructions) (a) <input type="checkbox"/> (b) <input checked="" type="checkbox"/>	
3.	SEC USE ONLY	
4.	Source of Funds (See Instructions) AF	
5.	Check if Disclosure of Legal Proceedings Is Required Pursuant to Items 2(d) or 2(e) <input type="checkbox"/>	
6.	Citizenship or Place of Organization United States Citizen	
Number of Shares Beneficially Owned by Each Reporting Person With:	7.	Sole Voting Power 29,325 shares (1)
	8.	Shared Voting Power 3,148,517 shares (2)
	9.	Sole Dispositive Power 29,325 shares (1)
	10.	Shared Dispositive Power 3,148,517 shares (2)
11.	Aggregate Amount Beneficially Owned by Each Reporting Person 3,177,842 shares (1)(2)	
12.	Check 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) 10.0% (3)	
14.	Type of Reporting Person (See Instructions) IN	

- (1) Consists of 29,325 shares of Common Stock issuable to James N. Topper pursuant to stock options exercisable within 60 days of September 17, 2021.
- (2) Consists of (i) 1,371,450 shares of Common Stock held directly by Frazier Life Sciences VIII, L.P., (ii) 654,431 shares of Common Stock issuable to Frazier Life Sciences VIII, L.P. pursuant to warrants exercisable within 60 days of September 17, 2021, (iii) 400,394 shares of Common Stock held directly by Frazier Life Sciences Public Fund L.P. and (iv) 722,242 shares of Common Stock issuable to Frazier Life Sciences Public Fund L.P. pursuant to warrants exercisable within 60 days of September 17, 2021. FHM Life Sciences VIII, L.P. is the general partner of Frazier Life Sciences VIII, L.P. and FHM Life Sciences VIII, L.L.C. is the general partner of FHM Life Sciences VIII, L.P. James N. Topper and Patrick J. Heron are the sole members of FHM Life Sciences VIII, L.L.C. and therefore share voting and investment power over the shares held by Frazier Life Sciences VIII, L.P. FHMLSP, L.P. is the general partner of Frazier Life Sciences Public Fund L.P. and FHMLSP, L.L.C. is the general partner of FHMLSP, L.P. Patrick J. Heron, James N. Topper, Albert Cha and James Brush are the members of FHMLSP, L.L.C. and therefore share voting and investment power over the shares held by Frazier Life Sciences Public Fund L.P.
- (3) The actual percentage is 9.99%. Such percentage was based on (i) 29,325 shares of Common Stock issuable to James N. Topper pursuant to stock options exercisable within 60 days of September 17, 2021, (ii) 23,914,879 shares of Common Stock outstanding on July 30, 2021 as set forth in the Issuer's Form 10-Q filed with the SEC on August 10, 2021, (iii) 6,489,357 shares of Common Stock that were sold on September 17, 2021 as described in the Issuer's Current Form 8-K filed with the SEC on September 15, 2021, (iv) 654,431 shares of Common Stock issuable to Frazier Life Sciences VIII, L.P. pursuant to warrants exercisable within 60 days of September 17, 2021 and (v) 722,242 shares of Common Stock issuable to Frazier Life Sciences Public Fund L.P. pursuant to warrants exercisable within 60 days of September 17, 2021.

1.	Name of Reporting Persons. Patrick J. Heron	
2.	Check the Appropriate Box if a Member of a Group (See Instructions) (a) <input type="checkbox"/> (b) <input checked="" type="checkbox"/>	
3.	SEC USE ONLY	
4.	Source of Funds (See Instructions) AF	
5.	Check if Disclosure of Legal Proceedings Is Required Pursuant to Items 2(d) or 2(e) <input type="checkbox"/>	
6.	Citizenship or Place of Organization United States Citizen	
Number of Shares Beneficially Owned by Each Reporting Person With:	7.	Sole Voting Power 0 shares
	8.	Shared Voting Power 3,148,517 shares (1)
	9.	Sole Dispositive Power 0 shares
	10.	Shared Dispositive Power 3,148,517 shares (1)
11.	Aggregate Amount Beneficially Owned by Each Reporting Person 3,148,517 shares (1)	
12.	Check 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) 9.9% (2)	
14.	Type of Reporting Person (See Instructions) IN	

- (1) Consists of (i) 1,371,450 shares of Common Stock held directly by Frazier Life Sciences VIII, L.P., (ii) 654,431 shares of Common Stock issuable to Frazier Life Sciences VIII, L.P. pursuant to warrants exercisable within 60 days of September 17, 2021, (iii) 400,394 shares of Common Stock held directly by Frazier Life Sciences Public Fund L.P. and (iv) 722,242 shares of Common Stock issuable to Frazier Life Sciences Public Fund L.P. pursuant to warrants exercisable within 60 days of September 17, 2021. FHM Life Sciences VIII, L.P. is the general partner of Frazier Life Sciences VIII, L.P. and FHM Life Sciences VIII, L.L.C. is the general partner of FHM Life Sciences VIII, L.P. James N. Topper and Patrick J. Heron are the sole members of FHM Life Sciences VIII, L.L.C. and therefore share voting and investment power over the shares held by Frazier Life Sciences VIII, L.P. FHMLSP, L.P. is the general partner of Frazier Life Sciences Public Fund L.P. and FHMLSP, L.L.C. is the general partner of FHMLSP, L.P. Patrick J. Heron, James N. Topper, Albert Cha and James Brush are the members of FHMLSP, L.L.C. and therefore share voting and investment power over the shares held by Frazier Life Sciences Public Fund L.P.
- (2) Based on (i) 23,914,879 shares of Common Stock outstanding on July 30, 2021 as set forth in the Issuer's Form 10-Q filed with the SEC on August 10, 2021, (ii) 6,489,357 shares of Common Stock that were sold on September 17, 2021 as described in the Issuer's Current Form 8-K filed with the SEC on September 15, 2021, (iii) 654,431 shares of Common Stock issuable to Frazier Life Sciences VIII, L.P. pursuant to warrants exercisable within 60 days of September 17, 2021 and (iv) 722,242 shares of Common Stock issuable to Frazier Life Sciences Public Fund L.P. pursuant to warrants exercisable within 60 days of September 17, 2021.

1.	Name of Reporting Persons. Albert Cha	
2.	Check the Appropriate Box if a Member of a Group (See Instructions) (a) <input type="checkbox"/> (b) <input checked="" type="checkbox"/>	
3.	SEC USE ONLY	
4.	Source of Funds (See Instructions) AF	
5.	Check if Disclosure of Legal Proceedings Is Required Pursuant to Items 2(d) or 2(e) <input type="checkbox"/>	
6.	Citizenship or Place of Organization United States Citizen	
Number of Shares Beneficially Owned by Each Reporting Person With:	7.	Sole Voting Power 0 shares
	8.	Shared Voting Power 1,122,636 shares (1)
	9.	Sole Dispositive Power 0 shares
	10.	Shared Dispositive Power 1,122,636 shares (1)
11.	Aggregate Amount Beneficially Owned by Each Reporting Person 1,122,636 shares (1)	
12.	Check 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) 3.6% (2)	
14.	Type of Reporting Person (See Instructions) IN	

- (1) Consists of (i) 400,394 shares of Common Stock held directly by Frazier Life Sciences Public Fund L.P. and (ii) 722,242 shares of Common Stock issuable to Frazier Life Sciences Public Fund L.P. pursuant to warrants exercisable within 60 days of September 17, 2021. FHM Life Sciences VIII, L.P. is the general partner of Frazier Life Sciences Public Fund L.P. and FHM Life Sciences VIII, L.L.C. is the general partner of FHM Life Sciences VIII, L.P. James N. Topper and Patrick J. Heron are the sole members of FHM Life Sciences VIII, L.L.C. and therefore share voting and investment power over the shares held by Frazier Life Sciences Public Fund L.P.
- (2) Based on (i) 23,914,879 shares of Common Stock outstanding on July 30, 2021 as set forth in the Issuer's Form 10-Q filed with the SEC on August 10, 2021, (ii) 6,489,357 shares of Common Stock that were sold on September 17, 2021 as described in the Issuer's Current Form 8-K filed with the SEC on September 15, 2021 and (iii) 722,242 shares of Common Stock issuable to Frazier Life Sciences Public Fund L.P. pursuant to warrants exercisable within 60 days of September 17, 2021.

1.	Name of Reporting Persons. James Brush	
2.	Check the Appropriate Box if a Member of a Group (See Instructions) (a) <input type="checkbox"/> (b) <input checked="" type="checkbox"/>	
3.	SEC USE ONLY	
4.	Source of Funds (See Instructions) AF	
5.	Check if Disclosure of Legal Proceedings Is Required Pursuant to Items 2(d) or 2(e) <input type="checkbox"/>	
6.	Citizenship or Place of Organization United States Citizen	
Number of Shares Beneficially Owned by Each Reporting Person With:	7.	Sole Voting Power 0 shares
	8.	Shared Voting Power 1,122,636 shares (1)
	9.	Sole Dispositive Power 0 shares
	10.	Shared Dispositive Power 1,122,636 shares (1)
11.	Aggregate Amount Beneficially Owned by Each Reporting Person 1,122,636 shares (1)	
12.	Check 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) 3.6% (2)	
14.	Type of Reporting Person (See Instructions) IN	

- (1) Consists of (i) 400,394 shares of Common Stock held directly by Frazier Life Sciences Public Fund L.P. and (ii) 722,242 shares of Common Stock issuable to Frazier Life Sciences Public Fund L.P. pursuant to warrants exercisable within 60 days of September 17, 2021. FHM Life Sciences VIII, L.P. is the general partner of Frazier Life Sciences Public Fund L.P. and FHM Life Sciences VIII, L.L.C. is the general partner of FHM Life Sciences VIII, L.P. James N. Topper and Patrick J. Heron are the sole members of FHM Life Sciences VIII, L.L.C. and therefore share voting and investment power over the shares held by Frazier Life Sciences Public Fund L.P.
- (2) Based on (i) 23,914,879 shares of Common Stock outstanding on July 30, 2021 as set forth in the Issuer's Form 10-Q filed with the SEC on August 10, 2021, (ii) 6,489,357 shares of Common Stock that were sold on September 17, 2021 as described in the Issuer's Current Form 8-K filed with the SEC on September 15, 2021 and (iii) 722,242 shares of Common Stock issuable to Frazier Life Sciences Public Fund L.P. pursuant to warrants exercisable within 60 days of September 17, 2021.

Item 1. Security and Issuer.

This Amendment No. 3 (“Amendment No. 3”) to Schedule 13D amends the statement on Schedule 13D filed on July 31, 2017 (the “Original Schedule 13D”), as amended on January 23, 2019 and July 30, 2020 (the “Prior Amendments”, and together with the Original Schedule 13D and this Amendment No. 3, the “Schedule 13D”) with respect to the Common Stock of Alpine Immune Sciences, Inc (the “Issuer”), having its principal executive office at 188 East Blaine St., Suite 200, Seattle, WA 98102. Except as otherwise specified in Amendment No. 3, all items in the Schedule 13D are unchanged. All capitalized terms used in this Amendment No. 3 and not otherwise defined herein have the meanings ascribed to such terms in the Original Schedule 13D.

Item 2. Identity and Background

(a) Name:

The entities and persons filing this statement (collectively, the “Reporting Persons”) are:

Frazier Life Sciences VIII, L.P. (“FLS-VIII”)
FHM Life Sciences VIII, L.P. (“FHM-VIII L.P.”)
FHM Life Sciences VIII, L.L.C. (“FHM-VIII LLC”)
Frazier Life Sciences Public Fund L.P. (“FLSPF”)
FHMLSP, L.P.
FHMLSP, L.L.C.
James N. Topper (“Topper”)
Patrick J. Heron (“Heron”)
Albert Cha (“Cha”)
Jamie Brush (“Brush” and together with Topper, Heron and Cha, the “Members”)

(b) Residence or Business Address:

The address of the principal place of business for each of the Reporting Persons is:

c/o Frazier Healthcare Partners
601 Union Street, Suite 3200
Seattle, WA 98101

(c) Present principal occupation or employment and the name, principal business and address of any corporation or other organization in which such employment is conducted:

FLS-VIII and FLSPF are venture capital funds concentrating in life science fields. The sole business of FHM-VIII L.P. is to serve as general partner of FLS-VIII. The sole business of FHM-VIII LLC. is to serve as general partner of FHM-VIII L.P. The sole business of FHMLSP, L.P. is to serve as general partner of FLSPF. The sole business of FHMLSP, L.L.C. is to serve as general partner of FHMLSP, L.P. The principal business of Topper and Heron is to manage FLS-VIII, FHM-VIII L.P., FHM-VIII L.L.C., FLSPF, FHMLSP, L.P., FHMLSP, L.L.C. and a number of affiliated partnerships with similar businesses. The principal business of Cha and Brush is to manage FLSPF, FHMLSP, L.P., FHMLSP, L.L.C. and a number of affiliated partnerships with similar businesses.

- (d) Whether or not, during the last five years, such person has been convicted in a criminal proceeding (excluding traffic violations or similar misdemeanors) and, if so, give the dates, nature of conviction, name and location of court, and penalty imposed, or other disposition of the case:
- During the last five years, none of the Reporting Persons has been convicted in any criminal proceeding (excluding traffic violations or similar misdemeanors).
- (e) Whether or not, during the last five years, such person was 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; and, if so, identify and describe such proceedings and summarize the terms of such judgment, decree or final order:
- During the last five years, none of the Reporting Persons has been 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.
- (f) Citizenship:
- | | | | |
|--------------|----------------|---|-----------------------|
| Entities: | FLS-VIII | - | Delaware, U.S.A. |
| | FHM-VIII L.P. | | Delaware, U.S.A. |
| | FHM-VIII LLC | - | Delaware, U.S.A. |
| | FLSPF | - | Delaware, U.S.A. |
| | FHMLSP, L.P. | - | Delaware, U.S.A. |
| | FHMLSP, L.L.C. | - | Delaware, U.S.A. |
| Individuals: | Topper | - | United States Citizen |
| | Heron | - | United States Citizen |
| | Cha | - | United States Citizen |
| | Brush | - | United States Citizen |

Item 3. Source and Amount of Funds or Other Consideration

FLS-VIII purchased from a company then known as Alpine Immune Sciences, Inc. (“Old Alpine”) in a series of private transactions 3,558,719 shares of Series A-1 Preferred Stock (“Series A-1 Stock”) and 866,741 shares of Common Stock (the “Old Alpine Common Stock”) for an aggregate purchase price of \$15,483,870. Pursuant to the terms of that certain Agreement and Plan of Merger and Reorganization, dated as of April 18, 2017, by and among the Issuer, Nautilus Merger Sub, Inc. and Old Alpine (the “Merger Agreement”), at the closing of the merger provided for in the Merger Agreement (the “Merger”), each share of Old Alpine’s Common Stock and Series A-1 Stock held by FLS-VIII was automatically converted into 0.4969 shares of the Issuer’s Common Stock, which resulted in FLS-VIII holding a total of 2,199,011 shares of the Issuer’s Common Stock as of July 24, 2017.

On January 18, 2019, FLS-VIII participated in the Issuer’s private placement offering and (i) purchased 372,439 shares of the Issuer’s Common Stock and (ii) received a warrant exercisable for 145,251 shares of the Issuer’s Common Stock for an aggregate purchase price of \$1,999,997.

On September 17, 2021, FLS-VIII exchanged 1,200,000 shares of the Issuer’s Common Stock for a warrant to purchase 1,200,000 shares of the Issuer’s Common Stock, of which 509,180 shares of the Issuer’s Common Stock are exercisable within 60 days of the date of this filing. FLS-VIII holds 1,371,450 shares of the Issuer’s Common Stock and warrants that are exercisable for 654,431 shares of the Issuer’s Common Stock within 60 days of the date of this filing (the “FLS VIII Shares”).

On September 15, 2021, FLSPF purchased 394 shares of the Issuer's Common Stock for an aggregate purchase price of \$3,704.

On September 17, 2021, FLSPF participated in the Issuer's private placement offering (the "Offering") pursuant to which it purchased a pre-funded warrant for 1,702,127 shares of the Issuer's Common Stock for an aggregate purchase price of \$15,999,994. This warrant is currently exercisable for 722,242 shares of the Issuer's Common Stock. FLSPF also purchased 400,000 shares of the Issuer's Common Stock from another stockholder of the Issuer for a total purchase price of \$3,760,000. FLSPF holds 400,394 shares of the Issuer's Common Stock and a warrant that is exercisable for 722,242 shares of the Issuer's Common Stock within 60 days of the date of this filing (the "FLSPF Shares" and together with the FLS VIII Shares, the "Frazier Shares").

Item 4. Purpose of Transaction

FLS-VIII and FLSPF acquired the Frazier Shares for investment purposes. Depending on market conditions, their continuing evaluation of the business and prospects of the Issuer and other factors, FLS-VIII, FLSPF and other Reporting Persons may dispose of or acquire additional shares of the Issuer. Except as set forth above, none of the Reporting Persons has any present plans 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 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 present capitalization or dividend policy of the Issuer;
- (f) Any other material change in the Issuer's business or corporate structure;
- (g) Changes in the Issuer's charter, bylaws or instruments corresponding thereto or other actions which may impede the acquisition of control of the Issuer by any person;
- (h) Causing a class of securities of the Issuer to be 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 Securities Exchange Act of 1934, as amended; or
- (j) Any action similar to any of those enumerated above.

Item 5. Interest in Securities of the Issuer

- (a) State the aggregate number and percentage of the class of securities identified pursuant to Item 1 (which may be based on the number of securities outstanding as contained in the most recently available filing with the Commission by the issuer unless the filing person has reason to believe such information is not current) beneficially owned (identifying those shares which there is a right to

acquire) by each person named in Item 2. The information should also be furnished with respect to persons who, together with any of the persons named in Item 2, comprise a group within the meaning of Section 13(d)(3) of the Act:

FLS-VIII is the record owner of the FLS VIII Shares. As the sole general partner of FLS-VIII, FHM-VIII L.P. may be deemed to beneficially own the FLS VIII Shares. As the sole general partner of FHM-VIII, L.P., FHM-VIII LLC may be deemed to beneficially own the FLS VIII Shares. As individual members of FHM-VIII LLC, each of Topper and Heron may be deemed to beneficially own the FLS VIII Shares.

FLSPF is the record owner of the FLSPF VIII Shares. As the sole general partner of FLSPF, FHMLSP, L.P. may be deemed to beneficially own the FLSPF VIII Shares. As the sole general partner of FHMLSP, L.P., FHMLSP, L.L.C. may be deemed to beneficially own the FLSPF Shares. As individual members of FHMLSP, L.L.C., each of Topper, Heron, Cha and Brush may be deemed to beneficially own the FLSPF Shares.

Each Reporting Person disclaims beneficial ownership of all Frazier Shares other than those shares which such person owns of record, which in Topper's case, includes the 29,325 shares of Common Stock issuable pursuant to stock options exercisable within 60 days of September 17, 2021.

The percentage of outstanding Common Stock of the Issuer, which may be deemed to be beneficially owned by each of FLS-VIII, FHM-VIII L.P. and FHM-VIII LLC, is set forth on Line 13 of such Reporting Person's cover sheet. Such percentage was calculated based on (i) 23,914,879 shares of Common Stock outstanding on July 30, 2021 as set forth in the Issuer's Form 10-Q filed with the SEC on August 10, 2021, (ii) 6,489,357 shares of Common Stock that were sold on September 17, 2021 as described in the Issuer's Current Form 8-K filed with the SEC on September 15, 2021 and (iii) 654,431 shares of Common Stock issuable to FLS-VIII pursuant to warrants exercisable within 60 days of September 17, 2021.

The percentage of outstanding Common Stock of the Issuer, which may be deemed to be beneficially owned by each of FLSPF, FHMLSP, L.P., FHMLSP, L.L.C., Cha and Brush is set forth on Line 13 of such Reporting Person's cover sheet. Such percentage was calculated based on (i) 23,914,879 shares of Common Stock outstanding on July 30, 2021 as set forth in the Issuer's Form 10-Q filed with the SEC on August 10, 2021, (ii) 6,489,357 shares of Common Stock that were sold on September 17, 2021 as described in the Issuer's Current Form 8-K filed with the SEC on September 15, 2021 and (iii) 722,242 shares of Common Stock issuable to FLSPF pursuant to warrants exercisable within 60 days of September 17, 2021.

The percentage of outstanding Common Stock of the Issuer, which may be deemed to be beneficially owned by Heron, is set forth on Line 13 of Heron's cover sheet. Such percentage was calculated based on (i) 23,914,879 shares of Common Stock outstanding on July 30, 2021 as set forth in the Issuer's Form 10-Q filed with the SEC on August 10, 2021, (ii) 6,489,357 shares of Common Stock that were sold on September 17, 2021 as described in the Issuer's Current Form 8-K filed with the SEC on September 15, 2021, (iii) 654,431 shares of Common Stock issuable to FLS-VIII pursuant to warrants exercisable within 60 days of September 17, 2021 and (iv) 722,242 shares of Common Stock issuable to FLSPF pursuant to warrants exercisable within 60 days of September 17, 2021.

The percentage of outstanding Common Stock of the Issuer, which may be deemed to be beneficially owned by Topper, is set forth on Line 13 of Topper's cover sheet. Such percentage was calculated based on (i) 29,325 shares of Common Stock issuable to James N. Topper pursuant to stock options exercisable within 60 days of September 17, 2021, (ii) 23,914,879 shares of Common Stock outstanding on July 30, 2021 as set forth in the Issuer's Form 10-Q filed with the SEC on August 10,

2021, (iii) 6,489,357 shares of Common Stock that were sold on September 17, 2021 as described in the Issuer's Current Form 8-K filed with the SEC on September 15, 2021, (iv) 654,431 shares of Common Stock issuable to FLS-VIII pursuant to warrants exercisable within 60 days of September 17, 2021 and (v) 722,242 shares of Common Stock issuable to FLSPF pursuant to warrants exercisable within 60 days of September 17, 2021.

(b) Regarding the number of shares as to which such person has:

- a. Sole power to vote or to direct the vote: See line 7 of cover sheets.
- b. Shared power to vote or to direct the vote: See line 8 of cover sheets.
- c. Sole power to dispose or to direct the disposition: See line 9 of cover sheets.
- d. Shared power to dispose or to direct the disposition: See line 10 of cover sheets.

(c) Describe any transactions in the class of securities reported on that were effected during the past sixty days or since the most recent filing of Schedule 13D (§240.13d-191), whichever is less, by the persons named in response to paragraph (a):

Information with respect to transactions in the Securities which were effected within the past sixty days or since the most recent filing on Schedule 13D, whichever is less, by the Reporting Persons is set forth below.

On September 15, 2021, FLSPF purchased 394 shares of the Issuer's Common Stock for a total purchase Price of \$3,704.

On September 17, 2021, FLS-VIII exchanged 1,200,000 shares of the Issuer's Common Stock for a warrant to purchase 1,200,000 shares of the Issuer's Common Stock.

On September 17, 2021, FLSPF purchased a warrant for 1,702,127 shares of the Issuer's Common Stock for an aggregate purchase price of \$15,999,994.

On September 17, 2021, FLSPF purchase 400,000 shares of the Issuer's Common Stock from another stockholder of the Issuer for a total purchase price of \$3,760,000.

(d) If any other person is known to have the right to receive or the power to direct the receipt of dividends from, or the proceeds from the sale of, such securities, a statement to that effect should be included in response to this item and, if such interest relates to more than five percent of the class, such person should be identified. A listing of the shareholders of an investment company registered under the Investment Company Act of 1940 or the beneficiaries of an employee benefit plan, pension fund or endowment fund is not required:

No other person is known to have the right to receive or the power to direct the receipt of dividends from, or any proceeds from the sale of, the Frazier Shares beneficially owned by any of the Reporting Persons.

(e) If applicable, state the date on which the reporting person ceased to be the beneficial owner of more than five percent of the class of securities:

Not applicable.

Item 6. Contracts, Arrangements, Understandings or Relationships with Respect to Securities of the Issuer

2019 FLS-VIII Warrant. On January 18, 2019, FLS-VIII received a warrant exercisable for 145,251 shares of the Issuer's Common Stock (the "2019 Warrant"). The 2019 Warrant has an exercise price per share of \$12.74 and will expire on January 18, 2024 if it is not exercised on or prior to such date.

2021 FLS-VIII Warrant. On September 17, 2021, FLS-VIII received a warrant exercisable for 1,200,000 shares of the Issuer's Common Stock (the "2021 FLS-VIII Warrant"). The 2021 FLS-VIII Warrant has an exercise price per share of \$0.001 and has no expiration date. In addition, FLS-VIII is not entitled to exercise the 2021 FLS-VIII Warrant if it would cause (i) the aggregate number of shares of Common Stock beneficially owned by FLS-VIII, its affiliates and any persons who are members of a Section 13(d) group with FLS-VIII or its affiliates to exceed 9.99% (the "Maximum Percentage") of the total number of issued and outstanding shares of Common Stock of the Issuer following such exercise, or (ii) the combined voting power of the securities of the Issuer beneficially owned by FLS-VIII and its affiliates and any other persons who are members of a Section 13(d) group with FLS-VIII or its affiliates to exceed the Maximum Percentage of the combined voting power of all of the securities of the Issuer then outstanding following such exercise. The Maximum Percentage may be increased or decreased by the holder with written notice to the Issuer to any other percentage specified not in excess of 19.99%.

Purchase Agreement. In connection with the Offering, on September 14, 2021, the Issuer entered into a Securities Purchase Agreement (the "Purchase Agreement") with FLSPF and certain other parties, pursuant to which on September 17, 2021 FLSPF purchased a warrant for 1,702,127 shares of the Issuer's Common Stock for an aggregate purchase price of \$15,999,994.

2021 FLSPF Warrant. On September 17, 2021, FLSPF received a warrant exercisable for 1,702,127 shares of the Issuer's Common Stock (the "2021 FLSPF Warrant"). The 2021 FLSPF Warrant has an exercise price per share of \$0.001 and has no expiration date. In addition, FLSPF is not entitled to exercise the 2021 FLSPF Warrant if it would cause (i) the aggregate number of shares of Common Stock beneficially owned by FLSPF, its affiliates and any persons who are members of a Section 13(d) group with FLSPF or its affiliates to exceed 9.99% of the total number of issued and outstanding shares of Common Stock of the Issuer following such exercise, or (ii) the combined voting power of the securities of the Issuer beneficially owned by FLSPF and its affiliates and any other persons who are members of a Section 13(d) group with FLSPF or its affiliates to exceed the Maximum Percentage of the combined voting power of all of the securities of the Issuer then outstanding following such exercise. The Maximum Percentage may be increased or decreased by the holder with written notice to the Issuer to any other percentage specified not in excess of 19.99%.

Registration Rights Agreement. In connection with the Offering, on September 14, 2021, the Issuer, FLSPF 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 or prior November 15, 2021 (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.

Lockup Agreements. In connection with the Offering, all of the Issuer's directors (including Topper), and executive officers have entered into agreements (the "Lockup Agreements") pursuant to which such parties have agreed not to, except in limited circumstances, sell or transfer, or engage in swap or similar transactions with respect to, shares of the Issuer's Common Stock until the earlier of (i) 60 days from the closing date of the Offering and (ii) following the date of effectiveness of the registration statement registering the sale of the shares issued pursuant to the Securities Purchase Agreement.

The foregoing summaries of the 2021 FLS-VIII Warrant, 2019 FLS-VIII Warrant, Purchase Agreement, 2021 FLSPF Warrant, the Registration Rights Agreement and the Lock-up Agreements are not intended to be complete and are qualified in their entirety by reference to the full texts of such documents, which are filed as Exhibit 99.B, Exhibit 99.C, Exhibit 99.D, Exhibit 99.E, Exhibit 99.F and Exhibit 99.G to this Schedule 13D, respectively, and are incorporated herein by reference.

Other than as described in this Schedule 13D, 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. Material to Be Filed as Exhibits

- Exhibit 99.A - Agreement regarding filing of joint Schedule 13D.
- Exhibit 99.B - Form of Warrant reflecting the 2021 FLS-VIII Warrant
- Exhibit 99.C - Form of Warrant reflecting the 2019 FLS-VIII Warrant (incorporated by reference to Exhibit 10.3 to the Issuer's Current Report on Form 8-K filed on January 16, 2019).
- Exhibit 99.D - Securities Purchase Agreement by and among Alpine Immune Sciences, Inc. and the Purchasers set forth therein dated September 14, 2021 (incorporated by reference to Exhibit 10.1 to the Issuer's Current Report on Form 8-K filed on September 15, 2021).
- Exhibit 99.E - Form of Warrant reflecting the 2021 FLSPF Warrant (incorporated by reference to Exhibit 10.3 to the Issuer's Current Report on Form 8-K filed on September 15, 2021).
- Exhibit 99.F - Registration Rights Agreement by and between Alpine Immune Sciences, Inc. and the Purchasers set forth therein dated September 14, 2021 (incorporated by reference to Exhibit 10.2 to the Issuer's Current Report on Form 8-K filed on September 15, 2021).
- Exhibit 99.G - Form of Lock-up Agreement (incorporated by reference to Exhibit J to that certain Securities Purchase Agreement by and among Alpine Immune Sciences, Inc. and the Purchasers set forth therein dated September 14, 2021 filed as Exhibit 10.1 to the Issuer's Current Report on Form 8-K filed on September 15, 2021).

SIGNATURES

After reasonable inquiry and to the best of my knowledge and belief, I certify that the information set forth in this statement is true, complete and correct.

Date: September 21, 2021

FRAZIER LIFE SCIENCES VIII, L.P.

By FHM Life Sciences VIII, L.P., its general partner

By FHM Life Sciences VIII, L.L.C., its general partner

By: /s/ Steve R. Bailey

Steve R. Bailey, Chief Financial Officer

Date: September 21, 2021

FHM LIFE SCIENCES VIII, L.P.

By FHM Life Sciences VIII, L.L.C., its general partner

By: /s/ Steve R. Bailey

Steve R. Bailey, Chief Financial Officer

Date: September 21, 2021

FHM LIFE SCIENCES VIII, L.L.C.

By: /s/ Steve R. Bailey

Steve R. Bailey, Chief Financial Officer

Date: September 21, 2021

FRAZIER LIFE SCIENCES PUBLIC FUND L.P.

By: FHMLSP, L.P., its General Partner

By: FHMLSP, L.L.C., its General Partner

By: /s/ Steve R. Bailey

Steve R. Bailey, Chief Financial Officer

Date: September 21, 2021

FHMLSP, L.P.

By: FHMLSP, L.L.C., its General Partner

By: /s/ Steve R. Bailey

Steve R. Bailey, Chief Financial Officer

Date: September 21, 2021

FHMLSP, L.L.C.

By: /s/ Steve R. Bailey

Steve R. Bailey, Chief Financial Officer

Date: September 21, 2021

By: *

James N. Topper

Date: September 21, 2021

By: *

Patrick J. Heron

Date: September 21, 2021

By: **

Albert Cha

Date: September 21, 2021

By: **

James Brush

Date: September 21, 2021

By: /s/ Steve R. Bailey

Steve R. Bailey, as Attorney-in-Fact

* This Schedule 13D was executed by Steve R. Bailey on behalf of the individuals listed above pursuant to a Power of Attorney, a copy of which was filed with the SEC on July 31, 2017.

** This Schedule 13D was executed by Steve R. Bailey on behalf of the individuals listed above pursuant to a Power of Attorney, a copy of which was filed with the SEC on August 16, 2021.

AGREEMENT

Pursuant to Rule 13d-1(k)(1) under the Securities Exchange Act of 1934, the undersigned hereby agree that only one statement containing the information required by Schedule 13D need be filed with respect to the ownership by each of the undersigned of Common Stock of Alpine Immune Systems, Inc.

Date: September 21, 2021

FRAZIER LIFE SCIENCES VIII, L.P.

By FHM Life Sciences VIII, L.P., its general partner

By FHM Life Sciences VIII, L.L.C., its general partner

By: /s/ Steve R. Bailey

Steve R. Bailey, Chief Financial Officer

Date: September 21, 2021

FHM LIFE SCIENCES VIII, L.P.

By FHM Life Sciences VIII, L.L.C., its general partner

By: /s/ Steve R. Bailey

Steve R. Bailey, Chief Financial Officer

Date: September 21, 2021

FHM LIFE SCIENCES VIII, L.L.C.

By: /s/ Steve R. Bailey

Steve R. Bailey, Chief Financial Officer

Date: September 21, 2021

FRAZIER LIFE SCIENCES PUBLIC FUND L.P.

By: FHMLSP, L.P., its General Partner

By: FHMLSP, L.L.C., its General Partner

By: /s/ Steve R. Bailey

Steve R. Bailey, Chief Financial Officer

Date: September 21, 2021

FHMLSP, L.P.

By: FHMLSP, L.L.C., its General Partner

By: /s/ Steve R. Bailey

Steve R. Bailey, Chief Financial Officer

Date: September 21, 2021

FHMLSP, L.L.C.

By: /s/ Steve R. Bailey
Steve R. Bailey, Chief Financial Officer

Date: September 21, 2021

By: *
James N. Topper

Date: September 21, 2021

By: *
Patrick J. Heron

Date: September 21, 2021

By: **
Albert Cha

Date: September 21, 2021

By: **
James Brush

Date: September 21, 2021

By: /s/ Steve R. Bailey
Steve R. Bailey, as Attorney-in-Fact

* This Agreement was executed by Steve R. Bailey on behalf of the individuals listed above pursuant to a Power of Attorney, a copy of which was filed with the SEC on July 31, 2017.

** This Agreement was executed by Steve R. Bailey on behalf of the individuals listed above pursuant to a Power of Attorney, a copy of which was filed with the SEC on August 16, 2021.

THE OFFER AND SALE OF THESE SECURITIES AND THE SECURITIES ISSUABLE UPON EXERCISE OF THESE SECURITIES HAVE NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933, AS AMENDED (THE "SECURITIES ACT"), OR ANY APPLICABLE STATE SECURITIES LAWS. THE SECURITIES MAY NOT BE OFFERED FOR SALE, SOLD, TRANSFERRED, ASSIGNED OR OTHERWISE DISPOSED OF (I) IN THE ABSENCE OF (A) AN EFFECTIVE REGISTRATION STATEMENT FOR THE SECURITIES UNDER THE SECURITIES ACT OR (B) AN AVAILABLE EXEMPTION FROM, OR IN A TRANSACTION NOT SUBJECT TO, THE REGISTRATION REQUIREMENTS OF THE SECURITIES ACT AND IN EACH CASE IN ACCORDANCE WITH APPLICABLE STATE SECURITIES LAWS OR BLUE SKY LAWS AS EVIDENCED BY A LEGAL OPINION OF COUNSEL REASONABLY SATISFACTORY TO THE COMPANY AND ITS TRANSFER AGENT OR (II) UNLESS SOLD PURSUANT TO RULE 144 UNDER THE SECURITIES ACT. NOTWITHSTANDING THE FOREGOING, THE SECURITIES MAY BE PLEDGED IN CONNECTION WITH A BONA FIDE MARGIN ACCOUNT OR OTHER LOAN OR FINANCING ARRANGEMENT SECURED BY THE SECURITIES; PROVIDED THAT IN CONNECTION WITH ANY FORECLOSURE OR TRANSFER OF THE SECURITIES, THE TRANSFEROR SHALL COMPLY WITH THE PROVISIONS HEREIN, IN THE EXCHANGE AGREEMENT, AND UPON FORECLOSURE OR TRANSFER OF THE SECURITIES, SUCH FORECLOSING PERSON OR TRANSFEREE SHALL COMPLY WITH ALL PROVISIONS CONTAINED HEREIN, IN THE EXCHANGE AGREEMENT.

ALPINE IMMUNE SCIENCES, INC.

PREFUNDED WARRANT TO PURCHASE COMMON STOCK

Number of Shares: 1,200,000
(subject to adjustment)

Warrant No. PF2021-6
Original Issue Date: September 17, 2021

Alpine Immune Sciences, Inc., a Delaware corporation (the "*Company*"), hereby certifies that, for good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, Frazier Life Sciences VIII, L.P. or its registered assigns (the "*Holder*"), is entitled, subject to the terms set forth below, to purchase from the Company up to a total of 1,200,000 shares of common stock, \$0.001 par value per share (the "*Common Stock*"), of the Company (each such share, a "*Warrant Share*" and all such shares, the "*Warrant Shares*") at an exercise price per share equal to \$0.001 per share (as adjusted from time to time as provided in Section 9 herein, the "*Exercise Price*"), upon surrender of this *Prefunded Warrant to Purchase Common Stock* (including any Warrants to Purchase Common Stock issued in exchange, transfer or replacement hereof, the "*Warrant*") at any time and from time to time on or after the date hereof (the "*Original Issue Date*"), subject to the following terms and conditions:

This Warrant is being issued pursuant to that certain Exchange Agreement, dated September 14, 2021, by and among the Company and the Holder.

1. **Definitions.** In addition to the terms defined elsewhere in this Warrant, capitalized terms that are not otherwise defined herein have the meanings given to such terms in the Purchase Agreement. For purposes of this Warrant, the following terms shall have the following meanings:

(c) "*Closing Sale Price*" means, for any security as of any date, the last trade price for such security on the Principal Trading Market for such security, as reported by Bloomberg Financial Markets, or, if such Principal Trading Market begins to operate on an extended hours basis and does not designate the last trade price, then the last trade price of such security prior to 4:00 P.M., New York City time, as reported by Bloomberg Financial Markets, or if the foregoing do not apply, the last trade price of such security in the over-the-counter market on the electronic bulletin

board for such security as reported by Bloomberg Financial Markets, or, if no last trade price is reported for such security by Bloomberg Financial Markets, the average of the bid prices, or the ask prices, respectively, of any market makers for such security as reported in the “pink sheets” by Pink Sheets LLC. If the Closing Sale Price cannot be calculated for a security on a particular date on any of the foregoing bases, the Closing Sale Price of such security on such date shall be the fair market value as determined by the Board of Directors using its good faith judgment. The Board of Directors’ determination shall be binding upon all parties absent demonstrable error. All such determinations shall be appropriately adjusted for any stock dividend, stock split, stock combination or other similar transaction during the applicable calculation period.

2. Registration of Warrants. The Company shall register ownership of this Warrant, upon records to be maintained by or on behalf of the Company for that purpose (the “*Warrant Register*”), in the name of the record Holder (which shall include the initial Holder or, as the case may be, any registered assignee to which this Warrant is permissibly assigned hereunder) from time to time. The Company may deem and treat the registered Holder of this Warrant as the absolute owner hereof for the purpose of any exercise hereof or any distribution to the Holder, and for all other purposes, absent actual notice to the contrary.

3. Registration of Transfers. Subject to the restrictions on transfer set forth in Section 4.1 of the Purchase Agreement and compliance with all applicable securities laws, the Company shall register the transfer of all or any portion of this Warrant in the Warrant Register, upon surrender of this Warrant, with the Form of Assignment attached as Schedule 2 hereto duly completed and signed, to the Company’s transfer agent or to the Company at its address specified in the Purchase Agreement and (x) delivery, at the request of the Company, of an opinion of counsel reasonably satisfactory to the Company to the effect that the transfer of such portion of this Warrant may be made pursuant to an available exemption from the registration requirements of the Securities Act and all applicable state securities or blue sky laws and (y) delivery by the transferee of a written statement to the Company certifying that the transferee is an “accredited investor” as defined in Rule 501(a) under the Securities Act and making the representations and certifications set forth in Section 3.2 of the Purchase Agreement, to the Company at its address specified in the Purchase Agreement. Upon any such registration or transfer, a new warrant to purchase Common Stock in substantially the form of this Warrant (any such new warrant, a “*New Warrant*”) evidencing the portion of this Warrant so transferred shall be issued to the transferee, and a New Warrant evidencing the remaining portion of this Warrant not so transferred, if any, shall be issued to the transferring Holder. The acceptance of the New Warrant by the transferee thereof shall be deemed the acceptance by such transferee of all of the rights and obligations in respect of the New Warrant that the Holder has in respect of this Warrant. The Company shall prepare, issue and deliver at the Company’s own expense any New Warrant under this Section 3. Until due presentment for registration of transfer, the Company may treat the registered Holder hereof as the owner and holder for all purposes, and the Company shall not be affected by any notice to the contrary.

4. Exercise and Duration of Warrants.

(a) All or any part of this Warrant shall be exercisable by the registered Holder in any manner permitted by this Warrant at any time and from time to time on or after the Original Issue Date.

(b) The Holder may exercise this Warrant by delivering to the Company (i) an exercise notice, in the form attached as Schedule 1 hereto (the “*Exercise Notice*”), completed and duly signed, and (ii) payment of the Exercise Price for the number of Warrant Shares as to which this Warrant is being exercised (which may take the form of a “cashless exercise” if so indicated in the Exercise Notice pursuant to Section 10 below), and the date on which the last of such items is delivered to the Company (as determined in accordance with the notice provisions hereof) is an “*Exercise Date*.” Within two (2) days following the delivery of the Exercise Notice (the “*Payment Deadline*”), the Holder shall make payment with respect to the Exercise Price for the number of Warrant Shares as to which this Warrant is being exercised; provided that the Company’s obligations to deliver such Warrant Shares shall be delayed on a day-for-day basis each day after the Payment Deadline such payment of the Exercise Price is not paid. The delivery by (or on behalf of) the Holder of the Exercise Notice and the applicable Exercise Price as provided above shall constitute the Holder’s certification to the Company that its representations contained in Sections 3.2(b), (c) and (d) of the Purchase Agreement are true and correct as of the Exercise Date as if remade in their entirety (or, in the case of any transferee Holder that is not a party to the Purchase Agreement, such transferee Holder’s certification to the Company that such representations are true and correct as to such transferee Holder as of the Exercise Date). The Holder shall not be required to physically surrender this Warrant to the Company until the Holder has purchased all

of the Warrant Shares available hereunder and the Warrant has been exercised in full, in which case, the Holder shall surrender this Warrant to the Company for cancellation within three (3) Trading Days of the date the final Exercise Notice is delivered to the Company. Execution and delivery of the Exercise Notice shall have the same effect as cancellation of the original Warrant and issuance of a New Warrant evidencing the right to purchase the remaining number of Warrant Shares, if any. The aggregate exercise price of this Warrant, except for the Exercise Price, was pre-funded to the Company on or before the Original Issue Date, and consequently no additional consideration (other than the Exercise Price) shall be required to be paid by the Holder to effect any exercise of this Warrant. The Holder shall not be entitled to the return or refund of all, or any portion, of such pre-funded exercise price under any circumstance or for any reason whatsoever.

5. Delivery of Warrant Shares.

(a) Subject to Section 4(b), upon exercise of this Warrant, the Company shall promptly (but no later than three (3) Trading Days after the Exercise Date (or four (4) Trading Days after the Exercise Date if the last of the Exercise Notice, the Exercise Price (if applicable) and opinion of counsel referred to below in this Section 5(a) (if applicable) is delivered after 5:00 P.M., New York City time, on the Exercise Date) or as soon as reasonably practicable in the event that a certificate is requested (such time, the "Delivery Deadline")) issue or cause to be issued and cause to be delivered to or upon the written order of the Holder and in such name or names as the Holder may designate (provided that, if the Registration Statement is not effective and the Holder directs the Company to deliver a certificate for the Warrant Shares in a name other than that of the Holder or an Affiliate of the Holder, it shall deliver to the Company on the Exercise Date an opinion of counsel reasonably satisfactory to the Company to the effect that the issuance of such Warrant Shares in such other name may be made pursuant to an available exemption from the registration requirements of the Securities Act and all applicable state securities or blue sky laws), (i) an electronic delivery of the Warrant Shares to the Holder's account at the Depository Trust Company ("DTC") or a similar organization, or (ii) if requested by the Holder, a certificate for the Warrant Shares issuable upon such exercise, free of restrictive legends, unless in the case of clause (i) and (ii) a registration statement covering the resale of the Warrant Shares and naming the Holder as a selling stockholder thereunder is not then effective or the Warrant Shares are not freely transferable without volume and manner of sale restrictions pursuant to Rule 144 under the Securities Act, in which case such Holder shall receive a book-entry notation for the Warrant Shares issuable upon such exercise with appropriate restrictive legends. The Holder, or any Person permissibly so designated by the Holder to receive Warrant Shares, shall be deemed to have become the holder of record of such Warrant Shares as of the Exercise Date. If the Warrant Shares are to be issued free of all restrictive legends, the Company shall, upon the written request of the Holder, use its commercially reasonable efforts to deliver, or cause to be delivered, Warrant Shares hereunder electronically through DTC or another established clearing corporation performing similar functions, if available; provided, that, the Company may, but will not be required to, change its transfer agent if its current transfer agent cannot deliver Warrant Shares electronically through such a clearing corporation.

(b) To the extent permitted by law and subject to Section 5(c), the Company's obligations to issue and deliver Warrant Shares in accordance with and subject to the terms hereof (including the limitations set forth in Section 12 below) are absolute and unconditional, irrespective of any action or inaction by the Holder to enforce the same, any waiver or consent with respect to any provision hereof, the recovery of any judgment against any Person or any action to enforce the same, or any setoff, counterclaim, recoupment, limitation or termination, or any breach or alleged breach by the Holder or any other Person of any obligation to the Company or any violation or alleged violation of law by the Holder or any other Person, and irrespective of any other circumstance that might otherwise limit such obligation of the Company to the Holder in connection with the issuance of Warrant Shares. Subject to Section 5(c), nothing herein shall limit the Holder's right to pursue any other remedies available to it hereunder, at law or in equity including, without limitation, a decree of specific performance and/or injunctive relief with respect to the Company's failure to timely deliver the Warrant Shares upon exercise of the Warrant as required pursuant to the terms hereof.

(c) If by the close of the third (3rd) Trading Day after the Exercise Date, the Company fails to deliver to the Holder a certificate representing the required number of Warrant Shares in the manner required pursuant to Section 5(a) or fails to credit the Holder's balance account with DTC for such number of Warrant Shares to which the Holder is entitled, and if after such third (3rd) Trading Day and prior to the receipt of such Warrant Shares, the Holder purchases (in an open market transaction or otherwise) shares of Common Stock to deliver in satisfaction of a sale

by the Holder of the Warrant Shares which the Holder anticipated receiving upon such exercise (a “Buy-In”), then the Company shall, within three (3) Trading Days after the Holder’s request and in the Holder’s sole discretion, either (1) pay in cash to the Holder an amount equal to the Holder’s total purchase price (including brokerage commissions, if any) for the shares of Common Stock so purchased, at which point the Company’s obligation to deliver such certificate (and to issue such Warrant Shares) shall terminate or (2) promptly honor its obligation to deliver to the Holder a certificate or certificates representing such Warrant Shares and pay cash to the Holder in an amount equal to the excess (if any) of Holder’s total purchase price (including brokerage commissions, if any) for the shares of Common Stock so purchased in the Buy-In over the product of (A) the number of shares of Common Stock purchased in the Buy-In, times (B) the Closing Sale Price of a share of Common Stock on the Exercise Date.

6. Charges, Taxes and Expenses. Issuance and delivery of the Warrant Shares upon exercise of this Warrant shall be made without charge to the Holder for any issue or transfer tax, transfer agent fee or other incidental tax or expense (excluding any applicable stamp duties) in respect of the issuance of the Warrant Shares, all of which taxes and expenses shall be paid by the Company; *provided, however*, that the Company shall not be required to pay any tax that may be payable in respect of any transfer involved in the registration of Warrant Shares or the Warrant in a name other than that of the Holder or an Affiliate thereof. The Holder shall be responsible for all other tax liability that may arise as a result of holding or transferring this Warrant or receiving Warrant Shares upon exercise hereof.

7. Replacement of Warrant. If this Warrant is mutilated, lost, stolen or destroyed, the Company shall issue or cause to be issued in exchange and substitution for and upon cancellation hereof, or in lieu of and substitution for this Warrant, a New Warrant, but only upon receipt of evidence reasonably satisfactory to the Company of such loss, theft or destruction (in such case) and, in each case, a customary and reasonable indemnity and surety bond, if requested by the Company. Applicants for a New Warrant under such circumstances shall also comply with such other reasonable regulations and procedures and pay such other reasonable third-party costs as the Company may prescribe. If a New Warrant is requested as a result of a mutilation of this Warrant, then the Holder shall deliver such mutilated Warrant to the Company as a condition precedent to the Company’s obligation to issue the New Warrant.

8. Reservation of Warrant Shares. The Company covenants that it will, at all times while this Warrant is outstanding, reserve and keep available out of the aggregate of its authorized but unissued and otherwise unreserved Common Stock, solely for the purpose of enabling it to issue Warrant Shares upon exercise of this Warrant as herein provided, the number of Warrant Shares that are initially issuable and deliverable upon the exercise of this entire Warrant, free from preemptive rights or any other contingent purchase rights of persons other than the Holder (taking into account the adjustments and restrictions of Section 9). The Company covenants that all Warrant Shares so issuable and deliverable shall, upon issuance and the payment of the applicable Exercise Price (or upon a “cashless exercise” pursuant to Section 10) in accordance with the terms hereof, be duly and validly authorized, issued and fully paid and non-assessable. The Company will take all commercially reasonable actions as may be reasonably necessary to assure that such shares of Common Stock may be issued as provided herein without violation of any applicable law or regulation, or of any requirements of any securities exchange or automated quotation system upon which the Common Stock may be listed. The Company further covenants that it will not, without the prior written consent of the Holder, take any actions to increase the par value of the Common Stock at any time while this Warrant is outstanding.

9. Certain Adjustments. The Exercise Price and number of Warrant Shares issuable upon exercise of this Warrant are subject to adjustment from time to time as set forth in this Section 9.

(a) Stock Dividends and Splits. If the Company, at any time while this Warrant is outstanding, (i) pays a stock dividend on its Common Stock or otherwise makes a distribution on any class of capital stock that is payable in shares of Common Stock, (ii) subdivides its outstanding shares of Common Stock into a larger number of shares, or (iii) combines its outstanding shares of Common Stock into a smaller number of shares, then in each such case, the Exercise Price shall be multiplied by a fraction, the numerator of which shall be the number of shares of Common Stock outstanding immediately before such event and the denominator of which shall be the number of shares of Common Stock outstanding immediately after such event. Any adjustment made pursuant to clause (i) of this paragraph shall become effective immediately after the record date for the determination of stockholders entitled to receive such dividend or distribution, and any adjustment pursuant to clause (ii) or (iii) of this paragraph shall become effective immediately after the effective date of such subdivision or combination.

(b) **Pro Rata Distributions.** If the Company, at any time while this Warrant is outstanding, distributes to all holders of Common Stock for no consideration (i) evidences of its indebtedness, (ii) any security (other than a distribution of Common Stock covered by the preceding paragraph), (iii) rights or warrants to subscribe for or purchase any security, or (iv) any other asset (in each case, “*Distributed Property*”), then, upon any exercise of this Warrant that occurs after the record date fixed for determination of stockholders entitled to receive such distribution, the Holder shall be entitled to receive, in addition to the Warrant Shares otherwise issuable upon such exercise (if applicable), the Distributed Property that such Holder would have been entitled to receive in respect of such number of Warrant Shares had the Holder been the record holder of such Warrant Shares immediately prior to such record date without regard to any limitation on exercise contained therein. Notwithstanding anything herein to the contrary, the foregoing provisions in this Section 9(b) shall not apply to, or be triggered by, any rights issued by the Company (either separately or that attach to any securities of the Company) in connection with any stockholders rights agreement, poison pill or other similar anti-takeover provision under the Company’s certificate of incorporation, bylaws or other documents.

(c) **Fundamental Transactions.** If, at any time while this Warrant is outstanding, the Company effects a “*Fundamental Transaction*” (to be defined as (i) any merger or consolidation of the Company with or into another Person, (ii) any sale of all or substantially all of the Company’s and its subsidiaries’ assets, taken as a whole, (iii) any reclassification of the Common Stock (other than a change to par value, or from par value to no par value or changes resulting from a combination or subdivision), or (iv) any statutory exchange of the outstanding shares of Common Stock, as a result of which, the holders of the Common Stock would be entitled to receive, or their Common Stock would be converted into, or exchanged for, shares, stock, other securities, or other property or assets (including cash or any combination thereof), then, to the extent then permitted under applicable laws, rules and regulations (including the rules of the Nasdaq Stock Market or any exchange on which the Common Stock is then listed), upon any subsequent exercise of this Warrant, the Holder shall have the right to receive, for each Warrant Share that would have been issuable upon such exercise immediately prior to the occurrence of such Fundamental Transaction, the same kind and amount of securities, cash, assets or property as it would have been entitled to receive upon the occurrence of such Fundamental Transaction if it had been, immediately prior to such Fundamental Transaction, the holder of the number of Warrant Shares then issuable upon exercise in full of this Warrant without regard to any limitations on exercise contained herein (the “*Alternate Consideration*”), and after receipt of such Alternate Consideration, the obligations of the Company, surviving entity or corporation purchasing or otherwise acquiring such assets or other appropriate corporation or Person shall be deemed satisfied in full and this Warrant terminated with respect to the portion so exercised. The Company shall not effect any such Fundamental Transaction unless prior to or simultaneously with the consummation thereof, any successor to the Company, surviving entity or the corporation purchasing or otherwise acquiring such assets or other appropriate corporation or Person shall assume the obligation to deliver to the Holder, such Alternate Consideration as, in accordance with the foregoing provisions, the Holder may be entitled to receive, and the other obligations under this Warrant. The provisions of this Section 9(c) shall similarly apply to subsequent transactions analogous of a Fundamental Transaction type.

(d) **Number of Warrant Shares.** Simultaneously with any adjustment to the Exercise Price pursuant to Section 9, the number of Warrant Shares that may be purchased upon exercise of this Warrant shall be increased or decreased proportionately, so that after such adjustment the aggregate Exercise Price payable hereunder for the increased or decreased number of Warrant Shares shall be the same as the aggregate Exercise Price in effect immediately prior to such adjustment.

(e) **Calculations.** All calculations under this Section 9 shall be rounded down to the nearest whole cent or the nearest whole share, as applicable.

(f) **Notice of Adjustments.** Upon the occurrence of each adjustment pursuant to this Section 9, the Company at its expense will, at the written request of the Holder, promptly compute such adjustment, in good faith, in accordance with the terms of this Warrant and prepare a certificate setting forth such adjustment, including a statement of the adjusted Exercise Price and adjusted number or type of Warrant Shares or other securities issuable upon exercise of this Warrant (as applicable), describing the transactions giving rise to such adjustments and showing in detail the facts upon which such adjustment is based. Upon written request, the Company will promptly deliver a copy of each such certificate to the Holder and to the Company’s transfer agent.

(g) Notice of Corporate Events. If, while this Warrant is outstanding, the Company (i) declares a dividend or any other distribution of cash, securities or other property in respect of its Common Stock, including, without limitation, any granting of rights or warrants to subscribe for or purchase any capital stock of the Company, (ii) enters into any agreement contemplating or solicits stockholder approval for any Fundamental Transaction or (iii) authorizes the voluntary dissolution, liquidation or winding up of the affairs of the Company, then, except if such notice and the contents thereof shall be deemed to constitute material non-public information, the Company shall deliver to the Holder a notice of such transaction at least five (5) Trading Days prior to the applicable record or effective date on which a Person would need to hold Common Stock in order to participate in or vote with respect to such transaction; *provided, however*, that the failure to deliver such notice or any defect therein shall not affect the validity of the corporate action required to be described in such notice. In addition, if while this Warrant is outstanding, the Company authorizes or approves, enters into any agreement contemplating or solicits stockholder approval for any Fundamental Transaction contemplated by Section 9(c), the Company shall deliver to the Holder a notice of such Fundamental Transaction at least fifteen (15) days prior to the date such Fundamental Transaction is consummated. Holder agrees to maintain any information disclosed pursuant to this Section 9(g) in confidence until such information is publicly available, and shall comply with applicable law with respect to trading in the Company's securities following receipt any such information.

10. Payment of Exercise Price. The Holder shall pay the Exercise Price in immediately available funds by wire transfer to an account designated by the Company; provided, however, that if, on any Exercise Date either (i) there is not an effective Registration Statement (as defined in that certain Registration Rights Agreement, of even date herewith, by and among the Company and the several Purchasers signatory thereto) registering, or no current prospectus available for, the resale of the Warrant Shares by the Holder or (ii) upon the Holder's election, the Holder may, in its sole discretion, satisfy its obligation to pay the Exercise Price through a "cashless exercise", in which event the Company shall issue to the Holder the number of Warrant Shares in an exchange of securities effected pursuant to Section 3(a)(9) of the Securities Act, as determined as follows:

$$X = Y [(A-B)/A]$$

where:

"X" equals the number of Warrant Shares to be issued to the Holder;

"Y" equals the total number of Warrant Shares with respect to which this Warrant is then being exercised;

"A" equals the Closing Sale Price of the shares of Common Stock (as reported by Bloomberg Financial Markets) as of the Trading Day on the date immediately preceding the Exercise Date (the "*Fair Market Value*"); and

"B" equals the Exercise Price then in effect for the applicable Warrant Shares at the time of such exercise.

For purposes of Rule 144 promulgated under the Securities Act, it is intended, understood and acknowledged that the Warrant Shares issued in a "cashless exercise" transaction shall be deemed to have been acquired by the Holder, and the holding period for the Warrant Shares shall be deemed to have commenced, on the date this Warrant was originally issued pursuant to the Purchase Agreement (provided that the Commission continues to take the position that such treatment is proper at the time of such exercise).

11. Company-Elected Conversion. The Company shall provide to the Holder prompt written notice if after the Original Issue Date the Company is unable to issue the Warrant Shares without restrictive legend, because the Commission has issued a stop order with respect to, or the Commission or Company has otherwise suspended or withdrawn, a Registration Statement covering the resale of the Warrant Shares, either temporarily or permanently, or otherwise (each a "*Restrictive Legend Event*"). To the extent that (A) a Restrictive Legend Event occurs, (B) at such time the Warrant Shares would be saleable under Rule 144 without compliance with the manner of sale or volume restrictions, (C) the Company has delivered the notice described in the immediately preceding sentence, and (D) the Holder attempts to exercise the Warrant after receipt of such notice by paying cash, the Company shall (i) if the Fair Market Value (as calculated above) of the Warrant Shares is greater than the Exercise Price, provide written notice to the Holder that the Company will deliver that number of Warrant Shares to the Holder as should be delivered in a

cashless exercise in accordance with Section 10, and return to the Holder all consideration paid to the Company in connection with the Holder's attempted exercise of this Warrant (a "*Company-Elected Conversion*"), or (ii) at the election of the Holder to be given within five (5) days of receipt of notice of a Company-Elected Conversion, the Holder shall be entitled to rescind the previously submitted Exercise Notice and the Company shall return all consideration paid by Holder for such Warrant Shares upon such rescission.

12. Limitations on Exercise.

(a) Notwithstanding anything to the contrary herein, the Company shall not effect any exercise of this Warrant, and the holder shall not be entitled to exercise this Warrant for a number of Warrant Shares in excess of that number of Warrant Shares which, upon giving effect or immediately prior to such exercise, would cause (i) the aggregate number of shares of Common Stock beneficially owned by the Holder, its Affiliates and any Persons who are members of a Section 13(d) group with such Holder or its Affiliates to exceed 9.99% (the "*Maximum Percentage*") of the total number of issued and outstanding shares of Common Stock of the Company following such exercise, or (ii) the combined voting power of the securities of the Company beneficially owned by the Holder and its Affiliates and any other Persons who are members of a Section 13(d) group with such Holder or its Affiliates to exceed the Maximum Percentage of the combined voting power of all of the securities of the Company then outstanding following such exercise. For purposes of this paragraph, beneficial ownership and whether a holder is a member of a Section 13(d) group shall be calculated and determined in accordance with Section 13(d) of the Exchange Act and the rules promulgated thereunder. For purposes of this Warrant, in determining the number of outstanding shares of Common Stock, the Holder may rely on the number of outstanding shares of Common Stock as reflected in (x) the Company's most recent Quarterly Report on Form 10-Q or Annual Report on Form 10-K, as the case may be, filed with the Commission prior to the date hereof, (y) a more recent public announcement by the Company or (z) any other notice by the Company or the Transfer Agent setting forth the number of shares of Common Stock outstanding. Upon the written request of the Holder, the Company shall within three (3) Trading Days confirm in writing or by electronic mail to the Holder the number of shares of Common Stock then outstanding. In any case, the number of outstanding shares of Common Stock shall be determined after giving effect to the conversion or exercise of securities of the Company, including this Warrant, by the Holder since the date as of which such number of outstanding shares of Common Stock was reported. By written notice to the Company, the Holder may from time to time increase or decrease the Maximum Percentage to any other percentage specified not in excess of 19.99% specified in such notice; provided that any such increase will not be effective until the sixty-first (61st) day after such notice is delivered to the Company. For purposes of this Section 12(a), the aggregate number of shares of Common Stock or voting securities beneficially owned by the Holder and its Affiliates and any other Persons who are members of a Section 13(d) group with such Holder or its Affiliates shall include the shares of Common Stock issuable upon (x) the exercise of this Warrant with respect to which such determination is being made, but shall exclude the number of shares of Common Stock which would be issuable upon exercise of the remaining unexercised and non-cancelled portion of this Warrant by the Holder and (y) the exercise or conversion of the unexercised, non-converted or non-cancelled portion of any other securities of the Company that do not have voting power (including without limitation any securities of the Company which would entitle the holder thereof to acquire at any time Common Stock, including without limitation any debt, preferred stock, right, option, warrant or other instrument that is at any time convertible into or exercisable or exchangeable for, or otherwise entitles the holder thereof to receive, Common Stock), is subject to a limitation on conversion or exercise analogous to the limitation contained herein and is beneficially owned by the Holder or any of its Affiliates and other Persons who are members of a Section 13(d) group with such Holder or its Affiliates.

(b) This Section 12 shall not restrict the number of shares of Common Stock which a Holder may receive or beneficially own in order to determine the amount of securities or other consideration that such Holder may receive in the event of a Fundamental Transaction as contemplated in Section 9(c) of this Warrant.

13. No Fractional Shares. No fractional Warrant Shares will be issued in connection with any exercise of this Warrant. In lieu of any fractional shares that would otherwise be issuable, the number of Warrant Shares to be issued shall be rounded down to the next whole number and the Company shall pay the Holder in cash the fair market value (based on the Closing Sale Price) for any such fractional shares.

14. **Notices.** Any and all notices or other communications or deliveries hereunder (including, without limitation, any Exercise Notice) shall be in writing and shall be deemed given and effective on the earliest of (i) the date of transmission, if such notice or communication is delivered via facsimile or confirmed e-mail at the facsimile number or e-mail address specified in the Purchase Agreement prior to 5:30 P.M., New York City time, on a Trading Day, (ii) the next Trading Day after the date of transmission, if such notice or communication is delivered via facsimile or confirmed e-mail at the facsimile number or e-mail address specified in the Purchase Agreement on a day that is not a Trading Day or later than 5:30 P.M., New York City time, on any Trading Day, (iii) the Trading Day following the date of mailing, if sent by nationally recognized overnight courier service specifying next business day delivery, and (iv) upon actual receipt by the Person to whom such notice is required to be given, if by hand delivery. The address and facsimile number of a Person for such notices or communications shall be as set forth in the Purchase Agreement unless changed by such Person by two (2) Trading Days' prior written notice to the other Persons in accordance with this Section 14.

15. **Warrant Agent.** The Company shall initially serve as warrant agent under this Warrant. Upon fifteen (15) days' notice to the Holder, the Company may appoint a new warrant agent. Any corporation into which the Company or any new warrant agent may be merged or any corporation resulting from any consolidation to which the Company or any new warrant agent shall be a party or any corporation to which the Company or any new warrant agent transfers substantially all of its corporate trust or stockholders services business shall be a successor warrant agent under this Warrant without any further act. Any such successor warrant agent shall promptly cause notice of its succession as warrant agent to be mailed (by first class mail, postage prepaid) to the Holder at the Holder's last address as shown on the Warrant Register.

16. **Miscellaneous.**

(a) **No Rights as a Stockholder.** The Holder, solely in such Person's capacity as a holder of this Warrant, shall not be entitled to vote or receive dividends or be deemed the holder of share capital of the Company for any purpose, nor shall anything contained in this Warrant be construed to confer upon the Holder, solely in such Person's capacity as the Holder of this Warrant, any of the rights of a stockholder of the Company or any right to vote, give or withhold consent to any corporate action (whether any reorganization, issue of stock, reclassification of stock, consolidation, merger, amalgamation, conveyance or otherwise), receive notice of meetings, receive dividends or subscription rights, or otherwise, prior to the issuance to the Holder of the Warrant Shares which such Person is then entitled to receive upon the due exercise of this Warrant. In addition, nothing contained in this Warrant shall be construed as imposing any liabilities on the Holder to purchase any securities (except upon exercise of this Warrant or otherwise) or as a stockholder of the Company, whether such liabilities are asserted by the Company or by creditors of the Company.

(b) **Authorized Shares.** (i) Except and to the extent as waived or consented to by the Holder, the Company shall not by any action, including, without limitation, amending its certificate or articles of incorporation or through any reorganization, transfer of assets, consolidation, merger, dissolution, issue or sale of securities or any other voluntary action, avoid or seek to avoid the observance or performance of any of the terms of this Warrant, but will at all times in good faith assist in the carrying out of all such terms and in the taking of all such actions as may be necessary or appropriate to protect the rights of Holder as set forth in this Warrant against impairment. Without limiting the generality of the foregoing, the Company will (a) not increase the par value of any Warrant Shares above the amount payable therefor upon such exercise immediately prior to such increase in par value, (b) take all such action as may be necessary or appropriate in order that the Company may validly and legally issue fully paid and non-assessable Warrant Shares upon the exercise of this Warrant, and (c) use commercially reasonable efforts to obtain all such authorizations, exemptions or consents from any public regulatory body having jurisdiction thereof as may be necessary to enable the Company to perform its obligations under this Warrant.

(ii) Before taking any action which would result in an adjustment in the number of Warrant Shares for which this Warrant is exercisable or in the Exercise Price, the Company shall obtain all such authorizations or exemptions thereof, or consents thereto, as may be necessary from any public regulatory body or bodies having jurisdiction thereof.

(c) Successors and Assigns. Subject to the restrictions on transfer set forth in this Warrant and in Section 4.1 of the Purchase Agreement, and compliance with applicable securities laws, this Warrant may be assigned by the Holder. This Warrant may not be assigned by the Company without the written consent of the Holder, except to a successor in the event of a Fundamental Transaction. This Warrant shall be binding on and inure to the benefit of the Company and the Holder and their respective successors and permitted assigns. Subject to the preceding sentence, nothing in this Warrant shall be construed to give to any Person other than the Company and the Holder any legal or equitable right, remedy or cause of action under this Warrant. This Warrant may be amended only in writing signed by the Company and the Holder, or their successors and assigns.

(d) Amendment and Waiver. Except as otherwise provided herein, the provisions of the Warrant may be amended and the Company may take any action herein prohibited, or omit to perform any act herein required to be performed by it, only if the Company has obtained the written consent of the Holder.

(e) Acceptance. Receipt of this Warrant by the Holder shall constitute acceptance of and agreement to all of the terms and conditions contained herein.

(f) Governing Law; Jurisdiction. ALL QUESTIONS CONCERNING THE CONSTRUCTION, VALIDITY, ENFORCEMENT AND INTERPRETATION OF THIS WARRANT SHALL BE GOVERNED BY AND CONSTRUED AND ENFORCED IN ACCORDANCE WITH THE LAWS OF THE STATE OF NEW YORK WITHOUT REGARD TO THE PRINCIPLES OF CONFLICTS OF LAW THEREOF. EACH OF THE COMPANY AND THE HOLDER HEREBY IRREVOCABLY SUBMITS TO THE EXCLUSIVE JURISDICTION OF THE STATE AND FEDERAL COURTS SITTING IN THE CITY OF NEW YORK, BOROUGH OF MANHATTAN, FOR THE ADJUDICATION OF ANY DISPUTE HEREUNDER OR IN CONNECTION HERewith OR WITH ANY TRANSACTION CONTEMPLATED HEREBY OR DISCUSSED HEREIN (INCLUDING WITH RESPECT TO THE ENFORCEMENT OF ANY OF THE TRANSACTION DOCUMENTS), AND HEREBY IRREVOCABLY WAIVES, AND AGREES NOT TO ASSERT IN ANY SUIT, ACTION OR PROCEEDING, ANY CLAIM THAT IT IS NOT PERSONALLY SUBJECT TO THE JURISDICTION OF ANY SUCH COURT. EACH OF THE COMPANY AND THE HOLDER HEREBY IRREVOCABLY WAIVES PERSONAL SERVICE OF PROCESS AND CONSENTS TO PROCESS BEING SERVED IN ANY SUCH SUIT, ACTION OR PROCEEDING BY MAILING A COPY THEREOF VIA REGISTERED OR CERTIFIED MAIL OR OVERNIGHT DELIVERY (WITH EVIDENCE OF DELIVERY) TO SUCH PERSON AT THE ADDRESS IN EFFECT FOR NOTICES TO IT UNDER THE PURCHASE AGREEMENT AND AGREES THAT SUCH SERVICE SHALL CONSTITUTE GOOD AND SUFFICIENT SERVICE OF PROCESS AND NOTICE THEREOF. NOTHING CONTAINED HEREIN SHALL BE DEEMED TO LIMIT IN ANY WAY ANY RIGHT TO SERVE PROCESS IN ANY MANNER PERMITTED BY LAW. EACH OF THE COMPANY AND THE HOLDER HEREBY WAIVES ALL RIGHTS TO A TRIAL BY JURY.

(g) Headings. The headings herein are for convenience only, do not constitute a part of this Warrant and shall not be deemed to limit or affect any of the provisions hereof.

(h) Severability. In case any one or more of the provisions of this Warrant shall be invalid or unenforceable in any respect, the validity and enforceability of the remaining terms and provisions of this Warrant shall not in any way be affected or impaired thereby, and the Company and the Holder will attempt in good faith to agree upon a valid and enforceable provision which shall be a commercially reasonable substitute therefor, and upon so agreeing, shall incorporate such substitute provision in this Warrant.

[REMAINDER OF PAGE INTENTIONALLY LEFT BLANK]

IN WITNESS WHEREOF, the Company has caused this Warrant to be duly executed by its authorized officer as of the date first indicated above.

ALPINE IMMUNE SCIENCES, INC.

By: /s/ Paul Rickey
Name: Paul Rickey
Title: Senior Vice President and Chief Financial Officer

SCHEDULE 1

FORM OF EXERCISE NOTICE

[To be executed by the Holder to purchase shares of Common Stock under the Warrant]

Ladies and Gentlemen:

(1) The undersigned is the Holder of Warrant No. ___ (the “*Warrant*”) issued by Alpine Immune Sciences, Inc., a Delaware corporation (the “*Company*”). Capitalized terms used herein and not otherwise defined herein have the respective meanings set forth in the Warrant.

(2) The undersigned hereby exercises its right to purchase _____ Warrant Shares pursuant to the Warrant.

(3) The Holder intends that payment of the Exercise Price shall be made as (check one):

- Cash Exercise
- “Cashless Exercise” under Section 10 of the Warrant

(4) If the Holder has elected a Cash Exercise, the Holder shall pay the sum of \$ _____ in immediately available funds to the Company in accordance with the terms of the Warrant.

(5) Pursuant to this Exercise Notice, the Company shall deliver to the Holder Warrant Shares determined in accordance with the terms of the Warrant.

(6) By its delivery of this Exercise Notice, the undersigned represents and warrants to the Company that in giving effect to the exercise evidenced hereby the Holder will not beneficially own in excess of the number of shares of Common Stock (as determined in accordance with Section 13(d) of the Securities Exchange Act of 1934, as amended) permitted to be owned under Section 12(a) of the Warrant to which this notice relates.

(7) By its delivery of this Exercise Notice and pursuant to Section 4(b) of the Warrant, the undersigned certifies to the Company that its representations contained in Sections 3.2(b), (c) and (d) of the Purchase Agreement are true and correct as of the date hereof as if remade in their entirety (or, in the case of any transferee Holder that is not a party to the Purchase Agreement, such transferee Holder’s certification to the Company that such representations are true and correct as to such transferee Holder as of the date hereof).

Dated: _____

Name of Holder: _____

By: _____

Name: _____

Title: _____

(Signature must conform in all respects to name of Holder as specified on the face of the Warrant)

SCHEDULE 2

FORM OF ASSIGNMENT

[To be completed and executed by the Holder only upon transfer of the Warrant]

FOR VALUE RECEIVED, the undersigned hereby sells, assigns and transfers unto _____ (the "Transferee") the right represented by the within Warrant to purchase _____ shares of Common Stock of Alpine Immune Sciences, Inc. (the "Company") to which the within Warrant relates and appoints _____ attorney to transfer said right on the books of the Company with full power of substitution in the premises. In connection therewith, the undersigned represents, warrants, covenants and agrees to and with the Company that:

- (a) the offer and sale of the Warrant contemplated hereby is being made in compliance with Section 4(a)(1) of the United States Securities Act of 1933, as amended (the "Securities Act") or another valid exemption from the registration requirements of Section 5 of the Securities Act and in compliance with all applicable securities laws of the states of the United States;
- (b) the undersigned has not offered to sell the Warrant by any form of general solicitation or general advertising, including, but not limited to, any advertisement, article, notice or other communication published in any newspaper, magazine or similar media or broadcast over television or radio, and any seminar or meeting whose attendees have been invited by any general solicitation or general advertising;
- (c) the undersigned has read the Transferee's investment letter included herewith, and to its actual knowledge, the statements made therein are true and correct; and
- (d) the undersigned understands that the Company may condition the transfer of the Warrant contemplated hereby upon the delivery to the Company by the undersigned or the Transferee, as the case may be, of a written opinion of counsel (which opinion shall be in form, substance and scope customary for opinions of counsel in comparable transactions) to the effect that such transfer may be made without registration under the Securities Act and under applicable securities laws of the states of the United States.

Dated: _____

(Signature must conform in all respects to name of holder as specified on the face of the Warrant)

Address of Transferee

In the presence of:
