UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, DC 20549

FORM 10-Q

(Mark One)

☒ **QUARTERLY REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the quarterly period ended June 30, 2019

OR

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the transition period from to

Commission File Number: 001-37449

ALPINE IMMUNE SCIENCES, INC.

(Exact Name of Registrant as Specified in its Charter)

Delaware	20-8969493
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**

201 Elliott Avenue West, Suite 230
Seattle, WA 98119
(206) 788-4545
(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading symbol(s)	Name of each exchange on which registered
Common Stock, par value $0.001 per share	ALPN	The Nasdaq Global Market

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes ☒ No ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer	☐	Accelerated filer	☐
Non-accelerated Filer	☒	Smaller reporting company	☒
Emerging growth company	☒		

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☒

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes ☐ No ☒

As of August 8, 2019, the registrant had 18,587,644 shares of common stock, $0.001 par value per share, outstanding.

ALPINE IMMUNE SCIENCES, INC.
FORM 10-Q
FOR THE QUARTER ENDED JUNE 30, 2019

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In this report, unless otherwise stated or as the context otherwise requires, references to "Alpine," "the Company," "we," "us," "our" and similar references refer to Alpine Immune Sciences, Inc. "Variant Immunoglobulin Domain", "vIgD", "Transmembrane Immunomodulatory Protein", "TIP", "Secreted Immunomodulatory Protein", and "SIP" are registered trademarks of Alpine Immune Sciences, Inc. All rights reserved. This report also contains registered marks, trademarks, and trade names of other companies. All other trademarks, registered marks, and trade names appearing in this report are the property of their respective holders.

PART I. FINANCIAL INFORMATION

Item 1. Financial Statements (unaudited)

ALPINE IMMUNE SCIENCES, INC.

CONDENSED CONSOLIDATED BALANCE SHEETS
(in thousands, except share and per share amounts)

	June 30, 2019 (unaudited)	December 31, 2018
Assets		
Current assets:		
Cash and cash equivalents	$ 15,468	$ 10,711
Short-term investments	40,097	41,592
Prepaid expenses and other current assets	1,657	1,242
Total current assets	57,222	53,545
Restricted cash	386	132
Property and equipment, net	1,176	1,196
Operating lease, right-of-use asset	11,303	—
Total assets	$ 70,087	$ 54,873
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 2,399	$ 1,716
Accrued liabilities	5,518	4,363
Deferred revenue	2,108	—
Operating lease liability, current	452	—
Current portion of long-term debt	2,079	2,048
Total current liabilities	12,556	8,127
Operating lease liability, noncurrent	10,919	—
Long-term debt	1,191	2,155
Total liabilities	24,666	10,282
Commitments and contingencies		
Stockholders' equity:		
Common stock, $0.001 par value per share; 200,000,000 shares authorized at June 30, 2019 and December 31, 2018; 18,635,197 shares issued and 18,584,730 shares outstanding at June 30, 2019; 13,904,672 shares issued and 13,854,205 shares outstanding at December 31, 2018	19	14
Treasury stock, at cost; 50,467 shares at June 30, 2019 and December 31, 2018	—	—
Additional paid-in capital	115,704	90,664
Accumulated other comprehensive gain (loss)	9	(13)
Accumulated deficit	(70,311)	(46,074)
Total stockholders' equity	45,421	44,591
Total liabilities and stockholders' equity	$ 70,087	$ 54,873

The accompanying notes are an integral part of these condensed consolidated financial statements.

ALPINE IMMUNE SCIENCES, INC.

CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE INCOME (LOSS)
(in thousands, except share and per share amounts)

	Three Months Ended June 30,		Six Months Ended June 30,	
	2019	2018	2019	2018
	(unaudited)			
Collaboration revenue	$ 567	$ 390	$ 567	$ 705
Operating expenses:				
Research and development	10,166	5,718	20,516	9,510
General and administrative	2,553	1,883	4,898	3,991
Loss on sale of intangible asset	—	1,203	—	1,203
Total operating expenses	12,719	8,804	25,414	14,704
Loss from operations	(12,152)	(8,414)	(24,847)	(13,999)
Other income (expense):				
Interest expense	(61)	(83)	(131)	(161)
Interest and other income	357	337	741	642
Loss before taxes	(11,856)	(8,160)	(24,237)	(13,518)
Income tax benefit	—	253	—	305
Net loss	$ (11,856)	$ (7,907)	$ (24,237)	$ (13,213)
Comprehensive income (loss):				
Unrealized gain on investments	17	50	32	4
Unrealized gain (loss) on foreign currency translation	4	—	(10)	—
Comprehensive loss	$ (11,835)	$ (7,857)	$ (24,215)	$ (13,209)
Weighted-average shares used to compute basic and diluted net loss per share	18,576,199	13,848,974	18,126,556	13,846,865
Basic and diluted net loss per share	$ (0.64)	$ (0.57)	(1.34)	$ (0.95)

The accompanying notes are an integral part of these condensed consolidated financial statements.

ALPINE IMMUNE SCIENCES, INC.
CONDENSED CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY (unaudited)
(in thousands, except share amounts)

	Common Stock		Treasury		Additional Paid-in Capital	Accumulated Other Comprehensive Loss	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount	Shares	Amount				
Balance, December 31, 2017	13,831,178	$ 14	50,467	$ —	$ 88,346	$ (59)	$ (9,384)	$ 78,917
Cumulative effect of changes related to adoption of new revenue standard	—	—	—	—	—	—	(202)	(202)
Exercise of stock options	14,906	—	—	—	7	—	—	7
Stock-based compensation	—	—	—	—	511	—	—	511
Unrealized loss on investments	—	—	—	—	—	(46)	—	(46)
Net loss	—	—	—	—	—	—	(5,306)	(5,306)
Balance, March 31, 2018	13,846,084	$ 14	50,467	$ —	$ 88,864	$ (105)	$ (14,892)	$ 73,881
Exercise of stock options	4,678	—	—	—	—	—	—	—
Stock-based compensation	—	—	—	—	523	—	—	523
Unrealized gain on investments	—	—	—	—	—	50	—	50
Net loss	—	—	—	—	—	—	(7,907)	(7,907)
Balance, June 30, 2018	13,850,762	$ 14	50,467	$ —	$ 89,387	$ (55)	$ (22,799)	$ 66,547
Balance, December 31, 2018	13,854,205	$ 14	50,467	$ —	$ 90,664	$ (13)	$ (46,074)	$ 44,591
Issuance of Units in Private Placement, net of offering costs	4,706,700	5	—	—	23,613	—	—	23,618
Exercise of stock options	124	—	—	—	—	—	—	—
Stock-based compensation	—	—	—	—	754	—	—	754
Unrealized gain on investments	—	—	—	—	—	15	—	15
Unrealized loss on foreign currency translation						(14)		(14)
Net loss	—	—	—	—	—	—	(12,381)	(12,381)
Balance, March 31, 2019	18,561,029	$ 19	50,467	$ —	$ 115,031	$ (12)	$ (58,455)	$ 56,583
Offering costs associated with Private Placement	—	—	—	—	(20)	—	—	(20)
Exercise of stock options	23,701	—	—	—	11	—	—	11
Stock-based compensation	—	—	—	—	682	—	—	682
Unrealized gain on investments	—	—	—	—	—	17	—	17
Unrealized gain on foreign currency translation	—	—	—	—	—	4	—	4
Net loss	—	—	—	—	—	—	(11,856)	(11,856)
Balance June 30, 2019	18,584,730	$ 19	50,467	$ —	$ 115,704	$ 9	$ (70,311)	$ 45,421

The accompanying notes are an integral part of these condensed consolidated financial statements.

ALPINE IMMUNE SCIENCES, INC.

CONDENSED CONSOLIDATED STATEMENTS OF CASH FLOWS
(in thousands)

	Six Months Ended June 30,	
	2019	**2018**
	(unaudited)	
Operating activities		
Net loss	$ (24,237)	$ (13,213)
Adjustments to reconcile net loss to net cash used in operating activities:		
Loss on sale of intangible asset	—	1,203
Amortization of right-of-use asset	454	—
Depreciation expense	229	170
Amortization of premium/discount on investments	(185)	(368)
Non-cash interest expense	67	88
Deferred income tax	—	(305)
Stock-based compensation and warrant expense	1,436	1,034
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	(415)	(536)
Accounts payable and accrued liabilities	1,829	760
Deferred revenue	2,108	(479)
Lease liabilities	(386)	—
Net cash used in operating activities	(19,100)	(11,646)
Investing activities		
Purchases of property and equipment	(200)	(278)
Proceeds from sale of intangible asset	—	250
Purchase of short-term investments	(39,804)	(41,390)
Maturities of short-term investments	40,125	48,626
Proceeds from the sale of short-term investments	1,391	—
Net cash provided by investing activities	1,512	7,208
Financing activities		
Proceeds from sale of common stock, net of offering costs	23,598	—
Repayment of debt	(1,000)	—
Proceeds from exercise of stock options	11	7
Net cash provided by financing activities	22,609	7
Effect of exchange rate changes on cash, cash equivalents and restricted cash	(10)	—
Net increase (decrease) in cash and cash equivalents and restricted cash	5,011	(4,431)
Cash and cash equivalents and restricted cash, beginning of period	10,843	8,132
Cash and cash equivalents and restricted cash, end of period	$ 15,854	$ 3,701
Supplemental Information		
Recognition of right-of-use asset	$ 11,757	$ —
Cash paid for interest	$ 67	$ 72

The accompanying notes are an integral part of these condensed consolidated financial statements.

1. Description of the Business

Alpine Immune Sciences, Inc. (the "Company", "Alpine", "we", "us", or "our"), together with its consolidated subsidiaries, is a clinical-stage immunotherapy company committed to leading a new wave of immune therapeutics, creating potentially powerful multifunctional immunotherapies to improve patients' lives via unique protein engineering technologies. Alpine has two lead programs. The first, ALPN-101 for autoimmune/inflammatory diseases, is a dual selective T-cell costimulation blocker engineered to reduce pathogenic T and B cell immune responses by blocking ICOS and CD28. ALPN-101 is currently enrolling a phase I healthy volunteer trial. The second, ALPN-202 for cancer, is a conditional CD28 costimulator and dual checkpoint inhibitor. Our proprietary scientific platform uses a process known as directed evolution to convert native immune system proteins from the Immunoglobulin Super Family, or IgSF, into multi-targeted therapeutics potentially capable of modulating the human immune system. We were incorporated under the laws of the State of Delaware and are headquartered in Seattle, Washington.

2. Summary of Significant Accounting Policies

Basis of Presentation

The accompanying unaudited condensed consolidated financial statements have been prepared in accordance with the rules and regulations of the Securities and Exchange Commission ("SEC") and generally accepted accounting principles in the United States of America ("GAAP"). The preparation of financial statements in conformity with GAAP requires management to make judgments, estimates and assumptions that affect the amounts reported in the unaudited condensed consolidated financial statements and accompanying notes. Significant estimates inherent in the preparation of the accompanying unaudited condensed consolidated financial statements include accruals for clinical trial activities and other accruals, and the estimated fair value of equity-based awards. We base our estimates and assumptions on historical experience when available and on various factors we believe to be reasonable under the circumstances. Actual results could differ materially from those estimates.

The accompanying unaudited condensed consolidated financial statements as of June 30, 2019 and for the three and six months ended June 30, 2019 and 2018 and the related interim information contained within the notes to the condensed consolidated financial statements are unaudited. The unaudited interim financial statements have been prepared on the same basis as the audited financial statements and in the opinion of management, reflect all normal recurring adjustments necessary for a fair statement of our financial position for the interim periods presented. The accompanying unaudited condensed consolidated financial statements should be read in conjunction with our audited consolidated financial statements and accompanying notes for the years December 31, 2018 and 2017 included in our Annual Report on Form 10-K for the year ended December 31, 2018, filed with the SEC on March 18, 2019 ("Annual Report"). The results of our operations for the three and six months ended June 30, 2019 are not necessarily indicative of the results to be expected for the full year.

Principles of Consolidation

Our unaudited condensed consolidated financial statements include the financial position and results of operations of Alpine and our wholly owned operating company and subsidiary, AIS Operating Co., Inc., and Alpine Immune Sciences Australia PTY LTD, respectively. All inter-company balances and transactions have been eliminated in consolidation.

Restricted Cash

Restricted cash represents cash drawn on lines of credit used to establish collateral to support the security deposit on our leases to rent office and laboratory space in Seattle, Washington.

Short-Term Investments

Our short-term investments include funds invested in highly liquid money market funds, U.S. Treasury securities, commercial paper, and corporate debt securities with a final maturity of each security of less than one year. All investments are classified as available-for-sale securities and are recorded at fair value based on quoted prices in active markets, with unrealized gains and losses excluded from earnings and reported in other comprehensive income (loss). Purchase premiums and discounts are recognized as interest income using the interest method over the terms of the securities. Realized gains and losses

and declines in fair value deemed to be other than temporary are reflected in the Condensed Consolidated Statements of Operations and Comprehensive Income (Loss) using the specific-identification method.

Leases (effective January 1, 2019)

We account for our leases under Accounting Standards Codification ("ASC") 842, Leases. Under this guidance, arrangements meeting the definition of a lease are classified as operating or financing leases, and are recorded on the condensed consolidated balance sheet as both a right-of-use asset and lease liability, calculated by discounting fixed lease payments over the lease term at the rate implicit in the lease or our incremental borrowing rate. Lease liabilities are increased by interest and reduced by payments each period, and the right-of-use asset is amortized over the lease term. For operating leases, interest on the lease liability and the amortization of the right-of-use asset result in straight-line rent expense over the lease term. For finance leases, interest on the lease liability and the amortization of the right-of-use asset results is front-loaded expense over the lease term. Variable lease expenses are recorded when incurred.

In calculating the right-of-use asset and lease liability, we elected to combine lease and non-lease components. We exclude short-term leases having initial terms of 12 months or less from the new guidance as an accounting policy election, and recognize rent expense on a straight-line basis over the lease term. We continue to account for leases in the prior period financial statements under ASC Topic 840.

Revenue Recognition

Revenue is recognized when control of the promised goods or services is transferred to our customers, in an amount that reflects the consideration we expect to be entitled to in exchange for those goods or services. Our steps for recognizing revenue consist of; (1) identifying the contract, (2) identifying the performance obligations as either distinct or bundled goods and services, (3) determining the transaction price associated with each performance obligation for which we expect to be entitled in exchange for transferring such goods and services, (4) allocating the transaction price to the performance obligations in the contract and (5) recognizing revenue upon satisfaction of performance obligations.

Our collaboration agreements principally contain multiple performance obligations, which may include (1) grants of, or options to obtain, intellectual property licenses; (2) research and development services; and/or (3) manufacturing or supply services. Payments typically received under these arrangements include one or more of the following: non-refundable upfront license fees, option exercise fees, payment for research and/or development efforts, amounts due upon the achievement of specified objectives, and/or royalties on future product sales. Our revenue is primarily derived from our collaboration agreements with Adaptimmune Therapeutics plc ("Adaptimmune") and Kite Pharma, a Gilead company ("Kite"). See further discussion of our collaboration agreements in Note 9.

We allocate revenue to each performance obligation based on its relative stand-alone selling price. We generally determine stand-alone selling prices at the inception of the contract based on our best estimate of what the selling price would be if the deliverable was regularly sold by us on a stand-alone basis. Payments received prior to satisfying the relevant revenue recognition criteria are recorded as deferred revenue in the accompanying Condensed Consolidated Balance Sheets and recognized as revenue when the related revenue recognition criteria are met. We recognize revenue under our collaboration agreements based on employee hours contributed to each performance obligation.

Our collaboration agreements provide for non-refundable milestone payments. We recognize revenue that is contingent upon the achievement of a substantive milestone in its entirety in the period in which the milestone is achieved. A milestone is considered substantive when the consideration payable to us for such milestone (1) is consistent with our performance necessary to achieve the milestone or the increase in value to the collaboration resulting from our performance; (2) relates solely to our past performance; and (3) is reasonable relative to all of the other deliverables and payments within the arrangement. In making this assessment, we consider all facts and circumstances relevant to the arrangement, including factors such as the scientific, regulatory, commercial, and other risks that must be overcome to achieve the milestone, the level of effort and investment required to achieve the milestone and whether any portion of the milestone consideration is related to future performance or deliverables.

We review the contributed employee hours for each performance obligation under our collaboration agreements, and adjust the revenue recognized to reflect changes in assumptions relating to the estimated satisfaction of the performance obligation. We could accelerate revenue recognition in the event of early termination of programs or if our expectations change. Alternatively, we could decelerate revenue recognition if programs are extended or delayed. While such changes to our estimates have no impact on our reported cash flows, the timing of revenue recorded in future periods could be materially impacted.

Revenue from Asset Purchase Agreement

In June 2018, we entered into an Asset Purchase Agreement ("Purchase Agreement") with Laurel Venture Capital Ltd. ("Laurel") and completed the sale of global rights to the indefinite-life GSNOR inhibitor in-process research and development asset acquired as part of the merger with Nivalis in 2017. As consideration under the Purchase Agreement, we received a non-refundable closing payment of $250,000, which was accounted for as a purchase of our intangible asset. Upon the sale of the GSNOR assets, we derecognized the full carrying value of the intangible asset on our accompanying Condensed Consolidated Balance Sheets and recognized a loss on the sale of the intangible asset of $1.2 million on the accompanying Condensed Consolidated Statements of Operations and Comprehensive Income (Loss). In June 2019, we recognized as revenue an additional milestone payment of $425,000, related to the asset purchase.

Foreign Currency Translation

Our functional currency is the U.S. dollar. All assets and liabilities of our subsidiaries are translated using period-end exchange rates and revenues and expenses are translated at average exchange rates for the year. Translation adjustments are included as components of comprehensive gain (loss) in the Condensed Consolidated Statements of Operations and Comprehensive Income (Loss).

Recently Issued Accounting Pronouncements

In November 2018, the Financial Accounting Standards Board ("FASB") issued Accounting Standards Update ("ASU") No. 2018-18, Collaborative Arrangements: Clarifying the Interaction between Topic 808 and Topic 606. This ASU clarifies that certain transactions between collaborative arrangement participants should be accounted for as revenue when the collaborative arrangement participant is a customer in the context of a unit of account and precludes recognizing as revenue consideration received from a collaborative arrangement participant if the participant is not a customer. This ASU is effective for public companies for annual reporting periods and interim periods within those annual periods beginning after December 15, 2019. We are currently evaluating the effect, if any, that ASU 2018-18 will have on our consolidated financial statements.

In August 2018, the FASB issued ASU No. 2018-13, Fair Value Measurement. ASU 2018-13 modifies the disclosure requirements for fair value measurements by removing, modifying, or adding certain disclosures. This ASU is effective for fiscal years beginning after December 15, 2019, and interim periods within those fiscal years, with early adoption permitted for any eliminated or modified disclosures. We are evaluating the effect of adopting this new accounting guidance to determine the impact it may have on our financial statements.

Recently Adopted Accounting Pronouncements

In June 2018, the FASB issued ASU No. 2018-07, which aligns the measurement and classification guidance for share-based payments to nonemployees with the guidance for share-based payments to employees, with certain exceptions. Under the guidance, the measurement of equity-classified nonemployee awards will be fixed at the grant date. Upon transition, nonemployee awards will be required to be measured at fair value as of the adoption date with a cumulative-effect adjustment recognized in retained earnings as of the beginning of the annual period of adoption. ASU 2018-07 is effective for fiscal years beginning after December 15, 2018, including interim periods within that fiscal year. We adopted this standard on January 1, 2019 and it did not have a material impact on our financial statements and related disclosures.

In February 2016, the FASB issued ASU No. 2016-02, Leases. ASU 2016-02 requires a lessee to separate the lease components from the non-lease components in a contract and recognize in the statement of financial position a liability to make lease payments (the lease liability) and a right-of-use asset representing its right to use the underlying asset for the lease term. It also aligns lease accounting for lessors with the revenue recognition guidance in ASU 2014-09. We adopted this ASU effective January 1, 2019 using the additional (optional) approach by recording an operating lease right-of-use asset of $797,000, a corresponding operating lease liability of $883,000, and reducing our deferred rent balance by $86,000 to $0 on our accompanying Condensed Consolidated Balance Sheets; there was no effect on opening retained earnings, and we continue to account for leases in the prior period financial statements under ASC Topic 840. In adopting the new standard, we elected to apply the practical expedients regarding the identification of leases, lease classification, indirect costs, and the combination of lease and non-lease components.

3. Net Loss Per Share

Basic net loss per share is computed by dividing net loss by the weighted-average number of common shares outstanding during the period. The net loss per share for the three and six months ended June 30, 2019 reflects 4,706,700 shares of our

common stock issued pursuant to a private placement financing completed in January 2019. The significant number of shares issued has affected the year-over-year comparability of our net loss per share calculations.

The common stock issuable upon the conversion or exercise of the following dilutive securities has been excluded from the diluted net loss per share calculation because their effect would have been anti-dilutive:

	June 30,	
	2019	2018
	(unaudited)	
Warrants to purchase common stock	1,859,733	24,123
Options to purchase common stock	3,266,572	1,990,793
Total	5,126,305	2,014,916

4. Cash Equivalents and Short-Term Investments

The amortized cost and fair value of our cash equivalents and short-term investments are as follows (in thousands):

	June 30, 2019			
Assets:	(unaudited)			
	Amortized Cost	Gross unrealized gains	Gross unrealized losses	Fair market value
Money market funds	$ 8,481	$ —	$ —	$ 8,481
U.S. treasury bills	11,509	6	—	11,515
Corporate debt securities and commercial paper	31,912	13	—	31,925
Total	$ 51,902	$ 19	$ —	$ 51,921

	December 31, 2018			
Assets:	Amortized Cost	Gross unrealized gains	Gross unrealized losses	Fair market value
Money market funds	$ 6,405	$ —	$ —	$ 6,405
U.S. treasury bills	13,966	—	(2)	13,964
Corporate debt securities and commercial paper	31,331	—	(11)	31,320
Total	$ 51,702	$ —	$ (13)	$ 51,689

All short-term investments held as of June 30, 2019 and December 31, 2018 were classified as available-for-sale securities and had contractual maturities of less than one year. There were no realized gains and losses on these securities for the periods presented.

5. Fair Value Measurements

Cash and cash equivalents, receivables, accounts payable and accrued liabilities, which are recorded at invoiced amount or cost, approximate fair value based on the short-term nature of these financial instruments. Fair value is defined as the exchange price received for an asset or paid to transfer a liability, or an exit price, in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. Valuation techniques used to measure fair value must maximize the use of observable inputs and minimize the use of unobservable inputs. The three-tier fair value hierarchy, which prioritizes the inputs used in measuring fair value, is as follows:

Level 1: Quoted prices in active markets for identical assets or liabilities.

Level 2: Observable inputs other than Level 1 prices, such as quoted prices for similar assets or liabilities, quoted prices in inactive markets, or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the assets or liabilities.

Level 3: Unobservable inputs supported by little or no market activity and significant to the fair value of the assets or liabilities.

As of June 30, 2019, and December 31, 2018, cash of $3.6 million and $614,000, respectively, is excluded from the following fair value table below. The following tables summarize our financial assets and liabilities measured at fair value on a recurring basis (in thousands):

	June 30, 2019 (unaudited)			
Assets:	**Level 1**	**Level 2**	**Level 3**	**Total**
Money market funds	$ 8,481	$ —	$ —	$ 8,481
U.S. treasury bills	11,515	—	—	11,515
Corporate debt securities and commercial paper	—	31,925	—	31,925
Total	$ 19,996	$ 31,925	$ —	$ 51,921

	December 31, 2018			
Assets:	**Level 1**	**Level 2**	**Level 3**	**Total**
Money market funds	$ 6,405	$ —	$ —	$ 6,405
U.S. treasury bills	13,964	—	—	13,964
Corporate debt securities and commercial paper	—	31,320	—	31,320
Total	$ 20,369	$ 31,320	$ —	$ 51,689

Our Level 2 assets consist of commercial paper and corporate debt securities. We review trading activity and pricing for our available-for-sale securities as of the measurement date. When sufficient quoted pricing for identical securities is not available, we use market pricing and other observable market inputs for similar securities obtained from various third-party data providers. These inputs either represent quoted prices for similar assets in active markets or have been derived from observable market data.

6. Accrued Liabilities

Accrued liabilities consisted of the following (in thousands):

	June 30, 2019 (unaudited)	December 31, 2018
Research and development services	$ 3,386	$ 2,457
Employee compensation	1,026	1,009
Legal and professional fees	113	646
Accrued other	993	251
Total	$ 5,518	$ 4,363

7. Long-term Debt

We maintain a long-term financing arrangement with Silicon Valley Bank. On June 30, 2017, we drew down a term loan of $5.0 million. The loan had an interest-only period that expired on July 1, 2018, at which point we became obligated to make thirty consecutive equal monthly payments of principal (each in an amount that will fully amortize the loan), plus accrued interest. Interest accrues at a floating per annum rate equal to the lender's prime rate minus 1.75%. As a condition to the loan, we agreed to pay a final payment fee of 7.5%, or $375,000, upon repayment of the loan. The final payment fee was recorded in long-term debt with an offsetting reduction in long-term debt and was accounted for as a debt discount.

Pursuant to the loan agreement we have pledged substantially all of our assets, excluding intellectual property, as collateral. The obligations under the loan agreement are subject to acceleration upon the occurrence of specified events of default, including a material adverse change in our business, operations, financial, or other condition. We assessed the likelihood of the lender accelerating payment of the loan due to a material adverse change in our business, operations, financial, or other condition as remote. As such, as of June 30, 2019, the classification of the loan is split between current and noncurrent based on the timing of payment obligations. The term loan agreement contains customary conditions to borrowings, events of default and negative covenants, including covenants that could limit our ability to, among other things, incur additional indebtedness, liens or other encumbrances; make dividends or other distributions; buy, sell or transfer assets; engage in any new

line of business; and enter into certain transactions with affiliates. We were in compliance with our covenants as of June 30, 2019.

Also, in connection with the drawdown of the loan, we granted Silicon Valley Bank 7,069 Series A-1 Preferred Stock warrants at an exercise price of $12.38 per share. The fair value of the warrants on the date of issuance was $53,000, determined using the Black-Scholes option-pricing model, and was recorded as a discount to the note and as a warrant liability. In connection with the merger and conversion of all outstanding Series A-1 preferred stock, the warrants became exercisable for 7,069 fully vested shares of our common stock. As a result of the change in the underlying shares, the warrants were equity-classified beginning on July 24, 2017.

The debt discount is being amortized to interest expense using the effective interest method over the repayment term of the initial loan amount. Non-cash interest expense associated with the amortization of the discount was $31,000 and $44,000 for the three months ended June 30, 2019 and 2018, respectively, and $67,000 and $88,000 for the six months ended June 30, 2019 and 2018, respectively. The unamortized discount was $105,000 as of June 30, 2019.

8. Commitments and Contingencies

Operating Leases

We lease office and laboratory space in Seattle, Washington, under an agreement classified as an operating lease that expires on December 31, 2019. This lease has two 12-month renewal options, which we did not include in the lease term when calculating our right-of-use asset and lease liability, as we are not reasonably certain to renew. This lease does not require any contingent rental payments, impose any financial restrictions, or contain any residual value guarantees. Variable expenses generally represent our share of the landlord's operating expenses. We do not act as a lessor or have any leases classified as financing leases. In May 2017, as required by the terms of the lease, we entered into a line of credit to establish collateral to support the security deposit in an amount of $132,000. This is recorded as restricted cash in the accompanying Condensed Consolidated Balance Sheets.

In March 2019, we entered into a lease with ARE-Seattle No. 28, LLC (the "Landlord") for 27,164 square feet of office and laboratory space located at 188 East Blaine Street, Seattle, Washington. The term of the lease is 10.8 years with one option to extend the term by 5 years. The lease term commenced in June 2019. The "Rent Commencement Date" will be nine months after the commencement date. The annual base rent under the lease is $1.7 million for the first year and will increase by 3.0% each year thereafter. We are not required to pay base rent from the Rent Commencement Date through the last day of the ninth month following the Rent Commencement Date. We will receive a maximum tenant improvement allowance of $5.4 million, which is included in our base rent, and a maximum additional tenant improvement allowance of $1.8 million, which will result in additional rent amortized over the term of the lease at an annual rate of 8.0%. The lease also requires us to pay additional amounts for operating and maintenance expenses. In March 2019, in connection with the lease, we provided a $254,000 letter of credit as a security deposit, which is recorded as restricted cash in our accompanying Condensed Consolidated Balance Sheets.

At June 30, 2019, our operating lease right-of-use assets and operating lease liability associated with these leases were $11.3 million and $11.4 million, respectively, which are included in the accompanying Condensed Consolidated Balance Sheets.

The components of our lease expense were as follows (in thousands):

	Three Months Ended June 30, 2019	Six Months Ended June 30, 2019
	(unaudited)	
Lease cost:		
Operating lease cost	$ 365	$ 572
Variable lease cost	80	171
Total lease cost	$ 445	$ 743
Other information:		
Cash paid for amounts included in the measurement of lease liabilities		$ 452
Right-of-use assets exchanged for new operating lease liabilities		$ 11,757
Weighted-average remaining lease term (in years), operating leases		10.3
Weighted-average discount rate, operating leases		10.5%

Maturities of our operating leases as of June 30, 2019 are as follows (in thousands):

2019 (remaining six months)	$	460
2020		228
2021		1,976
2022		2,027
2023		2,079
Thereafter		14,078
Total		20,848
Less: imputed interest		(9,477)
Operating lease liabilities included in the Consolidated Balance Sheets at June 30, 2019	$	11,371

Rent expense, which is recorded on a straight-line basis, was $206,000 and $398,000 for the three and six months ended June 30, 2018.

9. License and Collaboration Agreements

Adaptimmune

In May 2019, we entered into a collaboration and licensing agreement with Adaptimmune (the "Adaptimmune Collaboration Agreement") to develop next-generation SPEAR T-cell products. Under the Adaptimmune Collaboration Agreement, we are to perform certain research services and grant Adaptimmune an exclusive license to programs from our secreted immunomodulatory protein ("SIP") and transmembrane immunomodulatory protein ("TIP") technologies, in order to further enhance Adaptimmune's efforts to design and develop next-generation SPEAR T-cell therapies. In June 2019, under the terms of the Adaptimmune Collaboration Agreement, we received an upfront license payment of $2.0 million and an additional $250,000 in research support payments to fund ongoing programs. These payments were recorded as deferred revenue and will be recognized to revenue based on employee hours contributed to each performance obligation. We recorded revenue of $142,000 for the three months ended June 30, 2019. In addition, we are eligible for additional research support payments, one-time payments and downstream development and commercialization milestones of up to $288.0 million, if all pre-specified milestones for each program are achieved. We are also eligible to receive low-single digit royalties on worldwide net sales of the applicable products.

Kite

In October 2015, we entered into a collaboration and licensing agreement (the "Kite Collaboration Agreement") with Kite to discover and develop protein-based immunotherapies targeting the immune synapse to treat cancer. In May 2019, Kite provided us notice of termination of the Kite Collaboration Agreement following the expiration of the research term. Upon termination, the confidentiality and indemnity obligations of the parties survived and the licenses granted to Kite under the Kite Collaboration Agreement were terminated. Pursuant to the terms of the Kite Collaboration Agreement, the termination was effective in June 2019, thirty days after the effectiveness of Kite's notice.

Under the terms of the Kite Collaboration Agreement, in 2015, Kite made upfront payments to us of $5.5 million, which were initially recorded as deferred revenue. Under the Kite Collaboration Agreement, we recorded revenue of $0 and $390,000 for the three months ended June 30, 2019 and 2018, respectively, and $0 and $630,000 for the six months ended June 30, 2019 and 2018, respectively. In the second quarter of 2018, based on the completion of our research and development efforts in connection with the performance period, we recognized the remaining balance related to the Kite Collaboration Agreement in deferred revenue.

10. Stockholders' Equity

Securities Offerings

In January 2019, we entered into a securities purchase agreement (the "Purchase Agreement") with a limited number of accredited investors, pursuant to which we sold 4,706,700 units (the "Units") for an aggregate purchase price of $25.3 million in a private placement (the "Private Placement"). Each Unit has a purchase price of $5.37 and consists of one share of our common stock and a warrant to purchase 0.39 shares of common stock. Pursuant to the terms of the Purchase Agreement, we issued 4,706,700 shares of common stock and warrants to purchase an aggregate of 1,835,610 shares of common stock. The warrants have an exercise price of $12.74 and have a term of five years.

The issuance of the securities sold in the Private Placement was not registered under the Securities Act of 1933, as amended, or state securities laws and such securities could not be offered or sold in the United States absent registration with the SEC or an applicable exemption from such registration requirements. In March 2019, we filed a registration statement with the SEC covering the resale of the shares of common stock issuable in connection with the Private Placement and upon exercise of the warrants, which registration was declared effective by the SEC on April 4, 2019.

We have incurred legal, accounting and other direct costs related to our efforts to raise capital. These costs have been capitalized as deferred offering costs and are included within prepaid expenses and other current assets in our accompanying Condensed Consolidated Balance Sheets. These were deferred until completion of the Private Placement, at which time $1.7 million were reclassified to additional paid-in capital as a reduction of the proceeds. As of June 30, 2019, no sales under our Equity Distribution Agreement (as defined below) have occurred.

In June 2018, we entered into an equity distribution agreement, ("Equity Distribution Agreement"), with Piper Jaffray & Co., ("Piper Jaffray"), pursuant to which we may sell shares of our common stock through an "at the market" equity offering program for up to $50.0 million, in gross cash proceeds. Piper Jaffray will be entitled to compensation for its services of up to 3.0% of the gross sales price per share of all shares sold through Piper Jaffray under the Equity Distribution Agreement. The Equity Distribution Agreement may be terminated by us upon written notice to Piper Jaffray for any reason or by Piper Jaffray upon written notice to us for any reason or at any time under certain circumstances, including but not limited to if we experience a material adverse change.

Under the Equity Distribution Agreement, we will set the parameters for the sale of shares, including the number of shares to be issued, the time period during which sales are requested to be made, limitation on the number of shares that may be sold in any one trading day and any minimum price below which sales may not be made. We have no obligation to sell any shares under the Equity Distribution Agreement, and may at any time suspend solicitation and offers under the Equity Distribution Agreement. In July 2019, our Registration Statement on Form S-3 (File No. 333-212404) expired pursuant to Rule 415(a)(5) under the Securities Act of 1933, as amended. We will be unable to sell shares under the Equity Distribution Agreement until a new Registration Statement on Form S-3 is filed and declared effective by the SEC and a prospectus supplement relating to any sales under the Equity Distribution Agreement is filed with the SEC.

Stock-Based Compensation Expense

We use the Black-Scholes option pricing model to estimate the fair value of stock options granted at the grant date. We recognize the fair value of stock-based compensation as compensation expense over the requisite service period, which is the vesting period. Stock-based compensation and warrant expense is classified in the Condensed Consolidated Statements of Operations and Comprehensive Income (Loss) as follows (in thousands):

	Three Months Ended June 30,		Six Months Ended June 30,	
	2019	2018	2019	2018
	(unaudited)			
Employee:				
Research and development	$ 422	$ 205	$ 762	$ 402
General and administrative	248	247	631	555
Non-Employee:				
Research and development	11	7	40	8
General and administrative	1	64	3	69
Total stock-based compensation expense	$ 682	$ 523	$ 1,436	$ 1,034

11. Income Taxes

We are subject to income taxes in the United States and Australia and our effective tax rate is calculated quarterly based upon current assumptions relating to the full year's estimated operating results and various tax-related items. Each quarter an estimate of the annual effective tax rate is updated should we revise our forecast of earnings based upon our operating results. If there is a change in the estimated effective annual tax rate, a cumulative adjustment is made. Our effective tax rate for the three and six-month periods ended June 30, 2019 and 2018 was 0.0% and 0.98%, respectively. The difference between the effective tax rate of 0.00% and the U.S. federal statutory rate of 21% for the three and six-month periods ended June 30, 2019 was primarily due to recognizing a full valuation allowance on deferred tax assets. The difference between the effective tax rate of 0.98% and the U.S. federal statutory rate of 21% for the three and six-month periods ended June 30, 2018 was primarily due to recognizing a full valuation allowance on deferred tax assets, and the estimated annual benefit of the

removal of the deferred tax liability of $305,000 recorded as a result of a previously acquired in-process research and development intangible asset.

As of June 30, 2019, we determined that, based on an evaluation of the four sources of income and all available evidence, both positive and negative, including our latest forecasts and cumulative losses in recent years, it was more likely than not that none of our deferred tax assets would be realized and therefore we continued to record a full valuation allowance. No current tax liability or expense has been recorded in the financial statements.

Item 2. Management's Discussion and Analysis of Financial Condition and Results of Operations.

You should read the following management's discussion and analysis of financial condition and results of operations in conjunction with our unaudited condensed consolidated financial statements and notes thereto included in Part I, Item 1 of this Quarterly Report on Form 10-Q and with our audited financial statements and related notes thereto and Management's Discussion and Analysis of Financial Condition and Results of Operations for the year ended December 31, 2018, included in our Annual Report on Form 10-K, or the "Annual Report", filed with the SEC on March 18, 2019.

Forward-Looking Statements

This Quarterly Report on Form 10-Q contains forward-looking statements and information within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, which are subject to the "safe harbor" created by those sections. In some cases you can identify these statements by forward-looking words such as "believe," "may," "will," "estimate," "continue," "anticipate," "intend," "could," "would," "project," "plan," "expect," or similar expressions, or the negative or plural of these words or expressions. You should read these statements carefully because they discuss future expectations, contain projections of future results of operations or financial condition, or state other "forward-looking" information. These statements relate to our future plans, objectives, expectations, intentions and financial performance and the assumptions that underlie these statements. These forward-looking statements include, but are not limited to:

- our ability to identify, develop and commercialize additional products or product candidates;
- our estimates regarding our expenses, revenues, anticipated capital requirements and our needs for additional financing;
- our ability to obtain funding for our operations;
- the implementation of our business model and strategic plans for our business and technology;
- the timing of the commencement, progress and receipt of data from any of our preclinical and clinical trials;
- the expected results of any preclinical or clinical trial and the impact on the likelihood or timing of any regulatory approval;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our technology and product candidates;
- the timing or likelihood of regulatory filings and approvals;
- the therapeutic benefits, effectiveness and safety of our product candidates;
- the rate and degree of market acceptance and clinical utility of any future products;
- our ability to maintain and establish collaborations;
- our ability to achieve milestones in our current and any future collaborations;
- our expectations regarding market risk, including interest rate changes;
- developments relating to our competitors and our industry; and
- our expectations regarding licensing, acquisitions and strategic operations.

These forward-looking statements are subject to certain risks and uncertainties that could cause actual results to differ materially from those anticipated in the forward-looking statements. Factors that might cause such a difference include, but are not limited to, those discussed in this report in Part II, Item 1A — Risk Factors, and elsewhere in this report. Forward-looking statements are based on our management's beliefs and assumptions and on information currently available to our management. These statements, like all statements in this report, speak only as of their date, and we undertake no obligation to update or revise these statements in light of future developments, except as required by law.

In addition, statements that "we believe" and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this report, and while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain and investors are cautioned not to unduly rely upon these statements.

Overview

We are a clinical-stage immunotherapy company committed to leading a new wave of immune therapeutics, creating potentially powerful multifunctional immunotherapies to improve patients' lives via unique protein engineering technologies. Alpine has two lead programs. The first, ALPN-101 for autoimmune/inflammatory diseases, is a selective dual T-cell costimulation blocker engineered to reduce pathogenic T and B cell immune responses by blocking ICOS and CD28. ALPN-101 is currently enrolling a phase I healthy volunteer trial. The second, ALPN-202 for cancer, is a conditional CD28 costimulator and dual checkpoint inhibitor. Our proprietary scientific platform uses a process known as directed evolution to convert native immune system proteins from the Immunoglobulin Super Family, or IgSF, into multi-targeted therapeutics potentially capable of modulating the human immune system.

Our goal is to create modern therapies targeting the immune synapse, using our directed-evolution based scientific platform to treat patients with serious conditions such as cancer and inflammatory diseases. To achieve our goal, we intend to:

- move our lead inflammation/autoimmune therapeutic ALPN-101 through clinical development for the treatment of inflammatory diseases;
- move our lead oncology program, ALPN-202, to clinical trials for the treatment of cancer; and
- maximize the value of our pipeline and platform via partnering activities.

Our operations to date have been limited to business planning, raising capital, developing our platform technology, identifying potential immunotherapy candidates, and other research and development activities. To date, we have financed operations primarily through private placements of common stock and convertible preferred stock, funds received from a license and research agreement, debt financing and assets acquired upon the close of our merger with Nivalis Therapeutics Inc., or Nivalis. We do not have any products approved for sale and have not generated any product sales. Since inception and through June 30, 2019, excluding amounts borrowed through debt financing, we have raised an aggregate of $124.7 million to fund operations, of which $23.6 million was from the sale of common stock, $49.2 million was from the sale of convertible preferred stock, $7.8 million was through our license and collaboration agreements, and $44.1 million in cash, cash equivalents, and marketable securities acquired through the merger with Nivalis. As of June 30, 2019, we had cash, cash equivalents, and short-term investments totaling $55.6 million.

Our net loss was $11.9 million and $7.9 million for the three months ended June 30, 2019 and 2018, respectively, and $24.2 million and $13.2 million for the six months ended June 30, 2019 and 2018, respectively. We expect to continue incurring significant expenses and operating losses for at least the next several years as we:

- initiate and complete clinical trials for product candidates, including ALPN-101, a dual ICOS/CD28 antagonist program targeting autoimmune/inflammatory disorders and ALPN-202, a CD80 vIgD-Fc that mediates PD-L1-dependent CD28 costimulation and inhibits the PD-L1 and CTLA-4 checkpoints targeting cancer;
- contract to manufacture and perform additional process development for our product candidates;
- continue research and development efforts to build our pipeline beyond the current product candidates;
- maintain, expand, and protect our intellectual property portfolio;
- hire additional clinical, quality control, scientific, and management personnel; and
- add operational and financial personnel to support our product development efforts and operational capabilities applicable to operating as a public company.

We do not expect to generate product revenue unless and until we successfully complete development of, obtain marketing approval for and commercialize our product candidates, either alone or in collaboration with third parties. We expect these activities will take a number of years and our success in these efforts is subject to significant uncertainty. Accordingly, we will need to raise additional capital prior to the regulatory approval and commercialization of any of our product candidates. Until such time, if ever, as we can generate substantial product revenues, we expect to finance our operating activities through equity or debt financings, collaborations or licenses, capital lease transactions, or other available financing transactions. However, additional capital may not be available on reasonable terms, if at all, and if we raise additional funds through the issuance of additional equity or debt securities, it could result in dilution to our existing stockholders and increased fixed payment obligations.

Financial Overview

Collaboration Revenue

We derive our collaboration revenue primarily from our collaboration and licensing agreements. We may generate revenue in the future from milestone payments made pursuant to the Adaptimmune Collaboration Agreement, or from payments from future license or collaboration agreements, product sales, or government contracts and grants. We expect any revenue we generate, if any, will fluctuate from quarter to quarter.

Adaptimmune Therapeutics plc

In May 2019, we entered into a collaboration and licensing agreement, or the Adaptimmune Collaboration Agreement. with Adaptimmune Therapeutics plc, or Adaptimmune, a clinical-stage biopharmaceutical company primarily focused on providing novel cell therapies to patients, particularly for the treatment of solid tumors, to develop next-generation SPEAR T-cell products which incorporate the Company's secreted and transmembrane immunomodulatory protein (termed SIP™ and TIP™) technology. Under the Adaptimmune Collaboration Agreement, we are to perform certain research services and grant Adaptimmune an exclusive license to programs from our SIP and TIP technologies. In June 2019, under the terms of the Adaptimmune Collaboration Agreement, we received an upfront license payment of $2.0 million and an additional $250,000 in research support payments to fund ongoing programs. These payments were recorded as deferred revenue and will be recognized to revenue based on employee hours contributed to each performance obligation. We have recognized a total of $0.1 million in revenue through June 30, 2019 related to our collaboration agreement with Adaptimmune. In addition, we are eligible for additional research support payments, one-time payments and downstream development and commercialization milestones of up to $288.0 million, if all pre-specified milestones for each program are achieved. We are also eligible to receive low-single digit royalties on worldwide net sales of the applicable products.

Kite Pharma, a Gilead company

In October 2015, we entered into a collaboration and licensing agreement, or the Kite Collaboration Agreement, providing Kite Pharma, a Gilead company, or Kite, with access to two transmembrane immunomodulatory protein, or TIP, programs for use in Kite's engineered cellular therapy programs. In May 2019, Kite provided us notice of termination of the Agreement following the expiration of the research term. Upon termination, the confidentiality and indemnity obligations of the parties survived and the licenses granted to Kite under the Agreement terminated. Pursuant to the terms of the Kite Collaboration Agreement, the termination was effective in June 2019, thirty days after the effectiveness of Kite's notice. We have recognized a total of $5.6 million in revenue from inception through June 30, 2019 related to our collaboration agreement with Kite.

Research and Development Expenses

We focus our resources on research and development activities, including the conduct of preclinical and clinical studies and product development and expense such costs as they are incurred. Our research and development expenses consist of:

- employee-related expenses, including salaries, benefits, taxes, travel, and stock-based compensation expense for personnel in research and development functions;
- expenses related to process development and production of product candidates paid to contract manufacturing organizations;
- costs associated with preclinical activities and regulatory operations, including the cost of acquiring, developing, and manufacturing research material;
- clinical trials and activities related to regulatory filings for our product candidates; and
- allocation of facilities, depreciation, and amortization of laboratory equipment and other expenses.

We incurred $10.2 million and $5.7 million in research and development expenses for three months ended June 30, 2019 and 2018, respectively, and $20.5 million and $9.5 million for the six months ended June 30, 2019 and 2018, respectively. We plan to increase our research and development activities for the foreseeable future as we continue to develop our platform and product candidates.

The successful development of our platform and product candidates is highly uncertain. At this time, we cannot reasonably estimate the nature, timing, or costs of the efforts necessary to finish developing any of our product candidates or the period in which material net cash, if any, from these product candidates may commence. This is due to the numerous risks and uncertainties associated with developing therapeutics, including the uncertainty of:

- the scope, rate of progress, expense, and results of clinical trials;
- the scope, rate of progress, and expense of process development and manufacturing;
- preclinical and other research activities; and
- the timing of regulatory approvals.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries and related costs for employees in executive, business development, finance, and administrative functions. Other significant general and administrative expenses include professional fees for accounting and legal services, expenses associated with obtaining and maintaining patents and other intellectual property, and allocation of facilities costs.

We expect general and administrative expenses will increase as we expand infrastructure and support operating as a public company. These increases will include increased costs for director and officer liability insurance, costs related to the hiring of additional personnel, and increased fees for directors, outside consultants, lawyers, and accountants. We expect to incur significant costs to comply with corporate governance, internal controls, and similar requirements applicable to public companies.

Loss on Sale of Intangible Asset

Loss on sale of intangible asset relates solely to the sale of the GSNOR asset to Laurel in June 2018. For additional information regarding the sale of the GSNOR asset, please see Note 8 to our consolidated financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2018, filed with the SEC on March 18, 2019.

Interest Expense

Interest expense consists of accrued interest and the amortization of the debt discount associated with our $5.0 million term loan.

Interest and Other Income

Interest income consists of interest earned on our cash, cash equivalents, and short-term investments.

JOBS Act

On April 5, 2012, the JOBS Act was enacted. Section 107 of the JOBS Act provides that an emerging growth company can take advantage of the extended transition period provided in Section 7(a)(2)(B) of the Securities Act of 1933, as amended, or the Securities Act, for complying with new or revised accounting standards. Thus, an emerging growth company can delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this extended transition period and, as a result, we will adopt new or revised accounting standards on the relevant dates on which adoption of such standards is required for other public companies. In addition, for so long as we are an "emerging growth company," which is until as late as December 31, 2020, we will, among other things not be required to comply with the auditor attestation requirements of Section 404(b) of Sarbanes-Oxley.

Critical Accounting Policies and Estimates

Our management's discussion and analysis of our financial condition and results of operations is based on our financial statements, which we have prepared in accordance with generally accepted accounting principles in the United States of America, or GAAP. The preparation of these condensed consolidated financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the condensed consolidated financial statements, as well as the reported revenues and expenses during the reporting periods. We evaluate these estimates and judgments on an ongoing basis. We base our estimates on historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Our actual results may differ from these estimates under different assumptions or conditions. Our significant accounting policies are more fully described in Note 2 of the accompanying unaudited condensed consolidated financial statements and in Note 2 to the audited financial statements contained in our Annual Report. There have been no significant or material changes in our significant

accounting policies during the six months ended June 30, 2019, as compared to those disclosed in our Annual Report except the following:

Recently Adopted Accounting Pronouncements

In June 2018, the FASB issued ASU No. 2018-07, which aligns the measurement and classification guidance for share-based payments to nonemployees with the guidance for share-based payments to employees, with certain exceptions. Under the guidance, the measurement of equity-classified nonemployee awards will be fixed at the grant date. Upon transition, nonemployee awards will be required to be measured at fair value as of the adoption date with a cumulative-effect adjustment recognized in retained earnings as of the beginning of the annual period of adoption. ASU 2018-07 is effective for fiscal years beginning after December 15, 2018, including interim periods within that fiscal year. We adopted this standard on January 1, 2019 and it did not have a material impact on our financial statements and related disclosures.

In February 2016, the FASB issued ASU No. 2016-02, Leases. ASU 2016-02 requires a lessee to separate the lease components from the non-lease components in a contract and recognize in the statement of financial position a liability to make lease payments (the lease liability) and a right-of-use asset representing its right to use the underlying asset for the lease term. It also aligns lease accounting for lessors with the revenue recognition guidance in ASU 2014-09. We adopted this ASU effective January 1, 2019 using the additional (optional) approach by recording an operating lease right-of-use asset of $797,000, a corresponding operating lease liability of $883,000, and reducing our deferred rent balance by $86,000 to $0 on our accompanying Condensed Consolidated Balance Sheets; there was no effect on opening retained earnings, and we continue to account for leases in the prior period financial statements under ASC Topic 840. In adopting the new standard, we elected to apply the practical expedients regarding the identification of leases, lease classification, indirect costs, and the combination of lease and non-lease components.

For information regarding recent accounting pronouncements, see Note 2 of the Notes to Condensed Consolidated Financial Statements under Part I, Item 1 of this report.

Results of Operations

Comparison of Three Months Ended June 30, 2019 and 2018

The following table summarizes our results of operations for the three months ended June 30, 2019 and 2018 (in thousands):

	Three Months Ended June 30,		Increase/ (Decrease)
	2019	2018	
	(unaudited)		
Collaboration revenue	$ 567	$ 390	$ 177
Operating expenses:			
Research and development	10,166	5,718	4,448
General and administrative	2,553	1,883	670
Loss on sale of intangible asset	—	1,203	(1,203)
Total operating expenses	12,719	8,804	3,915
Loss from operations	(12,152)	(8,414)	(3,738)
Other income (expense):			
Interest expense	(61)	(83)	22
Interest and other income	357	337	20
Loss before taxes	(11,856)	(8,160)	(3,696)
Income tax benefit	—	253	(253)
Net loss	$ (11,856)	$ (7,907)	$ (3,949)

Collaboration Revenue

Revenue for the three months ended June 30, 2019 consists of $0.1 million related to the Adaptimmune Collaboration Agreement and $0.4 million related to the milestone payment from Laurel from the sale of our GSNOR assets. Revenue for the three months ended June 30, 2018 relates to the Kite Collaboration Agreement.

Research and Development Expenses

The $4.4 million increase in research and development expenses was primarily attributable to an increase of $1.5 million in clinical trial activity, an increase of $1.1 million in direct research activities, an increase of $1.1 million in personnel-related expenses as a result of growth in headcount to support ongoing discovery and development programs, an increase of $0.2 million in contract manufacturing and process development of our product candidates, an increase of $0.2 million in stock-based compensation, and an increase of $0.3 million in allocated overhead and facilities.

General and Administrative Expenses

The $0.7 million increase in general and administrative expenses was primarily attributable to a $0.7 million increase in personnel-related expenses related to an increase in administrative headcount.

Loss on Sale of Intangible Asset

Loss on sale of intangible asset relates solely to the sale of the GSNOR asset to Laurel in June 2018.

Comparison of Six Months Ended June 30, 2019 and 2018

The following table summarizes our results of operations for the six months ended June 30, 2019 and 2018 (in thousands):

	Six Months Ended June 30,		Increase/ (Decrease)
	2019	2018	
	(unaudited)		
Collaboration revenue	$ 567	$ 705	$ (138)
Operating expenses:			
Research and development	20,516	9,510	11,006
General and administrative	4,898	3,991	907
Loss on sale of intangible asset	—	1,203	(1,203)
Total operating expenses	25,414	14,704	10,710
Loss from operations	(24,847)	(13,999)	(10,848)
Other income (expense):			
Interest expense	(131)	(161)	30
Interest and other income	741	642	99
Loss before taxes	(24,237)	(13,518)	(10,719)
Income tax benefit	—	305	(305)
Net loss	$ (24,237)	$ (13,213)	$ (11,024)

Collaboration Revenue

Revenue for the six months ended June 30, 2019 consists of $0.1 million related to the Adaptimmune Collaboration Agreement and $0.4 million related to the milestone payment from Laurel from the sale of our GSNOR assets. Revenue for the six months ended June 30, 2018 relates primarily to the Kite Collaboration Agreement.

Research and Development Expenses

The $11.0 million increase in research and development expenses was primarily attributable to an increase of $3.8 million in contract manufacturing and process development of our product candidates, an increase of $2.4 million in clinical trial activity, an increase of $2.3 million in direct research activities, an increase of $1.7 million in personnel-related expenses as a result of growth in headcount to support ongoing discovery and development programs, an increase of $0.4 million in stock-based compensation, and an increase of $0.4 million in allocated overhead and facilities.

General and Administrative Expenses

The $0.9 million increase in general and administrative expenses was primarily attributable to increased personnel-related expenses related to an increase in administrative headcount.

Loss on Sale of Intangible Asset

Loss on sale of intangible asset relates solely to the sale of the GSNOR asset to Laurel in June 2018.

Liquidity and Capital Resources

As of June 30, 2019, we had cash, cash equivalents, and short-term investments totaling $55.6 million. Excluding amounts borrowed through debt financing, we have raised an aggregate of $124.7 million to fund operations, of which $23.6 million was from the sale of common stock, $49.2 million was from the sale of convertible preferred stock, $7.8 million was through our license and collaboration agreements, and $44.1 million in cash, cash equivalents, and marketable securities acquired through the merger with Nivalis. In June 2017, we drew down a term loan of $5.0 million. In addition to our existing cash, cash equivalents, and marketable securities, we are eligible to receive research and development funding and to earn milestone and other contingent payments for the achievement of defined collaboration objectives and certain development and regulatory milestones and royalty payments under our collaboration with Adaptimmune; however, our ability to earn these milestone and contingent payments and the timing of achieving these milestones is uncertain.

We have incurred operating losses since inception. We expect to continue to incur significant expenses and operating losses for the foreseeable future as we continue our research and preclinical and clinical development of our product candidates; expand the scope of our current studies for our product candidates; initiate additional preclinical, clinical or other studies for our product candidates, including under any collaboration agreements; change or add additional manufacturers or suppliers; seek regulatory and marketing approvals for any of our product candidates that successfully complete clinical studies; seek to identify, evaluate and validate additional product candidates; acquire or in-license other product candidates and technologies; maintain, protect and expand our intellectual property portfolio; attract and retain skilled personnel; and experience any delays or encounter issues with any of the above.

Until such time as we can generate substantial product revenue, if ever, we expect to finance our cash needs through a combination of equity or debt financings and collaboration agreements. Except for any obligations of our collaborator to make milestone payments under our agreement with them, we do not have any committed external sources of capital. To the extent that we raise additional capital through the future sale of equity or debt, the ownership interest of our stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our existing common stockholders. If we raise additional funds through collaboration agreements in the future, we may have to relinquish valuable rights to our technologies, future revenue streams or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Our future capital requirements are difficult to forecast and will depend on many factors, including:

- the number and characteristics of the future product candidates we pursue either from our internal research efforts or through acquiring or in-licensing other product candidates or technologies;
- the scope, progress, results and costs of independently researching and developing any of our future product candidates, including conducting preclinical research and clinical trials;
- whether our existing collaboration generates substantial milestone payments and, ultimately, royalties on future approved products for us;
- the timing of, and the costs involved in, obtaining regulatory approvals for any future product candidates we develop independently;
- the cost of future commercialization activities, if any;
- the cost of manufacturing our future product candidates and products, if any;
- our ability to maintain our existing collaboration and to establish new collaborations, licensing or other arrangements and the financial terms of such arrangements;
- the costs of preparing, filing, prosecuting, maintaining, defending and enforcing patents, including litigation costs and the outcome of such litigation; and

- the timing, receipt and amount of sales of, or royalties on, our current or future collaborators' product candidates, and our future products, if any.

Based on our research and development plans and our timing expectations related to the progress of our programs, we expect that our existing cash, cash equivalents and marketable securities as of the date of this report will enable us to fund our operating expenses and capital expenditure requirements for at least the next 12 months. We have based this estimate on assumptions that may prove to be wrong, and we could use our capital resources sooner than we expect. Additionally, the process of testing drug candidates in preclinical and clinical studies is costly, and the timing of progress in these studies remains uncertain.

Financing Agreements

In January 2019, we entered into a securities purchase agreement, or the Purchase Agreement, with a limited number of accredited investors, pursuant to which we sold approximately 4.7 million units, or the Units, for an aggregate purchase price of $25.3 million in a private placement, which we refer to as the Private Placement. Each Unit has a purchase price of $5.37 and consists of one share of our common stock and a warrant to purchase 0.39 shares of common stock. Pursuant to the terms of the Purchase Agreement, we issued approximately 4.7 million shares of common stock and warrants to purchase an aggregate of approximately 1.8 million shares of common stock. The warrants have an exercise price of $12.74 and have a term of five years.

Prior to execution and delivery of the merger agreement with Nivalis certain holders of our Series A-1 convertible preferred stock purchased shares of our Series A-1 convertible preferred stock. In March 2017, we issued and sold 707,330 shares of Series A convertible preferred stock and received a total of $4.0 million. In April 2017, we issued and sold 2,947,211 shares of our Series A-1 convertible preferred stock for an aggregate of $16.7 million in net proceeds. In addition, contemporaneously with the close of the Merger, certain existing stockholders of Alpine purchased 1,335,118 additional shares of Alpine's capital stock for an aggregate of $17.0 million in net proceeds.

In June 2018, we entered into an equity distribution agreement, or the Equity Distribution Agreement, with Piper Jaffray & Co., or Piper Jaffray, pursuant to which we may sell shares of our common stock through an "at the market" equity offering program for up to $50.0 million in gross cash proceeds. Piper Jaffray will be entitled to compensation for its services of up to 3.0% of the gross sales price per share of all shares sold through Piper Jaffray under the Equity Distribution Agreement. The Equity Distribution Agreement may be terminated by us upon written notice to Piper Jaffray for any reason, or by Piper Jaffray upon written notice to us for any reason, or at any time under certain circumstances, including but not limited to if we experience a material adverse change.

Under the Equity Distribution Agreement, we will set the parameters for the sale of shares, including the number of shares to be issued, the time period during which sales are requested to be made, limitation on the number of shares that may be sold in any one trading day and any minimum price below which sales may not be made. We have no obligation to sell any shares under the Equity Distribution Agreement and may at any time suspend solicitation and offers under the Equity Distribution Agreement. As of June 30, 2019, we have made no sales under the Equity Distribution Agreement. In July 2019, our Registration Statement on Form S-3 (File No. 333-212404) expired pursuant to Rule 415(a)(5) under the Securities Act of 1933, as amended. We will be unable to sell shares under the Equity Distribution Agreement until a new Registration Statement on Form S-3 is filed and declared effective by the SEC and a prospectus supplement relating to any sales under the Equity Distribution Agreement is filed with the SEC.

Long-Term Financing

In December 2016, we entered into a term loan agreement with Silicon Valley Bank pursuant to which up to $5.0 million could be borrowed. On June 30, 2017, we drew down a term loan of $5.0 million pursuant to the agreement. The loan's interest-only period expired on July 1, 2018, at which point we began making thirty consecutive equal monthly payments of principal (each in an amount that will fully amortize the loan), plus accrued interest. Interest accrues at a floating per annum rate equal to the lender's prime rate minus 1.75%. As a condition to the loan, we agreed to pay a final payment fee of 7.5%, or $375,000, upon repayment of the loan. The final payment fee was recorded in long-term debt with an offsetting reduction in long-term debt and was accounted for as a debt discount. As of June 30, 2019, we had $3.4 million outstanding principal amount under our term loan agreement.

Pursuant to the loan agreement we have pledged substantially all of our assets, excluding intellectual property, as collateral. The obligations under the loan agreement are subject to acceleration upon the occurrence of specified events of default, including a material adverse change in our business, operations or financial or other condition. The term loan agreement contains customary conditions to borrowings, events of default and negative covenants, including covenants that could limit our ability to, among other things, incur additional indebtedness, liens or other encumbrances, make dividends or

other distributions; buy, sell or transfer assets; engage in any new line of business; and enter into certain transactions with affiliates. We were in compliance with our covenants as of June 30, 2019.

Operating Lease

In March 2019, we entered into a lease with ARE-Seattle No. 28, LLC (the "Landlord") for 27,164 square feet of office and laboratory space located at 188 East Blaine Street, Seattle, Washington. The term of the lease is 10.8 years with one option to extend the term by 5 years. The lease term commenced in June 2019. The "Rent Commencement Date" will be nine months after the commencement date. We are not required to pay base rent from the Rent Commencement Date through the last day of the ninth month following the Rent Commencement Date. The annual base rent under the lease is $1.7 million for the first year and will increase by 3.0% each year thereafter. We will receive a maximum tenant improvement allowance of $5.4 million, which is included in our base rent, and a maximum additional tenant improvement allowance of $1.8 million, which will result in additional rent amortized over the term of the lease at an annual rate of 8.0%. The lease also requires us to pay additional amounts for operating and maintenance expenses. In March 2019, in connection with the lease, we provided a $254,000 letter of credit as a security deposit, which is recorded as restricted cash in our accompanying Condensed Consolidated Balance Sheets.

Cash Flows

The following is a summary of our cash flows (in thousands):

	Six Months Ended June 30,	
	2019	2018
	(unaudited)	
Net cash used in operating activities	$ (19,100)	$ (11,646)
Net cash provided by investing activities	1,512	7,208
Net cash provided by financing activities	22,609	7

Net Cash Used in Operating Activities:

Net cash used in operating activities was $19.1 million during the six months ended June 30, 2019, and consisted primarily of our net loss of $24.2 million. This was offset by increases of $3.1 million in our net operating assets and liabilities and $2.0 million in our net non-cash adjustments, which primarily relate to stock-based compensation, depreciation and amortization.

Net cash used in operating activities was $11.6 million during the six months ended June 30, 2018, and consisted primarily of our net loss of $13.2 million and a net decrease of $0.2 million in operating assets and liabilities. This was partially offset by net non-cash adjustments of $1.8 million, which primarily relate to the loss on the sale of our intangible asset, stock-based compensation, the write-off of our deferred tax liability, depreciation and amortization.

Net Cash Provided by Investing Activities:

Cash flows from investing activities primarily reflect cash used to purchase short-term investments and proceeds from the maturities of short-term investments, thus causing a shift between our cash and cash equivalents, and short-term investment balances. We manage our cash usage with respect to our total cash, cash equivalents and short-term investments.

Net cash provided by investing activities was $1.5 million during the six months ended June 30, 2019 and consisted primarily of our purchases, sales and maturities of short-term investments in U.S. Treasury securities, commercial paper, and corporate debt securities as well as purchases of property and equipment, primarily lab equipment, to support our research and development efforts.

Net cash provided by investing activities was $7.2 million during the six months ended June 30, 2018 and consisted primarily of our net purchases and maturities of short-term investments in U.S. Treasury securities, commercial paper, and corporate debt securities.

Net Cash Provided by Financing Activities:

Net cash provided by financing activities was $22.6 million during the six months ended June 30, 2019 and consisted primarily of the net proceeds of $23.6 million related to the sale of approximately 4.7 million Units under our Purchase Agreement, partially offset by $1.0 million related to principal payments on our debt.

Net cash provided by financing activities was $7,000 for the six months ended June 30, 2018 and consisted of proceeds from the exercise of stock options.

Contractual Obligations and Contingent Liabilities

As a "smaller reporting company," as defined by Rule 12b-2 of the Exchange Act, we are not required to provide additional information on our contractual obligations and contingent liabilities pursuant to Item 303 of Regulation S-K.

Off-Balance Sheet Arrangements

We did not have during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined under SEC rules.

Item 3. Quantitative and Qualitative Disclosures about Market Risk.

As a "smaller reporting company," as defined by Rule 12b-2 of the Exchange Act, and pursuant to Item 305 of Regulation S-K, we are not required to provide quantitative and qualitative disclosures about market risk.

Item 4. Controls and Procedures

Evaluation of Disclosure Controls and Procedures

Management, including our Chief Executive Officer and Chief Financial Officer, evaluated the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) of the Exchange Act), as of the end of the period covered by this report. Based upon the evaluation, our Chief Executive Officer and Chief Financial Officer concluded that, as of the end of the period covered by this report, our disclosure controls and procedures were effective, in design and operation, at the reasonable assurance level.

Changes in Internal Control over Financial Reporting

Our management, including our principal executive and principal financial officers, evaluated any changes in our internal control over financial reporting during the period ended June 30, 2019, and has concluded that there were no changes that materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Inherent Limitation on the Effectiveness of Internal Control

The effectiveness of any system of internal control over financial reporting, including ours, is subject to inherent limitations, including the exercise of judgment in designing, implementing, operating, and evaluating the controls and procedures, and the inability to eliminate misconduct completely. Accordingly, any system of internal control over financial reporting, including ours, no matter how well designed and operated, can only provide reasonable, not absolute assurances. In addition, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate. We intend to continue to monitor and upgrade our internal controls as necessary or appropriate for our business, but cannot assure you that such improvements will be sufficient to provide us with effective internal control over financial reporting.

PART II: OTHER INFORMATION

Item 1. Legal Proceedings

From time to time, we may become involved in legal proceedings or be subject to claims arising in the ordinary course of our business. We are not presently a party to any legal proceedings that, in the opinion of our management, would reasonably be expected to have a material adverse effect on our business, financial condition, operating results or cash flows if determined adversely to us. Regardless of the outcome, litigation can have an adverse impact on us because of defense and settlement costs, diversion of management resources and other factors.

Item 1A. Risk Factors

You should carefully consider the following risk factors, in addition to the other information contained in this Quarterly Report on Form 10-Q, including Management's Discussion and Analysis of Financial Condition and Results of Operations included in Part I, Item 2, and our consolidated financial statements and related notes. If any of the events described in the following risk factors and the risks described elsewhere in this report occurs, our business, operating results and financial condition could be seriously harmed. This report on Form 10-Q also contains forward-looking statements that involve risks and uncertainties. Our actual results could differ materially from those anticipated in the forward-looking statements as a result of factors that are described below and elsewhere in this report.

Risks Related to Our Financial Position, Capital Needs and Business

We will need to raise substantial additional funds to advance development of our therapeutic candidates, and we cannot guarantee we will have sufficient funds available in the future to develop and commercialize our current or future therapeutic candidates.

We will need to raise substantial additional funds to expand our development, regulatory, manufacturing, marketing, and sales capabilities or contract with other organizations to provide these capabilities to us. We have used substantial funds to develop our therapeutic candidates and will require significant funds to conduct further research and development, preclinical testing, and clinical trials of our therapeutic candidates, to seek regulatory approvals for our therapeutic candidates, and to manufacture and market products, if any are approved for commercial sale. As of June 30, 2019, we had $55.6 million in cash and cash equivalents and short-term investments. Based on our current operating plan, we believe our available cash and cash equivalents, will be sufficient to fund our planned level of operations for at least the next 12 months. Our future capital requirements and the period for which we expect our existing resources to support our operations may vary significantly from what we expect. Our monthly spending levels vary based on new and ongoing development and corporate activities. Because the length of time and activities associated with successful development of our therapeutic candidates are highly uncertain, we are unable to estimate the actual funds we will require for development and any approved marketing and commercialization activities. To execute our business plan, we will need, among other things:

- to obtain the human and financial resources necessary to develop, test, obtain regulatory approval for, manufacture, and market our therapeutic candidates;
- to build and maintain a strong intellectual property portfolio and avoid infringing intellectual property of third parties;
- to establish and maintain successful licenses, collaborations, and alliances;
- to satisfy the requirements of clinical trial protocols, including patient enrollment;
- to establish and demonstrate the clinical efficacy and safety of our therapeutic candidates;
- to obtain regulatory approvals;
- to manage our spending as costs and expenses increase due to preclinical studies, clinical trials, regulatory approvals, manufacturing scale-up, and commercialization;
- to obtain additional capital to support and expand our operations; and
- to market our products to achieve acceptance and use by the medical community in general.

If we are unable to obtain necessary funding on a timely basis or on acceptable terms, we may have to delay, reduce, or terminate our research and development programs, preclinical studies, or clinical trials, if any, limit strategic opportunities, or undergo reductions in our workforce or other corporate restructuring activities. We also could be required to seek funds through arrangements with collaborators or others requiring us to relinquish rights to some of our technologies or therapeutic candidates we would otherwise pursue on our own. We do not expect to realize revenue from product sales, or royalties in the

foreseeable future, if at all. Our revenue sources are, and will remain, extremely limited unless and until our therapeutic candidates are clinically tested, approved for commercialization, and successfully marketed.

To date, we have financed our operations primarily through the sale of equity securities and payments received under our collaboration agreements. We will be required to seek additional funding in the future and intend to do so through a combination of public or private equity offerings, debt financings, credit and loan facilities, research collaborations, and license agreements. Our ability to raise additional funds from these or other sources will depend on financial, economic, and other factors, many of which are beyond our control. Additional funds may not be available to us on acceptable terms or at all.

If we raise additional funds by issuing equity securities, our stockholders will suffer dilution, and the terms of any financing may adversely affect the rights of our stockholders. For example, in January 2019, we issued in a private placement 4,706,700 shares of common stock and warrants to purchase an additional 1,835,610 shares of common stock for gross proceeds of approximately $25.3 million. We also have an Equity Distribution Agreement in place with Piper Jaffray to sell up to $50.0 million of our common stock, from time to time, through an "at the market" equity offering program under which Piper Jaffray acts as sales agent; however, in July 2019, our Registration Statement on Form S-3 expired pursuant to Rule 415(a)(5), and until a new Registration Statement on Form S-3 is filed and declared effective by the SEC and a prospectus supplement relating to any sales under the Equity Distribution Agreement is filed with the SEC, the equity offering program will not be available to us.

In addition, as a condition to providing additional funds to us, future investors may demand, and may be granted, rights superior to those of existing stockholders. Debt financing, if available, may involve restrictive covenants limiting our flexibility in conducting future business activities, and, in the event of a liquidation or insolvency, debt holders would be repaid before holders of equity securities receive any distribution of corporate assets. Our failure to raise capital or enter into such other arrangements within a reasonable timeframe would have a negative impact on our financial condition, and we may have to delay, reduce, or terminate our research and development programs, preclinical or clinical trials, or undergo reductions in our workforce or other corporate restructuring activities.

We are an early stage biopharmaceutical company with a history of losses, we expect to continue to incur significant losses for the foreseeable future, we may never achieve or maintain profitability, and we have a limited operating history that may make it difficult for investors to evaluate the potential success of our business.

We are a clinical-stage immunotherapy company, with a limited operating history, focused on developing treatments for autoimmune/inflammatory diseases and cancer. Since inception, we have devoted our resources to developing novel protein-based immunotherapies using our proprietary scientific platform technology, which produces variant Ig domains or vIgDs. We have had significant operating losses since inception. For the six months ended June 30, 2019, our net loss was $24.2 million. Substantially all of our losses have resulted from expenses incurred in connection with our research programs and from general and administrative costs associated with our operations. Our technologies and therapeutic candidates are in early stages of development, and we are subject to the risks of failure inherent in the development of therapeutic candidates based on novel technologies.

We have historically generated revenue primarily from the receipt of research funding and upfront payments under our collaboration agreements. We have not generated, and do not expect to generate, any revenue from product sales for the foreseeable future, and we expect to continue to incur significant operating losses for the foreseeable future due to the cost of research and development, preclinical studies, clinical trials, and the regulatory approval process for therapeutic candidates. The amount of future losses is uncertain. Our ability to achieve profitability, if ever, will depend on, among other things, our or our existing collaborators, or any future collaborators, successfully developing therapeutic candidates, obtaining regulatory approvals to market and commercialize therapeutic candidates, manufacturing any approved products on commercially reasonable terms, establishing a sales and marketing organization or suitable third party alternatives for any approved product, and raising sufficient funds to finance business activities. If we or our existing collaborators, or any future collaborators, are unable to develop and commercialize one or more of our therapeutic candidates or if sales revenue from any therapeutic candidate receiving approval is insufficient, we will not achieve profitability, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

Our approach to the discovery and development of innovative therapeutic treatments based on our technology is unproven and may not result in marketable products.

We plan to develop novel protein-based immunotherapies using our proprietary vIgD technology for the treatment of cancer and autoimmune/inflammatory diseases. The potential to create therapies capable of working within and/or modulating an immune synapse, forcing a synapse to occur, or preventing a synapse from occurring is an important, novel attribute of our vIgDs. However, the scientific research forming the basis of our efforts to develop therapeutic candidates based on our platform

is relatively new. Further, the scientific evidence to support the feasibility of developing therapeutic treatments based on vIgDs is both preliminary and limited.

Relatively few therapeutic candidates based on immunoglobulin superfamily, or IgSF, domains have been tested in animals or humans, and a number of clinical trials conducted by other companies using IgSF domains technologies have not been successful. We may discover the therapeutic candidates developed using our scientific platform do not possess certain properties required for the therapeutic candidate to be effective, such as the ability to remain stable or active in the human body for the period of time required for the therapeutic candidate to reach the target tissue and/or cell. We currently have only limited data, and no conclusive evidence, to suggest we can introduce these necessary therapeutic properties into vIgD-based therapeutic candidates. We may spend substantial funds attempting to introduce these properties and may never succeed in doing so. In addition, vIgDs may demonstrate different chemical and pharmacological properties in human subjects or patients than they do in laboratory studies. Even if our programs, such as the ALPN-101 program, have successful results in animal studies, they may not demonstrate the same chemical and pharmacological properties in humans and may interact with human biological systems in unforeseen, ineffective, or harmful ways. For example, in the context of immunotherapies, in a Phase I clinical trial of TeGenero AG's product candidate TGN1412, healthy volunteer subjects receiving the product candidate experienced a systemic inflammatory response resulting in renal and pulmonary failure requiring interventions such as dialysis and critical care support. Following this experience, regulatory agencies now ask for evaluation of immunomodulatory antibodies with a number of in vitro assays with human cells. While we are currently performing in vitro and in vivo proof of concept studies for several of our vIgDs preclinically, and safety studies clinically for ALPN-101, the risk profile in humans has yet to be fully assessed. Undesirable side effects that may be caused by our therapeutic candidates could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or other comparable foreign authorities. Such side effects could also affect patient recruitment or the ability of enrolled patients to complete clinical trials or result in potential product liability claims. Any of these occurrences may harm our business, financial condition and prospects significantly. As a result, we may never succeed in developing a marketable therapeutic, we may not become profitable, and the value of our common stock will decline.

Further, we believe that the FDA has no prior experience with vIgDs and no regulatory authority has granted approval to any person or entity, including our company, to market and commercialize therapeutics using vIgDs, which may increase the complexity, uncertainty, and length of the regulatory approval process for our therapeutic candidates. Our company and our current collaborators, or any future collaborators, may never receive approval to market and commercialize any therapeutic candidate. Even if our company or a collaborator obtains regulatory approval, the approval may be for disease indications or patient populations not as broad as we intended or desired or may require labeling, including significant use or distribution restrictions or safety warnings. Our company or a collaborator may be required to perform additional or unanticipated clinical trials to obtain approval or be subject to post-marketing testing requirements to maintain regulatory approval. If therapeutic candidates we develop using our scientific platform prove to be ineffective, unsafe, or commercially unviable, our entire platform and pipeline would have little, if any, value, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

The market may not be receptive to our therapeutic products based on a novel therapeutic modality, and we may not generate any future revenue from the sale or licensing of therapeutic products.

Even if approval is obtained for a therapeutic candidate, we may not generate or sustain revenue from sales of the therapeutic product due to factors such as whether the therapeutic product can be sold at a competitive price and otherwise accepted in the market. Therefore, any revenue from sales of the therapeutic product may not offset the costs of development. The therapeutic candidates we are developing are based on new technologies and therapeutic approaches. Market participants with significant influence over acceptance of new treatments, such as physicians and third-party payors, may not adopt a treatment based on our therapeutic products, and we may not be able to convince the medical community and third-party payors to accept and use, or to provide favorable coverage or reimbursement for, any therapeutic products developed by our company, our existing collaborator, or any future collaborators. Market acceptance of our therapeutic products will depend on, among other factors:

- the timing of our receipt of any marketing and commercialization approvals;
- the terms of any approvals and the countries in which approvals are obtained;
- the safety and efficacy of our therapeutic products;
- the prevalence and severity of any adverse side effects associated with our therapeutic products;
- the prevalence and severity of any adverse side effects associated with therapeutics of the same type or class as our therapeutic products;
- limitations or warnings contained in any labeling approved by the FDA or other regulatory authority;

- relative convenience and ease of administration of our therapeutic products;
- the willingness of patients to accept any new methods of administration;
- the success of our physician education programs;
- the availability of adequate government and third-party payor coverage and reimbursement;
- the pricing of our products, particularly as compared to alternative treatments;
- our ability to compliantly market and sell our products; and
- availability of alternative effective treatments for the disease indications our therapeutic products are intended to treat and the relative risks, benefits, and costs of those treatments.

With our focus on engineering wild-type IgSFs proteins, these risks may increase to the extent this field becomes more competitive or less favored in the commercial marketplace. Additional risks apply in relation to any disease indications we pursue which are classified as rare diseases and allow for orphan drug designation by regulatory agencies in major commercial markets, such as the United States, European Union, and Japan. Because of the small patient population for a rare disease, if pricing is not approved or accepted in the market at an appropriate level for an approved therapeutic product with orphan drug designation, such drug may not generate enough revenue to offset costs of development, manufacturing, marketing, and commercialization despite any benefits received from the orphan drug designation, such as market exclusivity, assistance in clinical trial design, or a reduction in user fees or tax credits related to development expense. Market size is also a variable in disease indications classified as rare. Our estimates regarding potential market size for any rare indication may be materially different from what we discover to exist at the time we commence commercialization, if any, for a therapeutic product, which could result in significant changes in our business plan and have a material adverse effect on our business, financial condition, results of operations, and prospects.

If a therapeutic product with orphan drug designation subsequently receives the first FDA approval for the indication for which it has such designation, the therapeutic product is entitled to orphan product exclusivity, which means the FDA may not approve any other applications to market the same therapeutic product for the same indication, except in very limited circumstances, for seven years. Orphan drug exclusivity, however, could also block the approval of one of our therapeutic products for seven years if a competitor obtains approval of the same therapeutic product as defined by the FDA or if our therapeutic product is determined to be within the same class as the competitor's therapeutic product for the same indication or disease.

As in the United States, we may apply for designation of a therapeutic product as an orphan drug for the treatment of a specific indication in the European Union before the application for marketing authorization is made. Sponsors of orphan drugs in the European Union can enjoy economic and marketing benefits, including up to ten years of market exclusivity for the approved indication unless another applicant can show its therapeutic product is safer, more effective, or otherwise clinically superior to the orphan-designated therapeutic product. The respective orphan designation and exclusivity frameworks in the United States and in the European Union are subject to change, and any such changes may affect our ability to obtain EU or U.S. orphan designations in the future.

Our therapeutic candidates are in early stages of development and may fail in development or suffer delays that materially and adversely affect their commercial viability.

We have no products on the market and all of our therapeutic candidates are in early stages of development. Our ability to achieve and sustain profitability depends on obtaining regulatory approval and Institutional Review Board, or IRB, approval to conduct clinical trials at particular sites, obtaining regulatory approvals to market our therapeutic candidates and successfully commercializing our therapeutic candidates, either alone or with third parties, such as our collaborators. Before obtaining regulatory approval for the commercial distribution of our therapeutic candidates, we or a collaborator must conduct extensive preclinical tests and clinical trials to demonstrate the safety and efficacy in humans of our therapeutic candidates. Preclinical testing and clinical trials are expensive, difficult to design and implement, can take many years to complete, and are uncertain as to outcome. For example, in January 2019, we enrolled our first subjects in a Phase I healthy volunteer trial of ALPN-101. We are also working to advance our lead oncology program ALPN-202 for the treatment of cancer and preclinical development activities continue as planned, with the goal of filing an IND or IND-equivalent in the fourth quarter of 2019. Even with the significant investment of time and funding to advance ALPN-101 and ALPN-202, we cannot guarantee that our clinical and pre-clinical development efforts will be successful or that any of our product candidates will advance to human clinical trials. The start or end of a clinical study is often delayed or halted due to delays in or failure to obtain regulatory approval to commence the study, delays in or failure to reach agreement on acceptable terms with prospective contract research organizations or clinical trial sites, delays in or failure to obtain IRB approval at each site, changing regulatory requirements, manufacturing challenges, clinical sites or contract research organizations deviating from the trial protocol or failing to comply

with regulatory requirements or meet contractual obligations, slower than anticipated patient enrollment, changing standards of care, availability or prevalence of use of a comparative therapeutic or required prior therapy, clinical outcomes, failure of patients to complete the trial or return for post-treatment follow-up, or financial constraints. For instance, delays or difficulties in patient enrollment or difficulties in retaining trial participants can result in increased costs, longer development times, or termination of a clinical trial. Clinical trials of a new therapeutic candidate require the enrollment of a sufficient number of patients, which may include patients who are suffering from the disease the therapeutic candidate is intended to treat and who meet other eligibility criteria. Rates of patient enrollment are affected by many factors, including the size of the patient population, the eligibility criteria for the clinical trial, the age and condition of the patients, the stage and severity of disease, the nature of the protocol, the proximity of patients to clinical sites, and the availability of effective treatments or competing academic and other clinical trials for the relevant disease.

A therapeutic candidate can unexpectedly fail at any stage of preclinical and clinical development. The historical failure rate for therapeutic candidates is high due to scientific feasibility, safety, efficacy, changing standards of medical care, and other variables. The novelty of our platform may mean our failure rates are higher than historical norms. The results from preclinical testing or early clinical trials of a therapeutic candidate may not predict the outcome of later phase clinical trials of the therapeutic candidate, particularly in immuno-oncology and autoimmune/inflammatory disorders. To date, we have not conducted any clinical trials of our therapeutic candidates in patients with active disease. However, we will have to conduct trials in our proposed indications to verify the results obtained to date in our preclinical studies and to support any regulatory submissions for further clinical development. A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or adverse safety profiles despite promising results in earlier, smaller clinical trials. Moreover, clinical data are often susceptible to varying interpretations and analyses. We do not know whether Phase 1, Phase 2, Phase 3, or other clinical trials we may conduct will demonstrate consistent or adequate efficacy and safety with respect to the proposed indication for use sufficient to receive regulatory approval or market our therapeutic candidates.

We, the FDA, an IRB, an independent ethics committee, or other applicable regulatory authorities may suspend clinical trials of a therapeutic candidate at any time for various reasons, including a belief that subjects participating in such trials are being exposed to unacceptable health risks or adverse side effects. Similarly, an IRB or ethics committee may suspend a clinical trial at a particular trial site. We may not have the financial resources to continue development of, or to enter into collaborations for, a therapeutic candidate if we experience any problems or other unforeseen events delaying or preventing clinical development or regulatory approval of, or our ability to commercialize, therapeutic candidates, including:

- negative or inconclusive results from our clinical trials, or the clinical trials of others for therapeutic candidates similar to ours, leading to a decision or requirement to conduct additional preclinical testing or clinical trials or abandon a program;
- serious and unexpected drug-related side effects experienced by participants in our clinical trials or by individuals using therapeutics similar to our therapeutic candidates;
- serious drug-related side effects experienced in the past by individuals using therapeutics similar to our therapeutic candidates;
- delays in submitting Investigational New Drug, or IND, applications or clinical trial applications, or comparable foreign applications, or delays or failure in obtaining the necessary approvals from regulators or IRBs to commence a clinical trial, or a suspension or termination of a clinical trial once commenced;
- conditions imposed by the FDA or comparable foreign authorities, such as the European Medicines Agency, or EMA, regarding the scope or design of our clinical trials;
- delays in enrolling research subjects in clinical trials;
- high drop-out rates of research subjects;
- inadequate supply or quality of therapeutic candidate or therapeutic candidate components, or materials or other supplies necessary for the conduct of our clinical trials, including those owned, manufactured, or provided by companies other than ours;
- greater than anticipated clinical trial costs, including the cost of any approved drugs used in combination with our therapeutic candidates;
- poor effectiveness of our therapeutic candidates during clinical trials;
- unfavorable FDA or other regulatory agency inspection and review of a clinical trial site;
- failure of our third-party contractors or investigators to comply with regulatory requirements or otherwise meet their contractual obligations in a timely manner, or at all;

- delays and changes in regulatory requirements, policies, and guidelines, including the imposition of additional regulatory oversight around clinical testing generally or with respect to our technology in particular; or

- varying interpretations of data by the FDA and similar foreign regulatory agencies.

Product development involves a lengthy and expensive process with an uncertain outcome, and results of earlier pre-clinical and clinical trials may not be predictive of future clinical trial results.

Clinical testing is expensive and generally takes many years to complete, and the outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. The results of pre-clinical trials and early clinical trials of our product candidates may not be predictive of the results of larger, later-stage controlled clinical trials. Product candidates showing promising results in early-stage clinical trials may still suffer significant setbacks in subsequent clinical trials. In January 2019, we dosed the first subjects with ALPN-101 in a Phase I trial enrolling healthy volunteers. We have conducted no clinical trials to date with ALPN-202 and have not dosed ALPN-101 in patients with active inflammatory disease. We will have to conduct trials in our proposed indications to verify the results obtained to date and to support any regulatory submissions for further clinical development. A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or adverse safety profiles despite promising results in earlier, smaller clinical trials. Moreover, clinical data are often susceptible to varying interpretations and analyses. We do not know whether Phase 1, Phase 2, Phase 3, or other clinical trials we may conduct will demonstrate consistent or adequate efficacy and safety with respect to the proposed indication for use sufficient to receive regulatory approval or market our therapeutic candidates.

Additionally, disruptions at the FDA and other agencies may also slow the time necessary for new drugs to be reviewed by necessary government agencies, which would adversely affect our business. For example, over the last several years, the U.S. government has shut down multiple times and certain regulatory agencies, such as the FDA, have had to furlough critical FDA and other government employees. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

To date, our revenue has been primarily derived from our collaboration agreements, and our success is dependent, in part, on our collaborators' efforts to develop our therapeutic candidates.

Our success is dependent, in part, on our collaborators' efforts to develop our therapeutic candidates and, historically, our revenue has been primarily derived from our agreements with collaborators. For example, in October 2015, we entered into an exclusive, worldwide license and research agreement with Kite to research, develop, and commercialize engineered autologous T cell therapies incorporating two targets from our technology. In October 2017, Kite was acquired by Gilead Pharma, Inc. and in May 2019, Kite provided notice to us of termination of the research and license agreement, which was effective in June 2019. Also, in May 2019, we entered into the Adaptimmune Collaboration Agreement to develop next-generation SPEAR T-cell products.

Continued advancement of our product candidates and other development efforts depends, in part, upon the efforts of our collaborators. If our collaborators do not dedicate sufficient resources to the development of product candidates that are the subject of our agreements, such product candidates may never be successful and we may be ineligible to receive additional milestone payments or royalties pursuant to the terms of our arrangements, which could have a material adverse impact on our financial results and operations. Even if we and our collaborators dedicate sufficient resources to our collaboration agreements, neither we nor our collaborators may be effective in obtaining approvals for any therapeutic candidates or, if approved, the successful commercialization of any approved products. Collaborators may change their strategic focus or pursue alternative technologies after entering into a collaboration agreement with us, which could result in reduced, delayed or no revenue to us. Disputes regarding collaboration agreements, including disputes pertaining to ownership of intellectual property, may also arise and if we and our collaborators are unable to resolve such disputes, litigation proceedings may occur, which could further delay development, distract management and generate substantial expenses, any of which could materially and negatively impact our business.

If third parties on which we depend to conduct our clinical or preclinical studies, or any future clinical trials, do not perform as expected, fail to satisfy regulatory or legal requirements, or miss expected deadlines, our development program could be delayed, which may result in materially adverse effects on our business, financial condition, results of operations, and prospects.

We rely, in part, on third party clinical investigators, contract research organizations, or CROs, clinical data management organizations, and consultants to design, conduct, supervise, and monitor clinical trials and preclinical studies of our therapeutic candidates and may do the same for future clinical trials. Because we rely on third parties to conduct preclinical studies or clinical trials, we have less control over the timing, quality, compliance, and other aspects of preclinical studies and clinical trials than we would if we conducted all preclinical studies and clinical trials on our own. These investigators, CROs, and consultants are not our employees and we have limited control over the amount of time and resources they dedicate to our programs. These third parties may have contractual relationships with other entities, some of which may be our competitors, which may draw their time and resources away from our programs. The third parties with which we contract might not be diligent, careful, compliant, or timely in conducting our preclinical studies or clinical trials, resulting in the preclinical studies or clinical trials being delayed or unsuccessful. Further, if any of our relationships with third-party CROs terminate, we may not be able to enter into arrangements with alternative CROs or to do so on commercially reasonable terms.

If we cannot contract with acceptable third parties on commercially reasonable terms, or at all, or if these third parties do not carry out their expected duties, satisfy legal and regulatory requirements for the conduct of preclinical studies or clinical trials, or meet expected deadlines, our clinical development programs could be delayed and otherwise adversely affected. In all events, we are responsible for ensuring each of our preclinical studies and clinical trials is conducted in accordance with the general investigational plan and protocols for the trial and with legal, regulatory and scientific standards. The FDA and certain foreign regulatory authorities, such as the EMA, require preclinical studies to be conducted in accordance with applicable Good Laboratory Practices, or GLPs, and clinical trials to be conducted in accordance with applicable FDA regulations and Good Clinical Practices, or GCPs, including requirements for conducting, recording, and reporting the results of preclinical studies and clinical trials to assure data and reported results are credible and accurate and the rights, integrity, and confidentiality of clinical trial participants are protected. Our reliance on third parties we do not control does not relieve us of these responsibilities and requirements. If we or any of our CROs fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA, the EMA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials comply with GCP regulations. In addition, our clinical trials must be conducted with product produced under current good manufacturing practice, or cGMP, regulations. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process. Any such event could have a material adverse effect on our business, financial condition, results of operations, and prospects.

In addition, switching or adding additional CROs involves additional cost and requires management time and focus. There is also a natural transition period when a new CRO commences work. As a result, delays may occur, which could materially impact our ability to meet our desired clinical development timelines. There can be no assurance that we will not encounter such challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition and prospects.

Because we rely on third party manufacturing and supply partners, our supply of clinical trial materials may become limited or interrupted or may not be of satisfactory quantity or quality, and our dependence on these third parties may impair the advancement of our research and development programs.

We have established in-house recombinant protein generation capabilities for producing sufficient protein materials to enable a portion of our current preclinical studies. We rely on third party supply and manufacturing partners to supply the materials, components, and manufacturing services for a portion of preclinical studies and also rely on such third parties for all our clinical trial drug supplies. We do not own manufacturing facilities or supply sources for such components and materials for clinical trial supplies and our current manufacturing facilities are insufficient to supply such components and materials for all of our preclinical studies. Certain raw materials necessary for the manufacture of our therapeutic products, such as cell lines, are available from a single or limited number of source suppliers on a purchase order basis. There can be no assurance our supply of research and development, preclinical study, and clinical trial drugs and other materials will not be limited, interrupted, restricted in certain geographic regions, of satisfactory quality or quantity, or continue to be available at acceptable prices. In particular, any replacement of our therapeutic substance manufacturer could require significant effort and expertise and could result in significant delay of our preclinical or clinical activities because there may be a limited number of qualified replacements.

The manufacturing process for a therapeutic candidate is subject to FDA and foreign regulatory authority review, and the facilities used by our contract manufacturers to manufacture our therapeutic candidates must be approved by the FDA

pursuant to inspections that will be conducted after we submit our marketing application(s) to the FDA. Suppliers and manufacturers must meet applicable manufacturing requirements and undergo rigorous facility and process validation tests required by regulatory authorities in order to comply with cGMP regulations or other regulatory standards. In the event any of our suppliers or manufacturers fails to comply with such requirements or to perform its obligations to us in relation to quality, timing, or otherwise, or if our supply of components or other materials becomes limited or interrupted for other reasons, we may experience shortages resulting in delayed shipments, supply constraints, and/or stock-outs of our products, be forced to manufacture the materials alone, for which we currently do not have the capabilities or resources, or enter into an agreement with another third party, which we may not be able to do on reasonable terms, if at all. In some cases, the technical skills or technology required to manufacture our therapeutic candidates may be unique or proprietary to the original manufacturer and we may have difficulty, or there may be contractual and intellectual property restrictions prohibiting us from, transferring such skills or technology to another third party and a feasible alternative may not exist. These factors may increase our reliance on such manufacturer or require us to obtain a license from such manufacturer in order to have another third party manufacture our therapeutic candidates. If we are required to change manufacturers for any reason, we will be required to verify the new manufacturer maintains facilities and procedures complying with quality standards and with all applicable regulations. The delays associated with the verification of a new manufacturer could negatively affect our ability to develop therapeutic candidates in a timely manner, within budget, or at all.

We expect to continue to rely on third party manufacturers if we receive regulatory approval for any therapeutic candidate. To the extent we have existing, or enter into future, manufacturing arrangements with third parties, we will depend on these third parties to perform their obligations in a timely manner consistent with contractual and regulatory requirements, including those related to quality control and assurance. If we are unable to obtain or maintain third-party manufacturing for therapeutic candidates, or to do so on commercially reasonable terms, we may not be able to develop and commercialize our therapeutic candidates successfully. Our, or a third party's, failure to execute on our manufacturing requirements could adversely affect our business in a number of ways, including as a result of:

- an inability to initiate or continue preclinical studies or clinical trials of therapeutic candidates under development;
- delay in submitting regulatory applications, or receiving regulatory approvals, for therapeutic candidates;
- the loss of the cooperation of a collaborator;
- subjecting manufacturing facilities of our therapeutic candidates to additional inspections by regulatory authorities;
- requirements to cease distribution or to recall batches of our therapeutic candidates; and
- in the event of approval to market and commercialize a therapeutic candidate, an inability to meet commercial demands for our products.

We may not successfully engage in strategic transactions, including any additional collaborations we seek, which could adversely affect our ability to develop and commercialize therapeutic candidates, impact our cash position, increase our expenses, and present significant distractions to our management.

From time to time, we may consider strategic transactions, such as collaborations, acquisitions of companies, asset purchases, and out- or in-licensing of therapeutic candidates or technologies. In particular, we intend to evaluate and, if strategically attractive, seek to enter into additional collaborations, including with major biotechnology or pharmaceutical companies. The competition for collaborative partners is intense, and the negotiation process is time-consuming and complex. Any new collaboration may be on suboptimal terms for us, and we may be unable to maintain any new or existing collaboration if, for example, development or approval of a therapeutic candidate is delayed, sales of an approved therapeutic product do not meet expectations, or the collaborator terminates the collaboration. Any such collaboration, or other strategic transaction, may require us to incur non-recurring or other charges, increase our near- and long-term expenditures and pose significant integration or implementation challenges or disrupt our management or business.

These transactions would entail numerous operational and financial risks, including:

- exposure to unknown liabilities;
- disruption of our business and diversion of our management's time and attention in order to manage a collaboration or develop acquired therapeutic candidates, or technologies;
- incurrence of substantial debt or dilutive issuances of equity securities to pay transaction consideration or costs;
- higher than expected collaboration, acquisition, or integration costs;

- write-downs of assets or goodwill, or incurring impairment charges or increased amortization expenses; and

- difficulty and cost in facilitating the collaboration or combining the operations and personnel of any acquired business or impairment of relationships with key suppliers, manufacturers, or customers of any acquired business due to changes in management and ownership and the inability to retain key employees of any acquired business.

Accordingly, although there can be no assurance we will undertake or successfully complete any transactions of the nature described above, any transactions we do complete may be subject to the foregoing or other risks and have a material adverse effect on our business, results of operations, financial condition, and prospects. Conversely, any failure to enter any collaboration or other strategic transaction beneficial to us could delay the development and potential commercialization of our therapeutic candidates and have a negative impact on the competitiveness of any therapeutic candidate reaching market.

We face competition from entities that have developed or may develop therapeutic candidates for our target disease indications, including companies developing novel treatments and technology platforms based on modalities and technology similar to us. If these companies develop technologies or therapeutic candidates more rapidly than we do, or their technologies, including delivery technologies, are more effective, our ability to develop and successfully commercialize therapeutic candidates may be adversely affected.

We participate in the highly competitive sector of biotechnology and pharmaceuticals and in the subsector of immune modulation. This subsector has undergone tremendous technological advancement over the last decade due to advancements in understanding the role of the immune system across multiple therapeutic areas, including oncology and autoimmune/inflammatory disease. While we believe our novel technology platform, discovery programs, knowledge, experience, and scientific resources offer competitive advantages, we face competition from major pharmaceutical and biotechnology companies, academic institutions, governmental agencies, public and private research institutions, and others.

Any products we successfully develop and commercialize will face competition from currently approved therapies and new therapies potentially available in the future.

The availability of reimbursement from government and other third-party payors will also significantly affect the pricing and competitiveness of our products. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for our products, which could result in our competitors establishing a strong market position before we are able to enter the market.

Many of the companies we compete against may have significantly greater financial resources and expertise in research and development, manufacturing, pre-clinical testing, conducting clinical trials, obtaining regulatory approvals, and marketing approved products. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

Specifically, our competitors include companies developing therapies with the same target(s) as ALPN-101 and ALPN-202 as well as companies building novel platforms to generate multi-specific antibody or non-antibody-based targeting proteins.

ICOSL/CD28 Competitors

The competitors listed below have programs targeting either ICOS or CD28 (or one of their ligands). To our knowledge, there are currently no competitors with a single molecule targeting ICOS and CD28 simultaneously.

- an anti-BAFF, anti-ICOSL bispecific antibody being developed by Amgen, Inc. (AMG570/MEDI0700);

- an anti-CD28 monoclonal antibody fragment being developed by OSE ImmunoTherapeutics SA (FR104);

- an anti-CD28 peptide being developed by AtoxBio, Inc.; and

- an IL-10 - anti-CD86 cytokine-scFv fusion protein being developed by Aptevo, Inc. (APVO210).

ALPN-202 Program Competitors

There are numerous clinical trials for immuno-oncology products used as a single agent or in combination. One of the potentially novel attributes of the ALPN-202 program is it combines inhibitory receptor antagonism and activating costimulation with a single molecule interacting with multiple immune targets.

Examples of additional multi-target compounds for immuno-oncology are highlighted below. To our knowledge, there are currently no competitors with a single molecule capable of dual PD-L1/CTLA-4 antagonism and PD-L1-dependent CD28 agonism.

- wild-type CD80-Fc being developed by Five Prime Therapeutics, Inc. (FPT155);
- bifunctional fusion protein composed of monoclonal antibody against programmed death ligand 1 ("PD-L1") fused to the extracellular domain of human transforming growth factor–β ("TGF-β") receptor II being developed by EMD Serono, Inc and GSK plc (bintrafusp alfa, or M7824);
- bifunctional fusion protein composed of PD-1 and OX40L developed by Shattuck Labs, Inc. (SL-279252);
- bispecific fusion protein targeting 4-1BB and PD-L1 being developed by Pieris Pharmaceuticals, Inc. (PRS-344);
- bispecific monoclonal antibodies being developed by Xencor, Inc. including XmAb20717 targeting CTLA-4 and PD-1, XmAb22841 targeting CTLA-4 and LAG-3, and XmAb23104 targeting PD-1 and ICOS;
- bispecific constructs called "DARTs" being developed by Macrogenics, Inc., including MGD013 targeting PD-1 and LAG-3 and MGD019 targeting PD-1 and CTLA-4;
- bispecific monoclonal antibody being developed by Tesaro, Inc., targeting PD-1 and LAG-3;
- small molecule antagonists being developed by Aurigene Ltd and Curis, Inc., including CA-170 targeting PD-L1 and VISTA and CA-327 targeting PD-L1 and TIM-3;
- FS118, a bispecific monoclonal antibody targeting PD-L1 and LAG-3 being developed by F-star Biotechnology, Ltd.;
- various combinations of separate anti PD-1/L1 and anti-CTLA-4 monoclonal antibodies; and
- various combinations of separate anti PD-1/L1 and costimulatory monoclonal antibodies such as OX-40, 4-1BB, and others.

Novel Platform Competitors

Multifunctional therapeutic protein platforms potentially competitive with our platform include:

- Amgen, Inc. (BiTE®): fusion proteins consisting of two single-chain variable fragments to link T-cells to tumors;
- Macrogenics, Inc. (DART®): Dual-Affinity Re-Targeting and Trident technology platforms bind multiple targets with a single molecule;
- Xencor, Inc. (XmAb Bispecific): Optimized Fc domains for improved potency, half-life and stability;
- Zymeworks, Inc. (Azymetric™): Proprietary amino acid modifications to facilitate interaction of distinct heavy chains;
- Pieris Pharmaceuticals, Inc. (Anticalin®): Engineered proteins derived from natural lipocalins found in blood plasma;
- Compass Therapeutics, LLC (Targeted Immunomodulation™, StitchMabs™): Antibody discovery targeting the tumor-immune synapse;
- Harpoon Therapeutics, Inc.: TriTAC™ (Tri-specific T cell Activating Construct) contain CD3 binding domain, half-life extension domain, and antigen-binding domain;
- Shattuck Labs, Inc.: Agonist Redirected Antibody platform claimed to bind tumor-necrosis factor ("TNF") and checkpoint targets;
- Ablynx NV (Nanobody®), purchased by Sanofi Pharma, Inc.: Platform technology of single-domain, heavy-chain antibody fragments derived from camelidae (e.g., camels and llamas);
- Regeneron, Inc.: VEGF Trap and VelociSuite® antibody technology platforms;
- Five Prime Therapeutics, Inc.: Proprietary protein library and rapid protein production and testing platform; and
- Riada Therapeutics: developing and engineering next-generation immunocytokine therapies.

Additionally, there are a number of other therapies for autoimmune/inflammatory diseases or cancer approved or in development that are also competitive with our lead program and other programs in development. Many of the other therapies include other types of immunotherapies with different targets than our programs. Other potentially competitive therapies work in ways distinct from our development programs.

Many of our competitors have significantly greater financial, technical, manufacturing, marketing, sales, and supply resources or experience than we have. If we successfully obtain approval for any therapeutic candidate, we will face competition based on many different factors, including safety and effectiveness, ease with which our products can be administered and the extent to which patients accept relatively new routes of administration, timing and scope of regulatory approvals, availability and cost of manufacturing, marketing and sales capabilities, price, reimbursement coverage, and patent position of our products. Competing products could present superior treatment alternatives, including by being more effective, safer, less expensive, or marketed and sold more effectively than any products we may develop. Competitive products may make any products we develop obsolete or noncompetitive before we recover the expense of developing and commercializing our therapeutic candidates. Competitors could also recruit our employees, which could negatively impact our ability to execute our business plan.

Any inability to attract and retain qualified key management and technical personnel would impair our ability to implement our business plan.

Our success largely depends on the continued service of key management and other specialized personnel, including Mitchell H. Gold, M.D., our Executive Chairman and Chief Executive Officer, Stanford Peng, M.D., Ph.D., our President and Head of Research and Development, and Paul Rickey, our Senior Vice President and Chief Financial Officer.

The loss of one or more members of our management team or other key employees or advisors could delay our research and development programs and materially harm our business, financial condition, results of operations, and prospects. The relationships our key managers have cultivated within our industry make us particularly dependent upon their continued employment with us. We are dependent on the continued service of our technical personnel because of the highly technical nature of our therapeutic candidates and technologies, and the specialized nature of the regulatory approval process. Because our management team and key employees are not obligated to provide us with continued service, they could terminate their employment with us at any time without penalty. We do not maintain key person life insurance policies on any of our management team members or key employees. Our future success will depend in large part on our continued ability to attract and retain other highly qualified scientific, technical, and management personnel, as well as personnel with expertise in clinical testing, manufacturing, governmental regulation, and commercialization. We face competition for personnel from other companies, universities, public and private research institutions, government entities, and other organizations, including significant competition in the Seattle employment market.

As our therapeutic candidates advance into clinical trials, we may experience difficulties in managing our growth and expanding our operations.

We have limited experience in therapeutic development and very limited experience with clinical trials of therapeutic candidates. As our therapeutic candidates enter and advance through preclinical studies and clinical trials, we will need to expand our development, regulatory, and manufacturing capabilities or contract with other organizations to provide these capabilities for us. In the future, we expect to have to manage additional relationships with collaborators or partners, suppliers, and other organizations. Our ability to manage our operations and future growth will require us to continue to improve our operational, financial, and management controls, reporting systems, and procedures. We may not be able to implement improvements to our management information and control systems in an efficient or timely manner and may discover deficiencies in existing systems and controls.

If any of our therapeutic candidates are approved for marketing and commercialization and we are unable to develop sales, marketing and distribution capabilities on our own or enter into agreements with third parties to perform these functions on acceptable terms, we may be unable to successfully commercialize any such future products.

We currently have no sales, marketing, or distribution capabilities or experience. If any of our therapeutic candidates are approved, we will need to develop internal sales, marketing, and distribution capabilities to commercialize such products, which may be expensive and time-consuming, or enter into collaborations with third parties to perform these services. If we decide to market our products directly, we will need to commit significant financial, legal, and managerial resources to develop a marketing and sales force with technical expertise and supporting distribution, administration, and compliance capabilities. If we rely on third parties with such capabilities to market our approved products, or decide to co-promote products with collaborators, we will need to establish and maintain marketing and distribution arrangements with third parties, and there can be no assurance we will be able to enter into such arrangements on acceptable, compliant terms or at all. In entering into third-party marketing or distribution arrangements, any revenue we receive will depend upon the efforts of the third parties and there can be no assurance such third parties will establish adequate sales and distribution capabilities or be successful in gaining market acceptance of any approved therapeutic. If we are not successful in commercializing any therapeutic approved in the

future, either on our own or through third parties, our business, financial condition, results of operations, and prospects could be materially and adversely affected.

If we fail to comply with U.S. and foreign regulatory requirements, regulatory authorities could limit or withdraw any marketing or commercialization approvals we may receive and subject us to other penalties that could materially harm our business.

Our company, our therapeutic candidates, our suppliers, and our contract manufacturers, distributors, and contract testing laboratories are subject to extensive regulation by governmental authorities in the European Union, the United States, and other countries, with regulations differing from country to country.

Even if we receive marketing and commercialization approval of a therapeutic candidate, we and our third-party service providers will be subject to continuing regulatory requirements, including a broad array of regulations related to establishment registration and product listing, manufacturing processes, risk management measures, quality and pharmacovigilance systems, post-approval clinical studies, labeling and packaging, advertising and promotional activities, record keeping, distribution, adverse event reporting, import and export of pharmaceutical products, pricing, sales, and marketing, and fraud and abuse requirements.

We are required to submit safety and other post market information and reports, and are subject to continuing regulatory review, including in relation to adverse patient experiences with the product and clinical results reported after a product is made commercially available, both in the United States and in any foreign jurisdiction in which we seek regulatory approval. The FDA and certain foreign regulatory authorities, such as the EMA, have significant post-market authority, including the authority to require labeling changes based on new safety information and to require post-market studies or clinical trials to evaluate safety risks related to the use of a product or to require withdrawal of the product from the market.

The FDA also has the authority to require a Risk Evaluation and Mitigation Strategies, or REMS, plan either before or after approval, which may impose further requirements or restrictions on the distribution or use of an approved therapeutic. The EMA now routinely requires risk management plans, or RMPs, as part of the marketing authorization application process, and such plans must be continually modified and updated throughout the lifetime of the product as new information becomes available. In addition, the relevant governmental authority of any EU member state can request an RMP whenever there is a concern about the risk/ benefit balance of the product.

The manufacturers and manufacturing facilities we use to make a future product, if any, will also be subject to periodic review and inspection by the FDA and other regulatory agencies, including for continued compliance with cGMP requirements. The discovery of any new or previously unknown problems with our third-party manufacturers, manufacturing processes or facilities may result in restrictions on the product, manufacturers or facilities, including withdrawal of the product from the market. If we rely on third-party manufacturers, we will have limited control over compliance with applicable rules and regulations by such manufacturers.

If we or our collaborators, manufacturers, or service providers fail to comply with applicable continuing regulatory requirements in the U.S. or foreign jurisdictions in which we seek to market our products, we may be subject to, among other things, fines, warning and untitled letters, clinical holds, a requirement to conduct additional clinical trials, delay or refusal by the FDA or foreign regulatory authorities to approve pending applications or supplements to approved applications, suspension, refusal to renew or withdrawal of regulatory approval, product recalls, seizures, or administrative detention of products, refusal to permit the import or export of products, operating restrictions, inability to participate in government programs including Medicare and Medicaid, and total or partial suspension of production or distribution, injunction, restitution, disgorgement, debarment, civil penalties, and criminal prosecution.

Imposed price controls may adversely affect our future profitability.

In most countries, the pricing of prescription drugs is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after receipt of marketing approval for a product. In addition, there can be considerable pressure by governments and other stakeholders on prices and reimbursement levels, including as part of cost containment measures. Political, economic, and regulatory developments may further complicate pricing and reimbursement negotiations, and pricing negotiations may continue after reimbursement has been obtained.

Reference pricing used by various EU member states and parallel distribution, or arbitrage between low-priced and high-priced member states, can further reduce prices. In some countries, we or our collaborators may be required to conduct a clinical trial or other studies comparing the cost-effectiveness of our therapeutic candidates to other available therapies in order to obtain or maintain reimbursement or pricing approval. Publication of discounts by third-party payors or authorities may lead

to further pressure on the prices or reimbursement levels within the country of publication and other countries. If reimbursement of any product candidate approved for marketing is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business, financial condition, results of operations, or prospects could be adversely affected.

Our business entails a significant risk of product liability and our inability to obtain sufficient insurance coverage could harm our business, financial condition, results of operations, or prospects.

Our business exposes us to significant product liability risks inherent in the development, testing, manufacturing, and marketing of therapeutic treatments. Product liability claims could delay or prevent completion of our development programs. If we succeed in marketing products, such claims could result in an investigation by certain regulatory authorities, such as FDA or foreign regulatory authorities, of the safety and effectiveness of our products, our manufacturing processes and facilities, or our marketing programs and potentially a recall of our products or more serious enforcement action, limitations on the approved indications for which they may be used, or suspension or withdrawal of approvals. Regardless of the merits or eventual outcome, liability claims may also result in decreased demand for our products, injury to our reputation, costs to defend the related litigation, a diversion of management's time and our resources, substantial monetary awards to trial participants or patients, and a decline in our valuation. We currently have product liability insurance we believe is appropriate for our stage of development and may need to obtain higher levels of product liability insurance prior to marketing any therapeutic candidates. Any insurance we have or may obtain may not provide sufficient coverage against potential liabilities. Furthermore, clinical trial and product liability insurance is becoming increasingly expensive. As a result, we may be unable to obtain sufficient insurance at a reasonable cost to protect us against losses caused by product liability claims with a potentially material adverse effect on our business.

Our employees may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could have a material adverse effect on our business.

We are exposed to the risk of employee fraud or other misconduct. Misconduct by employees could include, but is not limited to:

- intentional failures to comply with FDA or U.S. health care laws and regulations, or applicable laws, regulations, guidance, or codes of conduct set by foreign governmental authorities or self-regulatory industry organizations;
- a provision of inaccurate information to any governmental authorities such as FDA;
- noncompliance with manufacturing standards we may establish;
- noncompliance with federal and state healthcare fraud and abuse laws and regulations; and
- a failure to report financial information or data accurately or a failure to disclose unauthorized activities to us.

In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws, regulations, guidance and codes of conduct intended to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws, regulations, guidance statements, and codes of conduct may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive program, health care professional, and other business arrangements.

Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions, including debarment or disqualification of those employees from participation in FDA regulated activities and serious harm to our reputation. This could include violations of provisions of the U.S. federal Health Insurance Portability and Accountability Act, or HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, other U.S. federal and state law, and requirements of non-U.S. jurisdictions, including the European Union Data Protection Directive.

It is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws, regulations, guidance or codes of conduct. If any such actions are instituted against us, and we are not successful in defending such actions or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant fines, exclusion from government programs, or other sanctions.

Our business involves the use of hazardous materials and we and our third-party manufacturers must comply with environmental laws and regulations, which may be expensive and restrict how we conduct business.

Our third-party manufacturers' activities and our own activities involve the controlled storage, use and disposal of hazardous and flammable materials, including the components of our pharmaceutical product candidates, test samples and reagents, biological materials and other hazardous compounds. We and our manufacturers are subject to federal, state, local, and foreign laws and regulations governing the use, generation, manufacture, storage, handling, and disposal of these hazardous materials. Although we believe our safety procedures for handling and disposing of these materials and waste products comply with the standards prescribed by these laws and regulations, we cannot eliminate the risk of accidental injury or contamination from the use, storage, handling, or disposal of hazardous materials. In the event of an accident, state, or federal or other applicable authorities may curtail our use of these materials and/or interrupt our business operations. In addition, if an accident or environmental discharge occurs, or if we discover contamination caused by prior operations, including by prior owners and operators of properties we acquire, we could be liable for cleanup obligations, damages, and fines. If such unexpected costs are substantial, this could significantly harm our financial condition and results of operations.

Compliance with governmental regulations regarding the treatment of animals used in research could increase our operating costs, which would adversely affect the commercialization of our technology.

The Animal Welfare Act, or AWA, is the federal law covering the treatment of certain animals used in research. Currently, the AWA imposes a wide variety of specific regulations governing the humane handling, care, treatment, and transportation of certain animals by producers and users of research animals, most notably relating to personnel, facilities, sanitation, cage size and feeding, watering, and shipping conditions. Third parties with whom we contract are subject to registration, inspections, and reporting requirements under the AWA. Furthermore, some states have their own regulations, including general anti-cruelty legislation, which establish certain standards in handling animals. Comparable rules, regulations, and or obligations exist in many foreign jurisdictions. If we or our contractors fail to comply with regulations concerning the treatment of animals used in research, we may be subject to fines and penalties and adverse publicity, and our operations could be adversely affected.

Our information technology systems could face serious disruptions adversely affecting our business.

Our information technology and other internal infrastructure systems, including corporate firewalls, servers, leased lines, and connection to the Internet, face the risk of systemic failure potentially disruptive to our operations. A significant disruption in the availability of our information technology and other internal infrastructure systems could cause interruptions in our collaborations with our partners and delays in our research and development work.

Our current operations are concentrated in one location and any events affecting this location may have material adverse consequences.

Our current operations are located in facilities situated in Seattle. Any unplanned event, such as flood, fire, explosion, earthquake, extreme weather condition, medical epidemics, power shortage, power outage, telecommunication failure, or other natural or manmade accidents or incidents resulting in our company being unable to fully utilize the facilities, may have a material adverse effect on our ability to operate our business, particularly on a daily basis, and have significant negative consequences on our financial and operating conditions. Loss of access to these facilities may result in increased costs, delays in the development of our therapeutic candidates, or interruption of our business operations. As part of our risk management policy, we maintain insurance coverage at levels we believe are appropriate for our business. However, in the event of an accident or incident at these facilities, we cannot assure you the amounts of insurance will be sufficient to satisfy any damages and losses or that the insurance covers all risks. If our facilities are unable to operate because of an accident or incident or for any other reason, even for a short period of time, any or all of our research and development programs may be harmed. Any business interruption may have a material adverse effect on our business, financial position, results of operations, and prospects.

The investment of our cash, cash equivalents, and fixed income in marketable securities is subject to risks which may cause losses and affect the liquidity of these investments.

As of June 30, 2019, we had $55.6 million in cash and cash equivalents, and short-term investments. We expect to invest our excess cash in marketable securities. These investments are subject to general credit, liquidity, market and interest rate risks, including potential future impacts similar to the impact of U.S. sub-prime mortgage defaults previously affecting various sectors of the financial markets and which caused credit and liquidity issues. We may realize losses in the fair value of

these investments, an inability to access cash in these investments for a potentially meaningful period, or a complete loss of these investments, which would have a negative effect on our financial statements.

Changes in accounting rules and regulations, or interpretations thereof, could result in unfavorable accounting charges or require us to change our compensation policies.

Accounting methods and policies for biopharmaceutical companies, including policies governing revenue recognition, research and development and related expenses, and accounting for stock-based compensation, are subject to review, interpretation, and guidance from our auditors and relevant accounting authorities, including the SEC. Changes to accounting methods or policies, or interpretations thereof, may require us to reclassify, restate, or otherwise change or revise our financial statements.

Our net operating loss carryforwards and certain other tax attributes are likely subject to limitations.

In general, a corporation that undergoes an "ownership change" is subject to limitations on its ability to utilize its pre-change net operating loss carryforwards, or NOLs, to offset future taxable income. In general, an ownership change occurs if the aggregate stock ownership of certain stockholders, generally stockholders beneficially owning five percent or more of a corporation's common stock, applying certain look-through and aggregation rules, increases by more than 50 percentage points over such stockholders' lowest percentage ownership during the testing period, generally three years. Nivalis may have experienced ownership changes in the past and may experience ownership changes in the future. In addition, the closing of the merger of Nivalis and Alpine in 2017 likely resulted in an ownership change for Nivalis. It is likely that, due to the method by which limitations on the utilization of NOL carryforwards are calculated, we will not be able to utilize any of Nivalis' net operating loss carryforwards and certain other tax attributes. It is also possible that Alpine's net operating loss carryforwards and certain other tax attributes may be subject to limitation as a result of ownership changes in the past and/or the closing of the merger. Consequently, even if we achieve profitability, we may not be able to utilize a material portion of Alpine's, or any of Nivalis' , net operating loss carryforwards and certain other tax attributes, which could have a material adverse effect on cash flow and results of operations.

Provisions of our debt instruments may restrict our ability to pursue our business strategies.

Our term loan agreement requires us, and any debt financing we may obtain in the future may require us, to comply with various covenants that limit our ability to, among other things:

- dispose of assets;
- complete mergers or acquisitions;
- incur indebtedness;
- encumber assets;
- pay dividends or make other distributions to holders of our capital stock;
- make specified investments;
- engage in any new line or business; and
- engagement in certain transactions with our affiliates.

These restrictions could inhibit our ability to pursue our business strategies. If we default under our term loan agreement, and such event of default is not cured or waived, the lenders could terminate commitments to lend and cause all amounts outstanding with respect to the debt to be due and payable immediately, which in turn could result in cross defaults under other debt instruments. Our assets and cash flow may not be sufficient to fully repay borrowings under our outstanding debt instruments if some or all of these instruments are accelerated upon a default. We may incur additional indebtedness in the future. The debt instruments governing such indebtedness could contain provisions that are as, or more, restrictive than our existing debt instruments. If we are unable to repay, refinance or restructure our indebtedness when payment is due, the lenders could proceed against the collateral granted to them to secure such indebtedness or force us into bankruptcy or liquidation.

Our business may be affected by litigation and government investigations.

We may from time to time receive inquiries and subpoenas and other types of information requests from government authorities and others and we may become subject to claims and other actions related to our business activities. While the ultimate outcome of investigations, inquiries, information requests, and legal proceedings is difficult to predict, defense of

litigation claims can be expensive, time-consuming and distracting, and adverse resolutions or settlements of those matters may result in, among other things, modification of our business practices, costs, and significant payments, any of which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

We believe our development programs and platform have a particular mechanism of action, but this mechanism of action has not been proven conclusively.

Our scientific platform is novel, and the underlying science is not exhaustively understood nor conclusively proven. In particular, the interaction of vIgDs with the immune synapse, the ability of vIgDs to slow, stop, restart, or accelerate immune responses, and the ability of vIgD domains to interact with multiple counter structures is still largely theoretical. Graphical representations of proposed mechanisms of action of our therapies, the size, actual or relative, of our therapeutics, and how our therapeutics might interface with other cells within the human body, inside the immune synapse, or inside the disease and/or the tumor microenvironment are similarly theoretical and not yet conclusively proven. The lack of a proven mechanism of action may adversely affect our ability to raise sufficient capital, complete preclinical studies, adequately manufacture drug product, obtain regulatory clearance for clinical trials, gain marketing approval, or conclude collaborations, or interfere with our ability to market our product to patients and physicians or achieve reimbursement from payors.

Any inability to present our data in scientific journals or at scientific conferences could adversely impact our business and stock price.

We may from time to time submit data related to our research and development activities in peer-reviewed scientific publications or apply to present data related to our research and development activities at scientific or other conferences. We have no control over whether these submissions or applications are accepted. Even if accepted for a conference, we have no control over whether presentations at scientific conferences will be accepted for oral presentation, poster presentation, or abstract publication only. Even when accepted for publication, we have no control over the timing of the release of the publication. Rejection by publications, delays in publication, rejection for presentation, or a less-preferred format for a presentation may adversely impact our stock price, ability to raise capital, and business.

Our business may be affected by adverse scientific publications or editorial or discussant opinions.

We may from time to time publish data related to our research and development activities in peer-reviewed scientific publications or present data related to our research and development activities at scientific or other conferences. Editorials or discussants unrelated to us may provide opinions on our presented data unfavorable to us. In addition, scientific publications or presentations may be made which are critical of our science or research or the field of immunotherapy in general. This may adversely affect our ability to raise necessary capital, complete clinical and preclinical studies, adequately manufacture drug product, obtain regulatory clearance for clinical trials, or approval for marketing, or interfere with our ability to market our product to patients and physicians or achieve reimbursement from payors.

Risks Related to Our Intellectual Property

If we are not able to obtain and enforce patent protection for our technology, including therapeutic candidates, therapeutic products, and platform technology, development of our therapeutic candidates and platform, and commercialization of our therapeutic products may be materially and adversely affected.

Our success depends in part on our ability to obtain and maintain patents and other forms of intellectual property rights, including in-licenses of intellectual property rights of others, for our technology, including platform and therapeutic candidates and products, methods used to manufacture our therapeutic candidates and products, and methods for treating patients using our therapeutic candidates and products, as well as our ability to preserve our trade secrets, to prevent third parties from infringing upon our proprietary rights, and to operate without infringing upon the proprietary rights of others. As of June 30, 2019, our patent portfolio consists of over 75 pending patent applications. We may not be able to apply for patents on certain aspects of our technology, including therapeutic candidates and products, in a timely fashion or at all. Any future patents we obtain may not be sufficiently broad to prevent others from using our technology or from developing competing therapeutics and technology. There is no guarantee that any of our pending patent applications will result in issued or granted patents, any of our issued or granted patents will not later be found to be invalid or unenforceable, or any issued or granted patents will include claims sufficiently broad to cover our technology, including therapeutic candidates and products, or to provide meaningful protection from our competitors. Moreover, the patent position of pharmaceutical and biotechnology companies can be highly uncertain because it involves complex legal and factual questions. We will be able to protect our proprietary rights from unauthorized use by third parties only to the extent our current and future technology, including

therapeutic candidates and products, are covered by valid and enforceable patents or are effectively maintained as trade secrets. If third parties disclose or misappropriate our proprietary rights, it may materially and adversely impact our competitive position in the market.

The U.S. Patent and Trademark Office, or USPTO, and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment, and other provisions during the patent process. There are situations in which noncompliance can result in abandonment or lapse of a patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, competitors might be able to enter the market earlier than would otherwise have been the case. Further, the standards applied by the USPTO and foreign patent offices in granting patents are not always applied uniformly or predictably. For example, there is no uniform worldwide policy regarding patentable subject matter or the scope of claims allowable in biotechnology and pharmaceutical patents. As such, we do not know the degree of future protection we will have on our technology, including therapeutic candidates and products. While we will endeavor to try to protect our technology, including therapeutic candidates and products, with intellectual property rights such as patents, as appropriate, the process of obtaining patents is time-consuming, expensive, and sometimes unpredictable, and we can provide no assurances our technology, including therapeutic candidates and products, will be adequately protected in the future against unauthorized uses or competing claims by third parties.

In addition, recent and future changes to the patent laws and to the rules of the USPTO or other foreign patent offices may have a significant impact on our ability to protect our technology, including therapeutic candidates and products, and enforce our intellectual property rights. For example, the Leahy-Smith America Invents Act enacted in 2011 involves significant changes in patent legislation. In addition, we cannot assure that court rulings or interpretations of any court decision will not adversely impact our patents or patent applications. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, there also may be uncertainty with respect to the value of patents, once obtained. Depending on decisions by the U.S. Congress, the federal courts, the USPTO, or made in foreign jurisdictions, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents we might obtain in the future.

Once granted, patents may remain open to opposition, interference, re-examination, post-grant review, inter partes review, nullification, or derivation action in court or before patent offices or similar proceedings before or after allowance or grant, during which time third parties can raise objections against such initial grant. In the course of such proceedings, which may continue for a protracted period of time, the patent owner may be compelled to limit the scope of the pending, allowed or granted claims thus attacked or may lose the allowed or granted claims altogether. Our patent risks include that:

- others may, or may be able to, make, use, offer to sell, or sell compounds that are the same as or similar to our therapeutic candidates and products but that are not covered by the claims of the patents we own or license;
- we or our licensors, collaborators, or any future collaborators may not be the first to file patent applications covering certain aspects of our technology, including therapeutic candidates and products;
- others may independently develop similar or alternative technology or duplicate any of our technology without infringing our intellectual property rights;
- a third party may challenge our patents and, if challenged, a court may not hold that our patents are valid, enforceable, or that a third party is infringing;
- a third party may challenge our patents in various patent offices and, if challenged, we may be compelled to limit the scope of our pending, allowed or granted claims or lose the allowed or granted claims altogether;
- any issued patents we own or have licensed may not provide us with any competitive advantages, or may be challenged by third parties;
- we may not develop additional proprietary technologies that are patentable;
- the patents of others could harm our business; and
- our competitors could conduct research and development activities in countries where we do not or will not have enforceable patent rights and then use the information learned from such activities to develop competitive products for sale in major commercial markets where we do not or will not have enforceable patent rights.

We may license patent rights from third-party owners or licensees. If such owners or licensees do not properly or successfully obtain, maintain or enforce the patents underlying such licenses, or if they retain or license to others any competing rights, our competitive position and business prospects may be materially and adversely affected.

We may rely upon intellectual property rights licensed from third parties to protect our technology, including platform technology and therapeutic candidates and products. To date, we have in-licensed some intellectual property on a non-exclusive

basis relating to commercially-available cell lines involved in the manufacture of our vIgD programs; however, we may also license additional third-party intellectual property in the future, to protect our technology, including intellectual property relating to our platform technology and therapeutic candidates and products. Our success will depend in part on the ability of our licensors to obtain, maintain, and enforce patent protection for our licensed intellectual property, in particular those patents to which we have secured exclusive rights. Our licensors may elect not to prosecute, or may be unsuccessful in prosecuting, any patent applications licensed to us. Even if patents issue or are granted, our licensors may fail to maintain these patents, may determine not to pursue litigation against other companies infringing these patents, or may pursue litigation less aggressively than we would. Further, any licenses we enter into may be non-exclusive and we may not be able to obtain exclusive rights, which would potentially allow third parties to develop competing products or technology. Without protection for, or exclusive right to, any intellectual property we may license, other companies might be able to offer substantially identical or similar product for sale, which could adversely affect our competitive business position and harm our business prospects. In addition, we may sublicense any rights we have under third-party licenses to current or future collaborators or any future strategic partners. Any impairment of these sublicensed rights could result in reduced revenue under or result in termination of an agreement by one or more of our collaborators or any future strategic partners.

We may be unable to protect our patent intellectual property rights throughout the world.

Obtaining a valid and enforceable issued or granted patent covering our technology, including therapeutic candidates and products, in the United States and worldwide can be extremely costly. In jurisdictions where we have not obtained patent protection, competitors may use our technology, including therapeutic candidates and products, to develop their own products, and further, may commercialize such products in those jurisdictions and export otherwise infringing products to territories where we have not obtained patent protection. In certain instances, a competitor may be able to export otherwise infringing products in territories where we will obtain patent protection. In jurisdictions outside the United States where we will obtain patent protection, it may be more difficult to enforce a patent as compared to the United States. Competitor products may compete with our future products in jurisdictions where we do not or will not have issued or granted patents or where our issued or granted patent claims or other intellectual property rights are not sufficient to prevent competitor activities in these jurisdictions. The legal systems of certain countries, particularly certain developing countries, make it difficult to enforce patents and such countries may not recognize other types of intellectual property protection, particularly relating to biopharmaceuticals. This could make it difficult for us to prevent the infringement of our patents or marketing of competing products in violation of our proprietary rights generally in certain jurisdictions. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial cost and divert our efforts and attention from other aspects of our business.

We generally file a provisional patent application first (a priority filing) at the USPTO. An international application under the Patent Cooperation Treaty, or PCT, is usually filed within twelve months after the priority filing, at times with a United States filing. Based on the PCT filing, national and regional patent applications may be filed in various international jurisdictions, such as in Europe, Japan, Australia, Canada, and the United States. We have so far not filed for patent protection in all national and regional jurisdictions where such protection may be available. In addition, we may decide to abandon national and regional patent applications before they are granted. Finally, the grant proceeding of each national or regional patent is an independent proceeding which may lead to situations in which applications might in some jurisdictions be refused by the relevant registration authorities, while granted by others. It is also quite common that, depending on the country, various scopes of patent protection may be granted on the same therapeutic candidate, product, or technology. The laws of some jurisdictions do not protect intellectual property rights to the same extent as the laws in the United States, and many companies have encountered significant difficulties in protecting and defending such rights in such jurisdictions. If we or our licensors encounter difficulties in protecting, or are otherwise precluded from effectively protecting, the intellectual property rights important for our business in such jurisdictions, the value of these rights may be diminished, and we may face additional competition from others in those jurisdictions. Many countries have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, many countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If we or any of our licensors are forced to grant a license to third parties with respect to any patents relevant to our business, our competitive position in the relevant jurisdiction may be impaired and our business and results of operations may be adversely affected.

We or our licensors, collaborators, or any future strategic partners may become subject to third party claims or litigation alleging infringement of patents or other proprietary rights or seeking to invalidate patents or other proprietary rights, and we may need to resort to litigation to protect or enforce our patents or other proprietary rights, all of which could be costly, time consuming, delay or prevent the development of our therapeutic candidates and commercialization of our therapeutic products, or put our patents and other proprietary rights at risk.

We or our licensors, licensees, collaborators, or any future strategic partners may be subject to third-party claims for infringement or misappropriation of patent or other proprietary rights. We are generally obligated under our license or collaboration agreements to indemnify and hold harmless our licensors, licensees, or collaborators for damages arising from intellectual property infringement by us. If we or our licensors, licensees, collaborators, or any future strategic partners are found to infringe a third-party patent or other intellectual property rights, we could be required to pay damages, potentially including treble damages, if we are found to have willfully infringed. In addition, we or our licensors, licensees, collaborators, or any future strategic partners may choose to seek, or be required to seek, a license from a third party, which may not be available on acceptable terms, if at all. Even if a license can be obtained on acceptable terms, the rights may be non-exclusive, which could give our competitors access to the same technology or intellectual property rights licensed to or from us. If we fail to obtain a required license, we or our licensee or collaborator, or any future licensee or collaborator, may be unable to effectively market therapeutic products based on our technology, which could limit our ability to generate revenue or achieve profitability and possibly prevent us from generating revenue sufficient to sustain our operations. In addition, we may find it necessary to pursue claims or initiate lawsuits to protect or enforce our patent or other intellectual property rights. The cost to us in defending or initiating any litigation or other proceeding relating to patent or other proprietary rights, even if resolved in our favor, could be substantial, and litigation would divert our management's attention. Some of our competitors may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could delay our research and development efforts and limit our ability to continue our operations.

Although we do not believe our technology infringes the intellectual property rights of others, we are aware of one or more patents or patent applications that may relate to our technology, and third parties may assert against our claims alleging infringement of their intellectual property rights regardless of whether their claims have merit. Infringement claims could harm our reputation, may result in the expenditure of significant resources to defend and resolve such claims, and could require us to pay monetary damages if we are found to have infringed the intellectual property rights of others.

If we were to initiate legal proceedings against a third party to enforce a patent covering our technology, including therapeutic candidates and products, the defendant could counterclaim that our patent is invalid or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, for example, patent ineligibility, lack of novelty, lack of written description, obviousness, or non-enablement. Grounds for an unenforceability assertion could be an allegation someone connected with prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during prosecution. The outcome following legal assertions of invalidity and unenforceability during patent litigation is unpredictable. With respect to the validity question, for example, we cannot be certain there is no invalidating prior art, of which we and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity or unenforceability, we would lose at least part, and perhaps all, of the patent protection on our technology, including therapeutic candidates and products. Such a loss of patent protection could have a material adverse impact on our business. Patents and other intellectual property rights also will not protect our technology, including therapeutic candidates and products, if competitors design around our protected technology, including therapeutic candidates and products, without legally infringing our patents or other intellectual property rights.

It is also possible we have failed to identify relevant third-party patents or applications. For example, patent applications in the United States and elsewhere are published approximately 18 months after the earliest filing for which priority is claimed, with such earliest filing date being commonly referred to as the priority date. Therefore, patent applications covering our technology, including therapeutic candidates and products, could have been filed by others without our knowledge. Additionally, pending patent applications which have been published can, subject to certain limitations, be later amended in a manner that could cover our technology, including therapeutic candidates and products. Third party intellectual property rights holders may also actively bring infringement claims against us. We cannot guarantee we will be able to successfully settle or otherwise resolve such infringement claims. If we are unable to successfully settle future claims on terms acceptable to us, we may be required to engage in or continue costly, unpredictable, and time-consuming litigation and may be prevented from, or experience substantial delays in, marketing our technology, including therapeutic candidates and products. If we fail in any such dispute, in addition to being forced to pay damages, we may be temporarily or permanently prohibited from commercializing our technology, including a therapeutic product, held to be infringing. We might, if possible, also be forced to redesign therapeutic candidates or products so we no longer infringe the third-party intellectual property rights. Any of these events, even if we were ultimately to prevail, could require us to divert substantial financial and management resources we would otherwise be able to devote to our business.

If we fail to comply with our obligations under any license, collaboration, or other agreements, we may be required to pay damages and could lose intellectual property rights necessary for developing and protecting our technology, including our platform technology, therapeutic candidates, and therapeutic products, or we could lose certain rights to grant sublicenses, either of which could have a material adverse effect on our results of operations and business prospects.

Our current licenses impose, and any future licenses we enter into are likely to impose, various development, commercialization, funding, milestone, royalty, diligence, sublicensing, insurance, patent prosecution and enforcement, and other obligations on us. If we breach any of these obligations, or use the intellectual property licensed to us in an unauthorized manner, we may be required to pay damages and the licensor may have the right to terminate the license, which could result in us being unable to develop, manufacture, and sell or offer to sell products covered by the licensed technology or enable a competitor to gain access to the licensed technology. Moreover, our licensors may own or control intellectual property that has not been licensed to us and, as a result, we may be subject to claims, regardless of their merit, that we are infringing or otherwise violating the licensor's rights. In addition, while we cannot currently determine the amount of the royalty obligations we would be required to pay on future sales of licensed products, if any, the amounts may be significant. The amount of our future royalty obligations will depend on the technology and intellectual property we use in therapeutic products we successfully develop and commercialize, if any. Therefore, even if we successfully develop and commercialize therapeutic products, we may be unable to achieve or maintain profitability.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

In addition to seeking patent protection for certain aspects of our technology, including platform technology and therapeutic candidates and products, we also consider trade secrets, including confidential and unpatented know-how, important to the maintenance of our competitive position. We protect trade secrets and confidential and unpatented know-how, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to such knowledge, such as our employees, corporate collaborators, outside scientific collaborators, CROs, contract manufacturers, consultants, advisors, and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants obligating them to maintain confidentiality and assign their inventions to us. Despite these efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. We also cannot guarantee that we have entered into such agreements with each party that may have or has had access to our trade secrets or proprietary technology and processes. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive, and time-consuming, and the outcome is unpredictable. In addition, some courts in the United States and certain foreign jurisdictions are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor, our competitive position would be harmed.

We are also subject both in the United States and outside the United States to various regulatory schemes regarding requests for the information we provide to regulatory authorities, which may include, in whole or in part, trade secrets or confidential commercial information. While we are likely to be notified in advance of any disclosure of such information and would likely object to such disclosure, there can be no assurance our challenge to the request would be successful.

We may be in the future subject to claims we or our employees or consultants have wrongfully used or disclosed alleged trade secrets of our employees' or consultants' former employers or their clients. These claims may be costly to defend and if we do not successfully do so, we may be required to pay monetary damages, may be prohibited from using some of our research and development and may lose valuable intellectual property rights or personnel.

Many of our employees were previously employed at universities or biotechnology or pharmaceutical companies, including our current and potential competitors. We may receive correspondence from other companies alleging the improper use or disclosure, and have received, and may in the future receive, correspondence from other companies regarding the use or disclosure, by certain of our employees who have previously been employed elsewhere in our industry, including with our competitors, of their former employer's trade secrets or other proprietary information. Responding to these allegations can be costly and disruptive to our business, even when the allegations are without merit, and can be a distraction to management. We may be subject to claims in the future that our employees have, or we have, inadvertently or otherwise used or disclosed trade secrets or other proprietary information of their former employers. Litigation may be necessary to defend against these claims. If we fail in defending current or future claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, personnel, or the ability to use some of our research and development. A loss of intellectual property, key research personnel, or their work product could hamper our ability to commercialize, or prevent us from commercializing, our therapeutic candidates, which could severely harm our business. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to management.

If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be materially and adversely affected.

Our trademarks or trade names may be challenged, infringed, circumvented, or declared generic or determined to be infringing on other marks. Any trademark litigation could be expensive. We may not be able to protect our rights to these trademarks and trade names or may be forced to stop using these names, which we need for name recognition by potential partners or customers in our markets of interest. If we are unable to establish name recognition based on our trademarks and trade names, we may not be able to compete effectively, and our business may be materially and adversely affected.

Third parties may independently develop similar or superior technology.

There can be no assurance others will not independently develop, or have not already developed, similar or more advanced technologies than our technology or that others will not design around, or have not already designed around, aspects of our technology or our trade secrets developed therefrom. If third parties develop technology similar or superior to our technology, or they successfully design around our current or future technology, our competitive position, business prospects, and results of operations could be materially and adversely affected.

Breaches of our internal computer systems, or those of our contractors, vendors, or consultants, may place our patents or proprietary rights at risk.

The loss of clinical or preclinical data or data from any future clinical trial involving our technology, including therapeutic candidates and products, could result in delays in our development and regulatory filing efforts and significantly increase our costs. In addition, theft or other exposure of data may interfere with our ability to protect our intellectual property, including trade secrets, and other information critical to our operations. We have experienced in the past, and may experience in the future, unauthorized intrusions into our internal computer systems, including portions of our internal computer systems storing information related to our platform technology, therapeutic candidates and products, and we can provide no assurances that certain sensitive and proprietary information relating to one or more of our therapeutic candidates or products has not been, or will not in the future be, compromised. Although we have invested significant resources to enhance the security of our computer systems, there can be no assurances we will not experience additional unauthorized intrusions into our computer systems, or those of our CROs, vendors, contractors, and consultants, that we will successfully detect future unauthorized intrusions in a timely manner, or that future unauthorized intrusions will not result in material adverse effects on our financial condition, reputation, or business prospects. Payments related to the elimination of ransomware may materially affect our financial condition and results of operations.

Certain data breaches must also be reported to affected individuals and the government, and in some cases to the media, under provisions of HIPAA, as amended by HITECH, other U.S. federal and state law, and requirements of non-U.S. jurisdictions, including the European Union Data Protection Directive, and financial penalties may also apply.

Risks Related to Government Regulation

We may be unable to obtain U.S. or foreign regulatory approval and, as a result, may be unable to commercialize our therapeutic candidates.

Our therapeutic candidates are subject to extensive governmental regulations relating to, among other things, research, development, testing, manufacture, quality control, approval, labeling, packaging, promotion, storage, record-keeping, advertising, distribution, sampling, pricing, sales and marketing, safety, post-approval monitoring and reporting, and export and import of drugs. Rigorous preclinical testing and clinical trials and an extensive regulatory approval process are required to be completed successfully in the United States and in many foreign jurisdictions before a new therapeutic can be marketed. Satisfaction of these and other regulatory requirements is costly, time consuming, uncertain, and subject to unanticipated delays. We have not obtained regulatory approval for any therapeutic candidates, and it is possible none of the therapeutic candidates we may develop will obtain the regulatory approvals necessary for us or our collaborators to begin selling them.

We have very limited experience in conducting and managing the clinical trials necessary to obtain regulatory approvals, including approval by the FDA as well as foreign regulatory authorities, such as the EMA. The time required to obtain FDA and foreign regulatory approvals is unpredictable but typically takes many years following the commencement of clinical trials, depending upon the type, complexity, and novelty of the therapeutic candidate, and at the substantial discretion of the regulatory authorities. The standards the FDA and its foreign counterparts use when regulating us are not always applied predictably or uniformly and can change. Any analysis we perform of data from preclinical and clinical activities is subject to confirmation and interpretation by regulatory authorities, who could delay, limit, or prevent regulatory approval. We may also encounter unexpected delays or increased costs due to new government regulations, future legislation or administrative action,

or from changes in the policy of FDA or foreign regulatory authorities during the period of product development, clinical trials, and regulatory review by the FDA or foreign regulatory authorities. It is impossible to predict whether legislative changes will be enacted, or whether FDA or foreign, regulations, guidance, or interpretations will be changed, or what the impact of such changes, if any, may be.

Because the therapeutic candidates we are developing may represent a new class of therapeutics, we are not aware of any definitive policies, practices, or guidelines that the FDA or its foreign counterparts have yet established in relation to these drugs. While we believe the therapeutic candidates we are currently developing are regulated as new biological products under the Public Health Service Act, or PHSA, the FDA could decide to regulate them or other products we may develop as drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA. The lack of policies, practices, or guidelines may hinder or slow review by the FDA or foreign regulatory authorities of any regulatory filings we may submit. Moreover, the FDA or foreign regulatory authorities may respond to these submissions by defining requirements we may not have anticipated. Such responses could lead to significant delays in the clinical development of our therapeutic candidates.

Our therapeutic candidates could fail to receive regulatory approval for many reasons, including the following:

- the FDA or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical trials;
- we may be unable to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that a therapeutic candidate is safe and effective for its proposed indication;
- the results of clinical trials may not meet the level of statistical significance required by the FDA or comparable foreign regulatory authorities for approval;
- we may be unable to demonstrate that a therapeutic candidate's clinical and other benefits outweigh its safety risks;
- the FDA or comparable foreign regulatory authorities may disagree with our interpretation of data from pre-clinical studies or clinical trials;
- the data collected from clinical trials of our therapeutic candidates may not be sufficient to support the submission of a Biologics License Application, or BLA, or other submission or to obtain regulatory approval in the United States, the European Union or elsewhere;
- the FDA or comparable foreign regulatory authorities may fail to approve the manufacturing processes or facilities of third-party manufacturers with which we contract for clinical and commercial supplies; and
- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

Any delay or failure in obtaining required approvals could have a material adverse effect on our ability to generate revenues from the particular therapeutic candidate for which we are seeking approval. The FDA, the EMA and other regulatory authorities have substantial discretion in the approval process, and in determining when or whether regulatory approval will be obtained for any of our therapeutic candidates. Even if we believe the data collected from preclinical and clinical trials of our therapeutic candidates are promising, such data may not be sufficient to support approval by the FDA, the EMA or any other regulatory authority. Furthermore, any regulatory approval to market a product may be subject to limitations on the approved uses for which we may market the product or in the product labeling or be subject to other restrictions. Regulatory authorities also may impose requirements for costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of the therapeutic. In addition, the FDA has the authority to require a REMS plan as part of the approval of a BLA or New Drug Application, or NDA, or after approval, which may impose further requirements or restrictions on the distribution or use of an approved drug or biologic, such as limiting prescribing to certain physicians or medical centers that have undergone specialized training, limiting treatment to patients who meet certain safe-use criteria, and requiring treated patients to enroll in a registry. These limitations and restrictions may limit the size of the market for the therapeutic and affect coverage and reimbursement by third-party payors.

We are also subject to numerous foreign regulatory requirements governing, among other things, the conduct of clinical trials, manufacturing, marketing authorization, pricing, and third-party reimbursement. The foreign regulatory approval process varies among countries and may include all of the risks associated with FDA approval described above as well as risks attributable to the satisfaction of local regulations in foreign jurisdictions. Moreover, the time required to obtain approval may differ from that required to obtain FDA approval. Approval by the FDA does not ensure approval by regulatory authorities outside the U.S. and vice versa.

If we fail to obtain orphan drug designation or obtain or maintain orphan drug exclusivity for certain of our products, our competitors may sell products to treat the same conditions and our revenue may be reduced.

Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is intended to treat a rare disease or condition, defined as a patient population of fewer than 200,000 in the United States, or a patient population greater than 200,000 in the United States where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the United States. In the United States, orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers. In addition, if a therapeutic product with orphan drug designation subsequently receives the first FDA approval for the indication for which it has such designation, the therapeutic product is entitled to orphan product exclusivity, which means the FDA may not approve any other applications to market the same therapeutic product for the same indication for seven years, except in limited circumstances such as a showing of clinical superiority over the product with orphan exclusivity or where the manufacturer is unable to assure sufficient product quantity.

As in the United States, we may apply for designation of a therapeutic candidate as an orphan drug for the treatment of a specific indication in the European Union before the application for marketing authorization is made. In the European Union, the EMA's Committee for Orphan Medicinal Products, grants orphan drug designation to promote the development of products that are intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting not more than five in 10,000 persons in the European Union. Additionally, designation is granted for products intended for the diagnosis, prevention or treatment of a life-threatening, seriously debilitating or serious and chronic condition when, without incentives, it is unlikely that sales of the drug in the European Union would be sufficient to justify the necessary investment in developing the drug or biological product or where there is no satisfactory method of diagnosis, prevention or treatment, or, if such a method exists, the medicine must be of significant benefit to those affected by the condition. Sponsors of orphan drugs in the European Union can enjoy economic and marketing benefits, including reduction of fees or fee waivers and up to ten years of market exclusivity for the approved indication unless another applicant can show its therapeutic product is safer, more effective, or otherwise clinically superior to the orphan-designated therapeutic product. This period may be reduced to six years if the orphan drug designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity.

We plan to seek orphan drug designation from the FDA and the EMA for certain of our product candidates. However, we may never receive such designation. Even if we are able to obtain orphan designation, we may not be the first to obtain marketing approval for any particular orphan indication due to the uncertainties associated with developing pharmaceutical products. In addition, exclusive marketing rights in the United States may be limited if we seek approval for an indication broader than the orphan-designated indication or may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition. Further, even if we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different drugs with different active moieties can be approved for the same condition. Even after an orphan drug is approved, regulatory authorities may subsequently approve the same drug with the same active moiety for the same condition if they conclude that the later drug is safer, more effective, or makes a major contribution to patient care. Orphan drug designation neither shortens the development time or regulatory review time of a product candidate nor gives the product candidate any advantage in the regulatory review or approval process. In addition, orphan drug exclusivity could block the approval of one of our therapeutic candidates if a competitor obtains approval of the same therapeutic product as defined by the FDA before we do, or if our therapeutic candidate is determined to be within the same class as the competitor's therapeutic product for the same indication or disease.

The respective orphan designation and exclusivity frameworks in the United States and in the European Union are subject to change, and any such changes may affect our ability to obtain EU or U.S. orphan designations in the future.

If we or our existing or future collaborators, manufacturers, or service providers fail to comply with healthcare laws and regulations, we or such other parties could be subject to enforcement actions, which could adversely affect our ability to develop, market, and sell our therapeutics and may harm our reputation.

Although we do not currently have any products on the market, once we begin commercializing our therapeutic candidates, if approved, we will be subject to additional healthcare statutory and regulatory requirements and enforcement by the federal, state, and foreign governments of the jurisdictions in which we conduct our business. Healthcare providers, physicians, and third-party payors play a primary role in the recommendation and prescription of any therapeutic candidates for which we obtain marketing approval. Our future arrangements with third-party payors and customers may expose us to broadly applicable fraud, abuse, and other healthcare laws and regulations constraining the business or financial arrangements and relationships through which we market, sell, and distribute the therapeutic candidates for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations include the following:

- the U.S. federal Anti-Kickback Statute, which prohibits, among other things, persons from soliciting, receiving, offering, or providing remuneration, directly or indirectly, to induce either the referral of an individual for a healthcare item or service, or the purchasing or ordering of an item or service, for which payment may be made, in whole or in part, under a federal healthcare program such as Medicare or Medicaid;

- the U.S. federal False Claims Act, which imposes criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, false or fraudulent claims for payment or making a false statement to avoid, decrease, or conceal an obligation to pay money to the federal government. In addition, the government may assert a claim including items and services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act;

- state all-payor fraud laws, which impose criminal and civil liability for executing a scheme to defraud any healthcare benefit program, or knowingly and willfully falsifying, concealing, or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services; similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;

- HIPAA, HITECH, and their implementing regulations, which impose obligations on certain covered entity healthcare providers, health plans, and healthcare clearinghouses as well as their business associates performing certain services involving the use or disclosure of individually identifiable health information, including mandatory contractual terms, with respect to safeguarding the privacy, security, and transmission of individually identifiable health information, and require notification to affected individuals and regulatory authorities of certain breaches of security of individually identifiable health information;

- the federal Physician Payment Sunshine Act and its implementing regulations, also referred to as "Open Payments," issued under the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or ACA, and any subsequent amending legislation or executive actions, which require manufacturers of pharmaceutical and biological drugs reimbursable under Medicare, Medicaid, and Children's Health Insurance Programs to report to the Department of Health and Human Services all consulting fees, travel reimbursements, research grants, and other payments, transfers of value or gifts made to physicians and teaching hospitals with limited exceptions; and

- analogous state laws and regulations, such as, state anti-kickback and false claims laws potentially applicable to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers; and some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring drug manufacturers to report information related to payments to physicians and other healthcare providers or marketing expenditures, and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Ensuring our future business arrangements with third-parties comply with applicable healthcare laws and regulations could involve substantial costs. If our operations are found to be in violation of any such requirements, we may be subject to penalties, including civil or criminal penalties, monetary damages, the curtailment or restructuring of our operations, or exclusion from participation in government contracting, healthcare reimbursement, or other government programs, including Medicare and Medicaid, any of which could adversely affect our financial results. Although effective compliance programs can mitigate the risk of investigation and prosecution for violations of these laws, these risks cannot be entirely eliminated. Any action against us for an alleged or suspected violation could cause our company to incur significant legal expenses and could divert our management's attention from the operation of our business, even if our defense is successful. In addition, achieving and sustaining compliance with applicable laws and regulations may be costly to us in terms of money, time, and resources.

If we or our current or future collaborators, manufacturers, or service providers fail to comply with applicable federal, state, or foreign laws or regulations, we could be subject to enforcement actions, which could affect our ability to develop, market, and sell our therapeutics successfully and could harm our reputation and lead to reduced acceptance of our therapeutics by the market. These enforcement actions include, among others:

- adverse regulatory inspection findings;

- warning or untitled letters;

- voluntary product recalls with public notification or medical product safety alerts to healthcare professionals;

- restrictions on, or prohibitions against, marketing our therapeutics;

- restrictions on, or prohibitions against, importation or exportation of our therapeutics;
- suspension of review or refusal to approve pending applications or supplements to approved applications;
- exclusion from participation in government-funded healthcare programs;
- exclusion from eligibility for the award of government contracts for our therapeutics;
- FDA debarment;
- suspension or withdrawal of therapeutic approvals;
- seizures or administrative detention of therapeutics;
- injunctions; and
- restitution, disgorgement of profits, or civil and criminal penalties and fines.

Enacted and future legislation may increase the difficulty and cost for us to obtain marketing approval of our therapeutic candidates.

The policies of the FDA or similar regulatory authorities may change, and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. For example, in 2016, the 21st Century Cures Act, or Cures Act, was signed into law. The Cures Act, among other things, is intended to modernize the regulation of drugs and biologics and spur innovation, but it is still being implemented and its ultimate implementation is unclear. If we or our collaborators are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we or our collaborators are not able to maintain regulatory compliance, our therapeutic candidates may not obtain or maintain regulatory approval, and we may not achieve or sustain profitability, which would adversely affect our business.

We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. For example, certain policies of the Trump administration may impact our business and industry. Namely, the Trump administration has taken several executive actions, including the issuance of a number of Executive Orders, that could impose significant burdens on, or otherwise materially delay, FDA's ability to engage in routine regulatory and oversight activities such as implementing statutes through rulemaking, issuance of guidance, and review and approval of marketing applications. It is difficult to predict how these requirements will be implemented, and the extent to which they will impact the FDA's ability to exercise its regulatory authority. If these executive actions impose constraints on FDA's ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted.

Any therapeutics we develop may become subject to unfavorable pricing regulations, third-party coverage and reimbursement practices, or healthcare reform initiatives, thereby harming our business.

The regulations governing marketing approvals, pricing, coverage, and reimbursement for new drugs and biologics vary widely from country to country. Many countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. Although we intend to monitor these regulations, our programs are currently in the early stages of development and we will not be able to assess the impact of price regulations for a number of years. As a result, we might obtain regulatory approval for a product in a particular country but then be subject to price regulations delaying our commercial launch of the product and negatively impacting the revenues we are able to generate from the sale of the product in that country.

Our ability to commercialize any therapeutics successfully also will depend in part on the extent to which coverage and reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers, and other organizations. However, there may be significant delays in obtaining coverage for newly-approved therapeutics. Moreover, eligibility for coverage does not necessarily signify a therapeutic will be reimbursed in all cases or at a rate covering our costs, including research, development, manufacture, sale, and distribution costs. Also, interim payments for new therapeutics, if applicable, may be insufficient to cover our costs and may not be made permanent. Thus, even if we succeed in bringing one or more therapeutics to the market, these products may not be considered cost-effective, and the amount reimbursed for any of them may be insufficient to allow us to sell them on a competitive basis. Because our programs are in the early stages of development, we are unable at this time to determine their cost effectiveness, coverage prospects, potential compendia listings, or the likely level or method of reimbursement, if covered. It is equally difficult for us to predict how Medicare coverage and reimbursement policies will be applied to our products in the future, and coverage and reimbursement under different federal healthcare programs are not always consistent. Medicare reimbursement rates may also reflect budgetary constraints placed on the Medicare program.

Third-party payors often rely upon Medicare coverage policies and payment limitations in setting their own reimbursement rates. These coverage policies and limitations may rely, in part, on compendia listings for approved therapeutics. Our inability to promptly obtain relevant compendia listings, coverage, and adequate reimbursement from both government-funded and private payors for new therapeutics we develop and for which we obtain regulatory approval could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products, and our financial condition.

We believe the efforts of governments and third-party payors to contain or reduce the cost of healthcare, and legislative and regulatory proposals to broaden the availability of healthcare, will continue to affect the business and financial condition of pharmaceutical and biopharmaceutical companies. A number of legislative and regulatory changes in the healthcare system in the United States and other major healthcare markets have been proposed, and such efforts have expanded substantially in recent years. These developments could, directly or indirectly, affect our ability to sell our products, if approved, at a favorable price. In addition, third-party payors who reimburse patients or healthcare providers, such as government and private insurance plans, are seeking greater upfront discounts, additional rebates, and other concessions to reduce the prices for therapeutics. If the price we are able to charge for any therapeutics we develop, or the reimbursement provided for such products, is inadequate, our return on investment could be adversely affected.

Pursuant to health reform legislation and related initiatives, the Centers for Medicare and Medicaid Services, or CMS, are working with various healthcare providers to develop, refine, and implement Accountable Care Organizations, or ACOs, and other innovative models of care for Medicare and Medicaid beneficiaries, including the Bundled Payments for Care Improvement Initiative, the Comprehensive Primary Care Initiative, the Duals Demonstration, and other models. The continued development and expansion of ACOs and other innovative models of care will have an uncertain impact on any future reimbursement we may receive for approved therapeutics administered by such organizations.

In addition, in recent years, the U.S. Congress has enacted various laws seeking to reduce the federal debt level and contain healthcare expenditures. For example, as a result of the Budget Control Act of 2011 and the Bipartisan Budget Act of 2015, an annual 2% reduction to Medicare payments that took effect in 2013 has been extended through 2025. These across-the-board spending cuts could adversely affect our future revenues, earnings, and cash flows.

From time to time, legislation is drafted, introduced, and passed in Congress that could significantly change the statutory provisions governing coverage, reimbursement, and marketing of products regulated by CMS or other government agencies. In addition to new legislation, CMS coverage and reimbursement policies are often revised or interpreted in ways that may significantly affect our business and our products. In particular, we expect the Administration and Congress will seek to modify, repeal, or otherwise invalidate all, or certain provisions of, U.S. healthcare legislation. A number of additional executive orders have been issued affecting, or potentially affecting, the ACA and other aspects of the healthcare market in the United States. There is a high degree of uncertainty with respect to the impact President Trump's Administration and Congress may have, and any changes will likely take time to unfold. Such reforms could have an adverse effect on anticipated revenues from therapeutic candidates we may successfully develop and for which we may obtain regulatory approval and may affect our overall financial condition and ability to develop therapeutic candidates. However, we cannot predict the ultimate content, timing, or effect of any healthcare reform legislation or executive orders or the impact of potential legislation and executive orders on us.

The healthcare industry is heavily regulated in the U.S. at the federal, state, and local levels, and our failure to comply with applicable requirements may subject us to penalties and negatively affect our financial condition.

As a healthcare company, our operations, clinical trial activities, and interactions with healthcare providers will be subject to extensive regulation in the United States, particularly if we receive FDA approval for any of our products in the future. For example, if we receive FDA approval for a therapeutic for which reimbursement is available under a federal healthcare program, it would be subject to a variety of federal laws and regulations, including those prohibiting the filing of false or improper claims for payment by federal healthcare programs, prohibiting unlawful inducements for the referral of business reimbursable by federal healthcare programs, and requiring disclosure of certain payments or other transfers of value made to U.S.-licensed physicians and teaching hospitals. We are not able to predict how government authorities will interpret these laws. They may challenge our practices and activities under one or more of these laws. If our past or present operations are found to be in violation of any of these laws, we could be subject to civil and criminal penalties, which could hurt our business, operations, and financial condition.

Similarly, some state laws prohibit, among other offenses, knowingly and willfully executing a scheme to defraud any health care benefit program, including private payors, or falsifying, concealing, or covering up a material fact or making any materially false, fictitious, or fraudulent statement in connection with the delivery of or payment for items or services under a health care benefit program. We may also be subject to the privacy and security provisions of HIPAA, as amended by HITECH, which restricts the use and disclosure of patient-identifiable health information, mandates the adoption of standards relating to

the privacy and security of patient-identifiable health information, and requires the reporting of certain security breaches to healthcare provider customers with respect to such information. Additionally, many states have enacted similar laws imposing more stringent requirements on entities like us. Failure to comply with applicable laws and regulations could result in substantial penalties and adversely affect our financial condition and results of operations.

Our ability to obtain services, reimbursement, or funding from the federal government may be impacted by possible reductions in federal spending.

The U.S. federal budget remains in flux and could, among other things, cut Medicare payments to providers. The Medicare program is frequently mentioned as a target for spending cuts. The full impact on our business of any future cuts in Medicare or other programs is uncertain. In addition, we cannot predict any impact President Trump's administration and Congress may have on the federal budget. If federal spending is reduced, anticipated budgetary shortfalls may also impact the ability of relevant agencies such as the FDA or the National Institutes of Health to continue to function at current levels. Amounts allocated to federal grants and contracts may be reduced or eliminated. These reductions may also impact the ability of relevant agencies to timely review and approve drug research and development, manufacturing, and marketing activities, which may delay our ability to develop, market, and sell any therapeutics we may develop.

If any of our therapeutic candidates receives marketing approval and we or others later identify undesirable side effects caused by the therapeutic product, our ability to market and derive revenue from the therapeutic products could be compromised.

In the event any of our therapeutic candidates receive regulatory approval and we or others identify undesirable side effects, adverse events, or other problems caused by one of our therapeutics, any of the following adverse events could occur, which could result in the loss of significant revenue to us and materially and adversely affect our results of operations and business:

- regulatory authorities may withdraw their approval of the product and require us to take the product off the market or seize the product;
- we may need to recall the therapeutic or change the way the therapeutic is administered to patients;
- additional restrictions may be imposed on the marketing and promotion of the particular therapeutic or the manufacturing processes for the therapeutic or any component thereof;
- we may not be able to secure or maintain adequate coverage and reimbursement for our proprietary therapeutic products from government (including U.S. federal health care programs) and private payors;
- we may lose or see adverse alterations to compendia listings or treatment protocols specified by accountable care organizations;
- we may be subject to fines, restitution, or disgorgement of profits or revenues, injunctions, or the imposition of civil penalties or criminal prosecution;
- regulatory authorities may require the addition of labeling statements, such as a "black box" warning, or equivalent, or a contraindication;
- regulatory authorities may require us to implement a REMS plan, or to conduct post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of the product;
- we may be required to create a Medication Guide outlining the risks of such side effects for distribution to patients;
- we could be sued and held liable for harm caused to patients;
- the therapeutic may become less competitive; and
- our reputation may suffer.

Our therapeutic candidates for which we intend to seek approval as biologic products may face competition sooner than anticipated.

The Patient Protection and Affordable Care Act, signed into law in 2010, includes a subtitle called the Biologics Price Competition and Innovation Act of 2009, or BPCIA, which created an abbreviated approval pathway for biological products that are biosimilar to or interchangeable with an FDA-licensed reference biological product. Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date that the reference product was first

licensed by the FDA. In addition, the approval of a biosimilar product may not be made effective by the FDA until 12 years from the date on which the reference product was first licensed. During this 12-year period of exclusivity, another company may still market a competing version of the reference product if the FDA approves a full BLA for the competing product containing the sponsor's own pre-clinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of their product. The law is complex and is still being interpreted and implemented by the FDA. As a result, its ultimate impact, implementation, and meaning are subject to uncertainty. While it is uncertain when such processes intended to implement BPCIA may be fully adopted by the FDA, any such processes could have a material adverse effect on the future commercial prospects for our biological products.

We believe that any of our therapeutic candidates approved as a biological product under a BLA should qualify for the 12-year period of exclusivity. However, there is a risk that this exclusivity could be shortened due to congressional action or otherwise, or that the FDA will not consider our therapeutic candidates to be reference products for competing products, potentially creating the opportunity for generic competition sooner than anticipated. Other aspects of the BPCIA, some of which may impact the BPCIA exclusivity provisions, have also been the subject of recent litigation. Moreover, the extent to which a biosimilar, once approved, will be substituted for any one of our reference products in a way that is similar to traditional generic substitution for non-biological products is not yet clear, and will depend on a number of marketplace and regulatory factors that are still developing.

Significant developments stemming from the United Kingdom's recent referendum on membership in the European Union could have a material adverse effect on us.

In June 2016, the United Kingdom held a referendum and voted in favor of leaving the European Union, and in March 2017, the government of the United Kingdom formally initiated the withdrawal process. This has created political and economic uncertainty, particularly in the United Kingdom and the European Union. Any business we conduct, now and in the future, in the United Kingdom, the European Union, and worldwide could be affected during this period of uncertainty, and perhaps longer, by the impact of the United Kingdom's referendum. There are many ways in which our business could be affected, only some of which we can identify as of the date of this filing.

The decision of the United Kingdom to withdraw from the European Union has caused and, along with events that could occur in the future as a consequence of the United Kingdom's withdrawal, may continue to cause significant volatility in global financial markets, including in global currency and debt markets. This volatility could cause a slowdown in economic activity in the United Kingdom, Europe, or globally, which could adversely affect our operating results and growth prospects. In addition, our business could be negatively affected by new trade agreements or data transfer agreements between the United Kingdom and other countries, including the United States, and by the possible imposition of trade or other regulatory barriers in the United Kingdom.

It is currently unknown how regulations affecting clinical trials, the approval of our future products, and the sale of these products will be affected by this referendum either in the United Kingdom or elsewhere in Europe.

These possible negative impacts, and others resulting from the United Kingdom's actual or threatened withdrawal from the EU, may adversely affect our operating results and growth prospects.

Risks Related to Ownership of Our Common Stock

Our stock price may be volatile, and an active, liquid, and orderly trading market may not develop for our common stock. As a result, stockholders may not be able to resell shares at or above their purchase price.

Although our common stock is listed on Nasdaq, an active trading market for our common stock may not develop or, if it develops, may not be sustained. The lack of an active market may impair the ability of our stockholders to sell their shares at the time they wish to sell them or at a price that they consider reasonable, which may reduce the fair market value of their shares. Further, an inactive market may also impair our ability to raise capital by selling our common stock should we determine additional funding is required.

The market price of our common stock could be subject to significant fluctuations. Market prices for securities of early-stage pharmaceutical, biotechnology, and other life sciences companies have historically been particularly volatile. Some of the factors that may cause the market price of our common stock to fluctuate include:

- our ability to obtain regulatory approvals for product candidates, and delays or failures to obtain such approvals;
- the failure of any of our product candidates, if approved, to achieve commercial success;
- issues in manufacturing our approved products, if any, or product candidates;

- the results of current, and any future, preclinical or clinical trials of our product candidates;
- the entry into, or termination of, key agreements, including key licensing, collaboration or acquisition agreements;
- the initiation or material developments in, or conclusion of, litigation to enforce or defend any of our intellectual property rights or defend against the intellectual property rights of others;
- announcements by commercial partners or competitors of new commercial products, clinical progress (or the lack thereof), significant contracts, commercial relationships, or capital commitments;
- adverse publicity relating to our markets, including with respect to other products and potential products in such markets;
- adverse publicity about our company, employees, therapeutic candidates, and/or therapeutic products in the media or on social media;
- the introduction of technological innovations or new therapies competing with our potential products;
- the loss of key employees;
- changes in estimates or recommendations by securities analysts, if any, who cover our common stock;
- general and industry-specific economic conditions potentially affecting our research and development expenditures;
- changes in the structure of health care payment systems;
- unanticipated serious safety concerns related to the use of any of our product candidates;
- failure to meet or exceed financial and development projections we may provide to the public;
- failure to meet or exceed the financial and development projections of the investment community;
- the perception of the pharmaceutical industry by the public, legislators, regulators, and the investment community;
- adverse regulatory decisions;
- disputes or other developments relating to proprietary rights, including patents, litigation matters, and our ability to obtain patent protection for our technologies;
- commencement of, or our involvement in, litigation;
- sales of our common stock by us or our stockholders in the future;
- trading volume of our common stock;
- period-to-period fluctuations in our financial results; and
- the other factors described in this "Risk Factors" section.

Moreover, the stock markets in general have experienced substantial volatility that has often been unrelated to the operating performance of individual companies or the biotechnology sector. These broad market fluctuations may also adversely affect the trading price of our common stock.

In the past, following periods of volatility in the market price of a company's securities, stockholders have often instituted class action securities litigation against those companies. Such litigation, if instituted, could result in substantial costs and diversion of management attention and resources, which could significantly harm our business and reputation.

Our officers and directors, and their respective affiliates, have a controlling influence over our business affairs and may make business decisions with which stockholders disagree and which may adversely affect the value of their investment.

Our executive officers and directors together with their respective affiliates, beneficially own approximately 76% of our common stock as of June 30, 2019. As a result, if some of these persons or entities act together, they will have the ability to exercise significant influence over matters submitted to the stockholders for approval, including the election of directors, amendments to the certificate of incorporation and bylaws and the approval of any strategic transaction requiring the approval of the stockholders. These actions may be taken even if they are opposed by other stockholders. This concentration of ownership may also have the effect of delaying or preventing a change of control of our company or discouraging others from making tender offers for our shares, which could prevent our stockholders from receiving a premium for their shares. Some of these persons or entities who make up our principal stockholders may have interests different from other stockholders. The

significant concentration of stock ownership may adversely affect the trading price of our common stock due to investors' perception that conflicts of interest may exist or arise.

Future sales, or the perception of future sales, of a substantial amount of our common stock could depress the trading price of our common stock.

Our stock price could decline as a result of sales of a large number of shares of our common stock or the perception that these sales could occur. These sales, or the possibility that these sales may occur, also might make it more difficult for us to sell equity securities in the future at a time and at a price that we deem appropriate.

For example, in connection with our January 2019 private placement, we entered into a registration rights agreement with the private placement investors that required us to prepare and file a registration statement on the date on which we filed our Annual Report on Form 10-K. The resale registration statement was declared effective by the SEC on April 4, 2019 and permits the resale by the private placement investors of approximately 4.7 million shares of our common stock as well as approximately 1.8 million shares of common stock issuable upon the exercise of warrants issued in the private placement. The shares subject to outstanding options and warrants, of which options and warrants to purchase 1,234,127 shares and 1,854,316 shares, respectively, were exercisable as of June 30, 2019, and the shares reserved for future issuance under our equity incentive plans will become available for sale immediately upon the exercise of such options.

We also register the offer and sale of all shares of common stock that we may issue under our equity incentive plans. Once we register the offer and sale of shares for the holders of registration rights and option holders, they can be freely sold in the public market upon issuance, subject to any related lock-up agreements or applicable securities laws.

In addition, in the future, we may issue additional shares of common stock or other equity or debt securities convertible into common stock in connection with a financing, acquisition, litigation settlement, employee arrangements or otherwise. Any such future issuance, including any issuances pursuant to our "at the market" equity offering program, could result in substantial dilution to our existing stockholders and could cause our stock price to decline.

We will have broad discretion over the use of the proceeds to us from our financing activities and may apply the proceeds to uses that do not improve our operating results or the value of your securities.

We will have broad discretion to use the net proceeds from our January 2019 private placement, and investors will be relying solely on the judgment of our board of directors and management regarding the application of these proceeds. Although we expect to use the net proceeds from our January 2019 private placement for general corporate purposes and to advance the development of our product candidates, we have not allocated these net proceeds for specific purposes. Investors will not have the opportunity, as part of their investment decision, to assess whether the proceeds are being used appropriately.

The JOBS Act allows us to postpone the date by which we must comply with certain laws and regulations intended to protect investors and to reduce the amount of information we provide in our reports filed with the SEC. We cannot be certain if this reduced disclosure will make our common stock less attractive to investors.

The JOBS Act is intended to reduce the regulatory burden on "emerging growth companies." As defined in the JOBS Act, we qualify as an "emerging growth company" and could remain an "emerging growth company" until as late as December 31, 2020. For so long as we are an "emerging growth company," we will, among other things:

- not be required to comply with the auditor attestation requirements of Section 404(b) of Sarbanes-Oxley;
- not be required to hold a nonbinding advisory stockholder vote on executive compensation pursuant to Section 14A of the Securities Exchange Act of 1934, as amended, or the Exchange Act;
- not be required to seek stockholder approval of any golden parachute payments not previously approved pursuant to Section 14A of the Exchange Act;
- be exempt from any rule adopted by the Public Company Accounting Oversight Board, requiring mandatory audit firm rotation or a supplemental auditor discussion and analysis; and
- be subject to reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements.

We have previously decided to opt out of an extended transition period under the JOBS Act that permits an emerging growth company to delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. Our decision is irrevocable. As a result, we will adopt new or revised accounting standards on the relevant dates on which adoption of such standards is required for other companies.

Furthermore, if we take advantage of some or all of the reduced disclosure requirements above, investors may find our common stock less attractive, which may result in a less active trading market for our common stock and greater stock price volatility.

If we fail to maintain proper and effective internal controls, our ability to produce accurate financial statements on a timely basis could be impaired.

We are subject to the reporting requirements of the Exchange Act, the Sarbanes-Oxley Act and the rules and regulations of The Nasdaq Stock Market LLC. The Sarbanes-Oxley Act requires, among other things, that we maintain effective disclosure controls and procedures and internal control over financial reporting. We must perform system and process evaluation and testing of our internal control over financial reporting to allow management to report on the effectiveness of our internal controls over financial reporting in our Annual Report on Form 10-K filing for that year, as required by Section 404 of the Sarbanes-Oxley Act.

We may discover weaknesses in our system of internal financial and accounting controls and procedures that could result in a material misstatement of our financial statements. Our internal control over financial reporting will not prevent or detect all errors and all fraud. An internal control system, no matter how well designed and operated, can provide only reasonable, not absolute, assurance that the internal control system's objectives will be met. Because of the inherent limitations in all internal control systems, no evaluation of internal controls can provide absolute assurance that misstatements due to error or fraud will not occur or that all internal control issues and instances of fraud will be detected.

If we are not able to comply with the requirements of Section 404 of the Sarbanes-Oxley Act, or if we are unable to maintain proper and effective internal controls, we may not be able to produce timely and accurate financial statements. If that were to happen, the market price of our common stock could decline and we could be subject to sanctions or investigations by The Nasdaq Stock Market LLC, the SEC, or other regulatory authorities.

Our disclosure controls and procedures may not prevent or detect all errors or acts of fraud.

Our disclosure controls and procedures are designed to reasonably ensure that information required to be disclosed by us in reports we file or submits under the Exchange Act is accumulated and communicated to management and recorded, processed, summarized and reported within the time periods specified in the rules and forms of the SEC. We believe that any disclosure controls and procedures as well as internal controls and procedures, no matter how well-conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are and will be met. These inherent limitations include the realities that judgments in decision-making can be faulty and that breakdowns can occur because of simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by an unauthorized override of the controls. Accordingly, because of the inherent limitations in our control system, misstatements due to error or fraud may occur and not be detected.

We will continue to incur costs and demands upon management as a result of complying with the laws and regulations affecting public companies.

We will incur significant legal, accounting, and other expenses associated with public company reporting requirements. We will also incur costs associated with corporate governance requirements, including requirements under the Sarbanes-Oxley Act, as well as new rules implemented by the SEC and The Nasdaq Stock Market LLC. Although the JOBS Act may for a limited period of time somewhat lessen the cost of complying with these additional regulatory and other requirements, we nonetheless expect that these rules and regulations will increase our legal and financial compliance costs and to make some activities more time-consuming and costlier. For example, our management team consists in part of the executive officers of Alpine prior to the merger, some of whom may not have previously managed and operated a public company. These executive officers and other personnel will need to devote substantial time to gaining expertise regarding operations as a public company and compliance with applicable laws and regulations. These rules and regulations may also make it difficult and expensive for us to obtain directors and officer's liability insurance. As a result, it may be more difficult for us to attract and retain qualified individuals to serve on our board of directors or as executive officers of our company, which may adversely affect investor confidence in us and could cause our business or stock price to suffer.

Anti-takeover provisions in our charter documents and under Delaware or Washington law could discourage, delay or prevent a change in control of our company, limit attempts by our stockholders to replace or remove our current management and may affect the trading price of our common stock.

Our corporate documents contain provisions that may delay or discourage transactions involving an actual or potential change in our control or change in our management, including transactions in which stockholders might otherwise receive a premium for their shares, or transactions that our stockholders might otherwise deem to be in their best interests. Therefore, these provisions could adversely affect the price of our stock. Among other things, our certificate of incorporation and bylaws:

- stagger the terms of our board of directors and require 66 and 2/3% stockholder voting to remove directors, who may only be removed for cause;
- provide that the authorized number of directors may be changed only by resolution of the board of directors;
- provide that all vacancies, including newly-created directorships, may, except as otherwise required by law, be filled by the affirmative vote of a majority of directors then in office, even if less than a quorum;
- authorize our board of directors to issue "blank check" preferred stock and to determine the rights and preferences of those shares, which may be senior to our common stock, without prior stockholder approval;
- establish advance notice requirements for nominating directors and proposing matters to be voted on by stockholders at stockholders' meetings;
- prohibit our stockholders from calling a special meeting and prohibit stockholders from acting by written consent;
- require 66 and 2/3% stockholder voting to effect certain amendments to our certificate of incorporation and bylaws; and
- prohibit cumulative voting in the election of directors, which limits the ability of minority stockholders to elect director candidates.

In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which generally prohibits a Delaware corporation from engaging in any of a broad range of business combinations with any "interested" stockholder for a period of three years following the date on which the stockholder became an "interested" stockholder. Likewise, because our principal executive offices are located in Washington, the anti-takeover provisions of the Washington Business Corporation Act may apply to us under certain circumstances now or in the future. These provisions prohibit a "target corporation" from engaging in any of a broad range of business combinations with any stockholder constituting an "acquiring person" for a period of five years following the date on which the stockholder became an "acquiring person." These provisions could discourage, delay or prevent a transaction involving a change in control of our company. These provisions could also discourage proxy contests and make it more difficult for stockholders to elect directors of their choosing and cause us to take other corporate actions our stockholders desire.

Claims for indemnification by our directors and officers may reduce our available funds to satisfy successful third-party claims against us and may reduce the amount of available cash.

Our amended and restated certificate of incorporation provides that we will indemnify our directors to the fullest extent permitted by Delaware law.

In addition, as permitted by Section 145 of the DGCL, our amended and restated bylaws and our indemnification agreements that we have entered into with our directors and officers provide that:

- we will indemnify our directors and officers for serving us in those capacities or for serving other business enterprises at our request, to the fullest extent permitted by Delaware law. Delaware law provides that a corporation may indemnify such person if such person acted in good faith and in a manner such person reasonably believed to be in or not opposed to the best interests of the corporation and, with respect to any criminal proceeding, had no reasonable cause to believe such person's conduct was unlawful.
- we may, in our discretion, indemnify other employees and agents in those circumstances where indemnification is permitted by applicable law.
- we are required to advance expenses, as incurred, to our directors and officers in connection with defending a proceeding, except that such directors or officers shall undertake to repay such advances if it is ultimately determined that such person is not entitled to indemnification.
- we will not be obligated pursuant to our amended and restated bylaws to indemnify any director or officer in connection with any proceeding (or part thereof) initiated by such person unless the proceeding was authorized in

the specific case by our board of directors or such indemnification is required to be made pursuant to our amended and restated bylaws.

- the rights conferred in our amended and restated bylaws are not exclusive, and we are authorized to enter into indemnification agreements with our directors, officers, employees and agents and to obtain insurance to indemnify such persons.

- we may not retroactively amend our amended and restated bylaw provisions to reduce our indemnification obligations to our directors or officers.

As a result, if we are required to indemnify one or more of our directors or officers, it may reduce our available funds to satisfy successful third-party claims against us, may reduce the amount of available cash and may have a material adverse effect on our business and financial condition.

Our amended and restated certificate of incorporation designates the Court of Chancery of the State of Delaware as the sole and exclusive forum for certain types of actions and proceedings that may be initiated by our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers, employees or agents.

Our amended and restated certificate of incorporation provides that, unless we consent in writing to an alternative forum, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for any derivative action or proceeding brought on our behalf, any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers, employees or agents to us or our stockholders, any action asserting a claim arising pursuant to any provision of the DGCL, our amended and restated certificate of incorporation or our amended and restated bylaws or any action asserting a claim that is governed by the internal affairs doctrine, in each case subject to the Court of Chancery having personal jurisdiction over the indispensable parties named as defendants therein and the claim not being one which is vested in the exclusive jurisdiction of a court or forum other than the Court of Chancery or for which the Court of Chancery does not have subject matter jurisdiction. Any person purchasing or otherwise acquiring any interest in any shares of our common stock shall be deemed to have notice of and to have consented to this provision of our amended and restated certificate of incorporation. This choice of forum provision may limit our stockholders' ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers, employees or agents, which may discourage such lawsuits against us and our directors, officers, employees and agents even though an action, if successful, might benefit our stockholders. Stockholders who do bring a claim in the Court of Chancery could face additional litigation costs in pursuing any such claim, particularly if they do not reside in or near Delaware. The Court of Chancery may also reach different judgments or results than would other courts, including courts where a stockholder considering an action may be located or would otherwise choose to bring the action, and such judgments or results may be more favorable to us than to our stockholders. Alternatively, if a court were to find this provision of our amended and restated certificate of incorporation inapplicable to, or unenforceable in respect of, one or more of the specified types of actions or proceedings, we may incur additional costs associated with resolving such matters in other jurisdictions, which could have a material adverse effect on our business, financial condition or results of operations.

We do not expect to pay any dividends on our common stock for the foreseeable future.

We currently expect to retain all future earnings, if any, for future operations and expansion, and have no current plans to pay any cash dividends to holders of our common stock for the foreseeable future. Any decision to declare and pay dividends in the future will be made at the discretion of our board of directors and will depend on, among other things, our results of operations, financial condition, cash requirements, contractual restrictions and other factors that our board of directors may deem relevant. As a result, stockholders may not receive any return on an investment in our common stock unless stockholders sell our common stock for a price greater than that which they paid for it.

If equity research analysts do not publish research or reports, or publish unfavorable research or reports, about us, our business or our market, our stock price and trading volume could decline.

The trading market for our common stock will be influenced by the research and reports that equity research analysts publish about us and our business. Equity research analysts may elect not to provide research coverage of our common stock or discontinue existing research coverage, and such lack of research coverage may adversely affect the market price of our common stock. We do not have any control over the analysts, or the content and opinions included in their reports. The price of our common stock could decline if one or more equity research analysts downgrade our stock or issue other unfavorable commentary or research. If one or more equity research analysts ceases coverage of us or fails to publish reports regularly, demand for our common stock could decrease, which in turn could cause our stock price or trading volume to decline.

Nasdaq may delist our common stock from its exchange, which could limit investors' ability to make transactions in our securities and subject us to additional trading restrictions.

Our common shares are listed on Nasdaq under the trading symbol "ALPN." Our securities may fail to meet the continued listing requirements to be listed on Nasdaq. If Nasdaq delists our common shares from trading on its exchange, we could face significant material adverse consequences, including:

- significant impairment of the liquidity for our common stock, which may substantially decrease the market price of our common stock;
- a limited availability of market quotations for our securities;
- a determination that our common stock qualifies as a "penny stock" which will require brokers trading in our common stock to adhere to more stringent rules and possibly resulting in a reduced level of trading activity in the secondary trading market for our common stock;
- a limited amount of news and analyst coverage for our company; and
- a decreased ability to issue additional securities or obtain additional financing in the future.

Item 2. Unregistered Sales of Equity Securities and Use of Proceeds

None.

Item 3. Defaults Upon Senior Securities

None.

Item 4. Mine Safety Disclosures

Not applicable.

Item 5. Other Information

None.

Item 6. Exhibits

Exhibit Number	Exhibit Description	Incorporation by Reference				Filed Herewith
		Form	File No.	Exhibit	Filing Date	
10.1+	Separation Agreement, dated April 24, 2019, by and between the Company and Mark Litton					X
31.1	Certification of Principal Executive Officer Required Under Rule 13a-14(a) and 15d-14(a) of the Securities Exchange Act of 1934, as amended					X
31.2	Certification of Principal Financial Officer Required Under Rule 13a-14(a) and 15d-14(a) of the Securities Exchange Act of 1934, as amended					X
32.1*	Certification of Principal Executive Officer Required Under Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended, and 18 U.S.C. §1350					X
32.2*	Certification of Principal Financial Officer Required Under Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended, and 18 U.S.C. §1350					X
101.INS	XBRL Instance Document					X
101.SCH	XBRL Taxonomy Extension Schema Linkbase Document					X
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document					X
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document					X
101.LAB	XBRL Taxonomy Extension Label Linkbase Document					X
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document					X

* The certifications attached as Exhibits 32.1 and 32.2 that accompany this Quarterly Report on Form 10-Q are not deemed filed with the Securities and Exchange Commission and are not to be incorporated by reference into any filing of Alpine Immune Sciences, Inc. under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, whether made before or after the date of this Form 10-Q, irrespective of any general incorporation language contained in such filing.

\+ Indicates a management contract or a compensatory plan, contract or arrangement.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

ALPINE IMMUNE SCIENCES, INC.

Date: August 13, 2019

By: /s/ Mitchell Gold

Name: Mitchell Gold

Title: Executive Chairman and Chief Executive Officer

ALPINE IMMUNE SCIENCES, INC.

Date: August 13, 2019

By: /s/ Paul Rickey

Name: Paul Rickey

Title: Senior Vice President and Chief Financial Officer

Exhibit 10.1

SEPARATION AGREEMENT AND RELEASE

This Separation Agreement and Release ("Agreement") is made by and between Mark Litton ("Employee") and Alpine Immune Sciences, Inc. (the "Company") (collectively referred to as the "Parties" or individually referred to as a "Party").

WHEREAS, Employee was employed at-will by the Company pursuant to that certain Executive Employment Agreement between the Company and Employee dated August 6, 2018 (the "Employment Agreement");

WHEREAS, Employee signed an At-Will Employment, Confidential Information, Invention Assignment, and Arbitration Agreement with the Company on August 6, 2018 (the "Confidentiality Agreement");

WHEREAS, on August 6, 2018, Employee and the Company entered into a Participation Agreement (the "Participation Agreement") under the Company's Change of Control and Severance Policy (the "Severance Policy");

WHEREAS, the Company and Employee have entered into (i) two Stock Option Agreements, dated as of August 6, 2018 and February 6, 2019, granting Employee the option to purchase shares of the Company's common stock subject to the terms and conditions of the Stock Option Agreements and the Company's 2018 Equity Incentive Plan and (ii) the Stand-Alone Inducement Stock Option Grant, dated as of August 6, 2018, granting Employee the option to purchase shares of the Company's common stock subject to the terms and conditions of the Stand-Alone Inducement Stock Option Grant (collectively the "Stock Agreements");

WHEREAS, Employee separated from employment with the Company effective April 16, 2019 (the "Separation Date");

WHEREAS, Employee's separation from employment with the Company constitutes a "Non-COC Qualified Termination" under the Severance Policy;

WHEREAS, this Agreement is the "Release" described in the Severance Policy; and

WHEREAS, the Parties wish to resolve any and all disputes, claims, complaints, grievances, charges, actions, petitions, and demands that the Employee may have against the Company and any of the Releasees as defined below, including, but not limited to, any and all claims arising out of or in any way related to Employee's employment with or separation from the Company;

NOW, THEREFORE, in consideration of the mutual promises made herein, the Company and Employee hereby agree as follows:

COVENANTS

1. Consideration. In consideration of Employee's execution of this Agreement and Employee's fulfillment of all of its terms and conditions, and provided that Employee does not revoke the Agreement under Section 6 below, the Company agrees as follows:

a. Separation Payment. The Company agrees to pay Employee a total of Three Hundred Eleven Thousand Two Hundred and Fifty Dollars and Zero Cents ($311,250.00), at the rate of Thirty-Four Thousand Five Hundred Eighty-Three Dollars and Thirty-Three Cents ($34,583.33) per month, less applicable withholdings, for nine (9) months following the Separation Date in accordance with the Company's regular payroll procedures; provided, however, that all payments shall be further subject to the timing and other provisions of the paragraphs in the Severance Policy bearing the headings "Release," "Section 409A," "Reduction of Severance Benefits," and "Determination of Excise Tax Liability" (together, the "Surviving Sections").

b. COBRA Reimbursement. Provided Employee timely elects and pays for continuation coverage pursuant to the Consolidated Omnibus Budget Reconciliation Act of 1985, as amended ("COBRA") within the time period prescribed pursuant to COBRA, the Company shall reimburse Employee for the payments Employee makes for COBRA coverage for Employee and Employee's eligible dependents that were covered under the Company's health care plans immediately prior to the Separation Date, for a period of up to the first nine (9) months of such coverage, or, if earlier, until the sooner of (i) Employee's securing of health insurance coverage through another employer or (ii) Employee ceasing to be eligible for coverage under COBRA. COBRA reimbursements shall be made by the Company to Employee consistent with the Company's normal expense reimbursement policy, provided that Employee submits documentation to the Company substantiating Employee's payments for COBRA coverage. Notwithstanding the preceding, if the Company determines in its sole discretion that it cannot provide COBRA reimbursement benefits without potentially violating applicable law (including, without limitation, Section 2716 of the Public Health Service Act), the Company will instead provide the Employee nine (9) taxable monthly payments each in an amount equal to the monthly COBRA premium that the Employee would be required to pay to continue the Employee's group health coverage in effect on the date of termination of employment (which amount will be based on the premium for the first month of COBRA coverage), regardless of whether the Employee elects COBRA continuation coverage, beginning on the Company's first regular payroll date that occurs on or after the 60th day following the Separation Date and continuing monthly thereafter. Notwithstanding any of the foregoing, all reimbursements or payments under this paragraph shall be subject to the timing and other provisions of the Surviving Sections.

c. General. Employee acknowledges that (i) without this Agreement, Employee is otherwise not entitled to the consideration listed in this Section 1, (ii) the consideration provided in this Section 1 fully satisfies all of the Company's

obligations to Employee under the Participation Agreement and the Severance Policy, and (iii) the considered provided in this Section 1 fully satisfies any other obligation that the Company would have had to pay Employee severance under the Employment Agreement or any other plan or agreement.

2. Stock. The Parties agree that for purposes of determining the number of shares of the Company's common stock that Employee is entitled to purchase from the Company, pursuant to the exercise of outstanding options, Employee will be considered to have vested only up to the Separation Date. Employee acknowledges that as of the Separation Date, Employee will have vested in 25,000 options and no more pursuant to the Stock Option Agreement dated as of August 6, 2018. The exercise of Employee's vested options and shares shall continue to be governed by the terms and conditions of the Company's Stock Agreements.

3. Benefits. Employee's health insurance benefits shall cease on April 30, 2019, subject to Employee's right to continue Employee's health insurance under COBRA. Employee's participation in all benefits and incidents of employment, including, but not limited to, vesting in stock options, and the accrual of bonuses, vacation, and paid time off, ceased as of the Separation Date.

4. Payment of Salary and Receipt of All Benefits. Employee acknowledges and represents that, other than the consideration set forth in this Agreement, the Company and its agents have paid or provided all salary, wages, bonuses, accrued vacation/paid time off, notice periods, premiums, leaves, housing allowances, relocation costs, interest, severance, outplacement costs, fees, reimbursable expenses, commissions, stock, stock options, vesting, and any and all other benefits and compensation due to Employee.

5. Release of Claims. Employee agrees that the foregoing consideration represents settlement in full of all outstanding obligations owed to Employee by the Company and its current and former officers, directors, employees, agents, investors, attorneys, shareholders, administrators, affiliates, benefit plans, plan administrators, insurers, trustees, divisions, and subsidiaries, and predecessor and successor corporations and assigns (collectively, the "Releasees"). Employee, on Employee's own behalf and on behalf of Employee's respective heirs, family members, executors, agents, and assigns, hereby and forever releases the Releasees from, and agrees not to sue concerning, or in any manner to institute, prosecute, or pursue, any claim, complaint, charge, duty, obligation, or cause of action relating to any matters of any kind, whether presently known or unknown, suspected or unsuspected, that Employee may possess against any of the Releasees arising from any omissions, acts, facts, or damages that have occurred up until and including the date Employee signs this Agreement, including, without limitation:

a. any and all claims relating to or arising from Employee's employment relationship with the Company and the termination of that relationship;

b. any and all claims relating to, or arising from, Employee's right to purchase, or actual purchase of shares of stock of the Company, including, without limitation, any claims for fraud, misrepresentation, breach of fiduciary duty, breach of duty under applicable state corporate law, and securities fraud under any state or federal law;

c. any and all claims under the law of any jurisdiction, including, but not limited to, wrongful discharge of employment; constructive discharge from employment; termination in violation of public policy; discrimination; harassment; retaliation; breach of contract, both express and implied; breach of covenant of good faith and fair dealing, both express and implied; promissory estoppel; negligent or intentional infliction of emotional distress; fraud; negligent or intentional misrepresentation; negligent or intentional interference with contract or prospective economic advantage; unfair business practices; defamation; libel; slander; negligence; personal injury; assault; battery; invasion of privacy; false imprisonment; conversion; and disability benefits;

d. any and all claims for violation of any federal, state, or municipal statute, including, but not limited to, Title VII of the Civil Rights Act of 1964; the Civil Rights Act of 1991; the Rehabilitation Act of 1973; the Americans with Disabilities Act of 1990; the Equal Pay Act; the Fair Labor Standards Act, except as prohibited by law; the Fair Credit Reporting Act; the Age Discrimination in Employment Act of 1967; the Older Workers Benefit Protection Act; the Employee Retirement Income Security Act of 1974; the Worker Adjustment and Retraining Notification Act; the Family and Medical Leave Act, except as prohibited by law; the Uniformed Services Employment and Reemployment Rights Act; the Washington State Law Against Discrimination, as amended (RCW 49.60.010 et seq.); the Washington equal pay law, as amended (RCW 49.12.175); the Washington sex discrimination law (RCW 49.12.200); the Washington age discrimination law (RCW 49.44.090); Washington whistleblower protection laws (RCW 49.60.210, 49.12.005, and 49.12.130); the Washington genetic testing protection law (RCW 49.44.180); the Washington Family Care Act (RCW 49.12.265 to 49.12.295); the Washington Minimum Wage Act (RCW 49.46.005 to 49.46.920); Washington wage, hour, and working conditions laws (RCW 49.12.005 to 49.12.020, 49.12.041 to 49.12.050, 49.12.091, 49.12.101, 49.12.105, 49.12.110, 49.12.121, 49.12.130 to 49.12.150, 49.12.170, 49.12.175, 49.12.185, 49.12.187, 49.12.450); and Washington wage payment laws (RCW 49.48.010 to 49.48.190);

e. any and all claims for violation of the federal or any state constitution;

f. any and all claims arising out of any other laws and regulations relating to employment or employment discrimination;

g. any claim for any loss, cost, damage, or expense arising out of any dispute over the nonwithholding or other tax treatment of any of the proceeds received by Employee as a result of this Agreement; and

h. any and all claims for attorneys' fees and costs.

Employee agrees that the release set forth in this section shall be and remain in effect in all respects as a complete general release as to

the matters released. This release does not extend to any obligations incurred under this Agreement. This release does not release claims that cannot be released as a matter of law, including any Protected Activity (as defined below). Any and all disputed wage claims that are released herein shall be subject to binding arbitration in accordance with Section 17, except as required by applicable law. This release does not extend to any right Employee may have to unemployment compensation benefits or workers' compensation benefits.

6. Acknowledgment of Waiver of Claims under ADEA . Employee understands and acknowledges that Employee is waiving and releasing any rights Employee may have under the Age Discrimination in Employment Act of 1967 ("ADEA"), and that this waiver and release is knowing and voluntary. Employee understands and agrees that this waiver and release does not apply to any rights or claims that may arise under the ADEA after the date Employee signs this Agreement. Employee understands and acknowledges that the consideration given for this waiver and release is in addition to anything of value to which Employee was already entitled. Employee further understands and acknowledges that Employee has been advised by this writing that: (a) Employee should consult with an attorney prior to executing this Agreement; (b) Employee has twenty-one (21) days within which to consider this Agreement; (c) Employee has seven (7) days following Employee's execution of this Agreement to revoke this Agreement; (d) this Agreement shall not be effective until after the revocation period has expired; and (e) nothing in this Agreement prevents or precludes Employee from challenging or seeking a determination in good faith of the validity of this waiver under the ADEA, nor does it impose any condition precedent, penalties, or costs for doing so, unless specifically authorized by federal law. In the event Employee signs this Agreement and returns it to the Company in less than the 21-day period identified above, Employee hereby acknowledges that Employee has freely and voluntarily chosen to waive the time period allotted for considering this Agreement. Employee acknowledges and understands that revocation must be accomplished by a written notification to the person executing this Agreement on the Company's behalf that is received prior to the Effective Date. The Parties agree that changes, whether material or immaterial, do not restart the running of the 21-day period.

7. Unknown Claims. Employee acknowledges that Employee has been advised to consult with legal counsel and that Employee is familiar with the principle that a general release does not extend to claims that the releaser does not know or suspect to exist in Employee's favor at the time of executing the release, which, if known by Employee, must have materially affected Employee's settlement with the Releasees. Employee, being aware of said principle, agrees to expressly waive any rights Employee may have to that effect, as well as under any other statute or common law principles of similar effect.

8. No Pending or Future Lawsuits. Employee represents that Employee has no lawsuits, claims, or actions pending in Employee's name, or on behalf of any other person or entity, against the Company or any of the other Releasees. Employee also represents that Employee does not intend to bring any claims on Employee's own behalf or on behalf of any other person or entity against the Company or any of the other Releasees.

9. Application for Employment. Employee understands and agrees that, as a condition of this Agreement, Employee shall not be entitled to any employment with the Company, and Employee hereby waives any right, or alleged right, of employment or re-employment with the Company. Employee further agrees not to apply for employment with the Company and not otherwise pursue an independent contractor or vendor relationship with the Company.

10. Confidentiality. Subject to Section 20 below governing Protected Activity, Employee agrees to maintain in complete confidence the existence of this Agreement, the contents and terms of this Agreement, and the consideration for this Agreement (hereinafter collectively referred to as "Separation Information"). Except as required by law, Employee may disclose Separation Information only to Employee's immediate family members, the Court in any proceedings to enforce the terms of this Agreement, Employee's counsel, and Employee's accountant and any professional tax advisor to the extent that they need to know the Separation Information in order to provide advice on tax treatment or to prepare tax returns, and must prevent disclosure of any Separation Information to all other third parties. Employee agrees that Employee will not publicize, directly or indirectly, any Separation Information.

11. Trade Secrets and Confidential Information/Company Property. Employee reaffirms and agrees to observe and abide by the terms of the Confidentiality Agreement, specifically including the provisions therein regarding nondisclosure of the Company's trade secrets and confidential and proprietary information, and all restrictive covenants. Employee acknowledges that the non-disclosure obligations in the Confidentiality Agreement do not restrict Employee from disclosing work-related sexual harassment or sexual assault to the extent such disclosures are protected under chapter 117, Washington Laws 2018. Employee also agrees that the above reaffirmation and agreement with the Confidentiality Agreement shall constitute a new and separately enforceable agreement to abide by the terms of the Confidentiality Agreement, entered and effective as of the Effective Date. Employee specifically acknowledges and agrees that any violation of the restrictive covenants in the Confidentiality Agreement shall constitute a material breach of this Agreement. Employee's signature below constitutes Employee's certification under penalty of perjury that Employee has returned all documents and other items provided to Employee by the Company, developed or obtained by Employee in connection with Employee's employment with the Company, or otherwise belonging to the Company, including, but not limited to, all passwords to any software or other programs or data that Employee used in performing services for the Company.

12. No Cooperation. Subject to Section 20 below governing Protected Activity, Employee agrees that Employee will not knowingly encourage, counsel, or assist any attorneys or their clients in the presentation or prosecution of any disputes, differences, grievances, claims, charges, or complaints by any third party against any of the Releasees, unless under a subpoena or other court order to do so or as related directly to the ADEA waiver in this Agreement. Employee agrees both to immediately notify the Company upon receipt of any such subpoena or court order, and to furnish, within three (3) business days of its receipt, a copy of such subpoena or other court order. If approached by anyone for counsel or assistance in the presentation or prosecution of any disputes, differences, grievances, claims, charges, or complaints against any of the Releasees, Employee shall state no more than that Employee cannot provide counsel or assistance.

13. Nondisparagement. Employee agrees to refrain from any disparagement, defamation, libel, or slander of any of the Releasees, and agrees to refrain from any tortious interference with the contracts and relationships of any of the Releasees. Employee shall direct any inquiries by potential future employers to the Company's human resources department, which shall use its best efforts to provide only the Employee's last position and dates of employment.

14. Breach. In addition to the rights provided in the "Attorneys' Fees" section below, Employee acknowledges and agrees that any material breach of this Agreement, unless such breach constitutes a legal action by Employee challenging or seeking a determination in good faith of the validity of the waiver herein under the ADEA, or of any provision of the Confidentiality Agreement shall entitle the Company immediately to recover and/or cease providing the consideration provided to Employee under this Agreement and to obtain damages, except as provided by law, provided, however, that the Company shall not recover One Hundred Dollars ($100.00) of the consideration already paid pursuant to this Agreement, and such amount shall serve as full and complete consideration for the promises and obligations assumed by Employee under this Agreement and the Confidentiality Agreement.

15. No Admission of Liability. Employee understands and acknowledges that this Agreement constitutes a compromise and settlement of any and all actual or potential disputed claims by Employee. No action taken by the Company hereto, either previously or in connection with this Agreement, shall be deemed or construed to be (a) an admission of the truth or falsity of any actual or potential claims or (b) an acknowledgment or admission by the Company of any fault or liability whatsoever to Employee or to any third party.

16. Costs. The Parties shall each bear their own costs, attorneys' fees, and other fees incurred in connection with the preparation of this Agreement.

17. ARBITRATION. THE PARTIES AGREE THAT ANY AND ALL DISPUTES ARISING OUT OF THE TERMS OF THIS AGREEMENT, THEIR INTERPRETATION, EMPLOYEE'S EMPLOYMENT WITH THE COMPANY OR THE TERMS THEREOF, AND ANY OF THE MATTERS HEREIN RELEASED, SHALL BE SUBJECT TO BINDING ARBITRATION UNDER THE FEDERAL ARBITRATION ACT (THE "FAA"). THE FAA'S SUBSTANTIVE AND PROCEDURAL RULES SHALL GOVERN AND APPLY TO THIS ARBITRATION AGREEMENT WITH FULL FORCE AND EFFECT, AND ANY STATE COURT OF COMPETENT JURISDICTION MAY STAY PROCEEDINGS PENDING ARBITRATION OR COMPEL ARBITRATION IN THE SAME MANNER AS A FEDERAL COURT UNDER THE FAA. EMPLOYEE AGREES THAT, TO THE FULLEST EXTENT PERMITTED BY LAW, EMPLOYEE MAY BRING ANY SUCH ARBITRATION PROCEEDING ONLY IN EMPLOYEE'S INDIVIDUAL CAPACITY. ANY ARBITRATION WILL OCCUR IN KING COUNTY, WASHINGTON, BEFORE JAMS, PURSUANT TO ITS EMPLOYMENT ARBITRATION RULES & PROCEDURES ("JAMS RULES"), EXCEPT AS EXPRESSLY PROVIDED IN THIS SECTION 17. THE PARTIES AGREE THAT THE ARBITRATOR SHALL HAVE THE POWER TO DECIDE ANY MOTIONS BROUGHT BY ANY PARTY TO THE ARBITRATION, INCLUDING MOTIONS FOR SUMMARY JUDGMENT AND/OR ADJUDICATION, AND MOTIONS TO DISMISS AND DEMURRERS, APPLYING THE STANDARDS SET FORTH UNDER THE WASHINGTON CIVIL RULES. THE PARTIES AGREE THAT THE ARBITRATOR SHALL ISSUE A WRITTEN DECISION ON THE MERITS. THE PARTIES ALSO AGREE THAT THE ARBITRATOR SHALL HAVE THE POWER TO AWARD ANY REMEDIES AVAILABLE UNDER APPLICABLE LAW, AND THAT THE ARBITRATOR MAY AWARD ATTORNEYS' FEES AND COSTS TO THE PREVAILING PARTY, WHERE PERMITTED BY APPLICABLE LAW. THE ARBITRATOR MAY GRANT INJUNCTIONS AND OTHER RELIEF IN SUCH DISPUTES. THE ARBITRATOR SHALL APPLY SUBSTANTIVE AND PROCEDURAL WASHINGTON LAW TO ANY DISPUTE OR CLAIM, WITHOUT REFERENCE TO ANY CONFLICT-OF-LAW PROVISIONS OF ANY JURISDICTION. THE DECISION OF THE ARBITRATOR SHALL BE FINAL, CONCLUSIVE, AND BINDING ON THE PARTIES TO THE ARBITRATION. THE PARTIES AGREE THAT THE PREVAILING PARTY IN ANY ARBITRATION SHALL BE ENTITLED TO INJUNCTIVE RELIEF IN ANY COURT OF COMPETENT JURISDICTION TO ENFORCE THE ARBITRATION AWARD. THE PARTIES TO THE ARBITRATION SHALL EACH PAY AN EQUAL SHARE OF THE COSTS AND EXPENSES OF SUCH ARBITRATION, AND EACH PARTY SHALL SEPARATELY PAY FOR ITS RESPECTIVE COUNSEL FEES AND EXPENSES; PROVIDED, HOWEVER, THAT THE ARBITRATOR SHALL AWARD ATTORNEYS' FEES AND COSTS TO THE PREVAILING PARTY, EXCEPT AS PROHIBITED BY LAW. THE PARTIES HEREBY AGREE TO WAIVE THEIR RIGHT TO HAVE ANY DISPUTE BETWEEN THEM RESOLVED IN A COURT OF LAW BY A JUDGE OR JURY. NOTWITHSTANDING THE FOREGOING, THIS SECTION WILL NOT PREVENT EITHER PARTY FROM SEEKING INJUNCTIVE RELIEF (OR ANY OTHER PROVISIONAL REMEDY) FROM ANY COURT HAVING JURISDICTION OVER THE PARTIES AND THE SUBJECT MATTER OF THEIR DISPUTE RELATING TO THIS AGREEMENT AND THE AGREEMENTS INCORPORATED HEREIN BY REFERENCE. SHOULD ANY PART OF THE ARBITRATION AGREEMENT CONTAINED IN THIS PARAGRAPH CONFLICT WITH ANY OTHER ARBITRATION AGREEMENT BETWEEN THE PARTIES, THE PARTIES AGREE THAT THIS ARBITRATION AGREEMENT SHALL GOVERN.

18. Tax Consequences. The Company makes no representations or warranties with respect to the tax consequences of the payments and any other consideration provided to Employee or made on Employee's behalf under the terms of this Agreement. Employee agrees and understands that Employee is responsible for payment, if any, of local, state, and/or federal taxes on the payments and any other consideration provided hereunder by the Company and any penalties or assessments thereon. Employee further agrees to indemnify and hold the Releasees harmless from any claims, demands, deficiencies, penalties, interest, assessments, executions, judgments, or recoveries by any government agency against the Company for any amounts claimed due on account of (a) Employee's failure to pay or delayed payment of, federal or state taxes, or (b) damages sustained by the Company by reason of any such claims, including attorneys' fees and costs.

19. Authority. The Company represents and warrants that the undersigned has the authority to act on behalf of the Company and to bind the Company and all who may claim through it to the terms and conditions of this Agreement. Employee represents and warrants that Employee has the capacity to act on Employee's own behalf and on behalf of all who might claim through Employee to bind them to the terms and conditions of this Agreement. Each Party warrants and represents that there are no liens or claims of lien or assignments in law or equity or otherwise of or against any of the claims or causes of action released herein.

20. Protected Activity Not Prohibited. Employee understands that nothing in this Agreement shall in any way limit or prohibit Employee from engaging in any Protected Activity. For purposes of this Agreement, "Protected Activity" shall mean filing a charge, complaint, or report with, or otherwise communicating, cooperating, or participating in any investigation or proceeding that may be conducted by, any federal, state or local government agency or commission, including the Securities and Exchange Commission, the Equal Employment Opportunity Commission, the Occupational Safety and Health Administration, and the National Labor Relations Board ("Government Agencies"). Employee understands that in connection with such Protected Activity, Employee is permitted to disclose documents or other information as permitted by law, and without giving notice to, or receiving authorization from, the Company. Notwithstanding the foregoing, Employee agrees to take all reasonable precautions to prevent any unauthorized use or disclosure of any information that may constitute Company confidential information under the Confidentiality Agreement to any parties other than the Government Agencies. Employee further understands that "Protected Activity" does not include the disclosure of any

Company attorney-client privileged communications or attorney work product. Any language in the Confidentiality Agreement regarding Employee's right to engage in Protected Activity that conflicts with, or is contrary to, this paragraph is superseded by this Agreement. In addition, pursuant to the Defend Trade Secrets Act of 2016, Employee is notified that an individual will not be held criminally or civilly liable under any federal or state trade secret law for the disclosure of a trade secret that (a) is made in confidence to a federal, state, or local government official (directly or indirectly) or to an attorney *solely* for the purpose of reporting or investigating a suspected violation of law, or (b) is made in a complaint or other document filed in a lawsuit or other proceeding, if (and only if) such filing is made under seal. In addition, an individual who files a lawsuit for retaliation by an employer for reporting a suspected violation of law may disclose the trade secret to the individual's attorney and use the trade secret information in the court proceeding, if the individual files any document containing the trade secret under seal and does not disclose the trade secret, except pursuant to court order. Finally, nothing in this Agreement constitutes a waiver of any rights Employee may have under the Sarbanes-Oxley Act or Section 7 of the National Labor Relations Act.

21. No Representations. Employee represents that Employee has had an opportunity to consult with an attorney, and has carefully read and understands the scope and effect of the provisions of this Agreement. Employee has not relied upon any representations or statements made by the Company that are not specifically set forth in this Agreement.

22. Severability. In the event that any provision or any portion of any provision hereof or any surviving agreement made a part hereof becomes or is declared by a court of competent jurisdiction or arbitrator to be illegal, unenforceable, or void, this Agreement shall continue in full force and effect without said provision or portion of provision.

23. Attorneys' Fees. Except with regard to a legal action challenging or seeking a determination in good faith of the validity of the waiver herein under the ADEA, in the event that either Party brings an action to enforce or effect its rights under this Agreement, the prevailing Party shall be entitled to recover its costs and expenses, including the costs of mediation, arbitration, litigation, court fees, and reasonable attorneys' fees incurred in connection with such an action.

24. Entire Agreement. This Agreement represents the entire agreement and understanding between the Company and Employee concerning the subject matter of this Agreement and Employee's employment with and separation from the Company and the events leading thereto and associated therewith, and supersedes and replaces any and all prior agreements and understandings between Employee and the Company concerning the subject matter of this Agreement and Employee's relationship with the Company, including the Employment Agreement, the Participation Agreement, and the Severance Policy, except for the Surviving Sections. Notwithstanding the foregoing, the respective rights and obligations of Employee and Company prescribed in the following agreements shall remain in full force and effect and survive Employee's termination from employment with the Company: (a) the Confidentiality Agreement, (b) the Stock Agreements, and (c) that certain Indemnification Agreement by and between Employee and the Company dated August 6, 2018.

25. No Oral Modification. This Agreement may only be amended in a writing signed by Employee and the Company's Chief Executive Officer.

26. Governing Law. This Agreement shall be governed by the laws of the State of Washington, without regard for choice-of-law provisions. Employee consents to personal and exclusive jurisdiction and venue in the State of Washington.

27. Effective Date. Employee understands that this Agreement shall be null and void if not executed by Employee within the twenty-one (21) day period set forth under Section 6 above. Each Party has seven (7) days after that Party signs this Agreement to revoke it. This Agreement will become effective on the eighth (8th) day after Employee signed this Agreement, so long as it has been signed by the Parties and has not been revoked by either Party before that date (the "Effective Date").

28. Counterparts. This Agreement may be executed in counterparts and by facsimile, and each counterpart and facsimile shall have the same force and effect as an original and shall constitute an effective, binding agreement on the part of each of the undersigned.

29. Voluntary Execution of Agreement. Employee understands and agrees that Employee executed this Agreement voluntarily, without any duress or undue influence on the part or behalf of the Company or any third party, with the full intent of releasing all of Employee's claims against the Company and any of the other Releasees. Employee acknowledges that:

(a) Employee has read this Agreement;

(b) Employee has been represented in the preparation, negotiation, and execution of this Agreement by legal counsel of Employee's own choice or has elected not to retain legal counsel;

(c) Employee understands the terms and consequences of this Agreement and of the releases it contains; and

(d) Employee is fully aware of the legal and binding effect of this Agreement.

IN WITNESS WHEREOF, the Parties have executed this Agreement on the respective dates set forth below.

MARK LITTON, an individual

Dated: 4/24/2019 /s/ Mark Litton

Mark Litton

ALPINE IMMUNE SCIENCES, INC.

Dated: 4/24/2019 By: /s/ Mitchell H. Gold

Mitchell H. Gold
Chief Executive Officer

Exhibit 31.1

CERTIFICATIONS

I, Mitchell Gold, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Alpine Immune Sciences, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervisions, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: August 13, 2019

/s/ Mitchell Gold

Mitchell Gold

Executive Chairman and Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATIONS

I, Paul Rickey, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Alpine Immune Sciences, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervisions, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: August 13, 2019

/s/ Paul Rickey

Paul Rickey

Senior Vice President and Chief Financial Officer (Principal Accounting Officer and Principal Financial Officer)

Exhibit 32.1

ALPINE IMMUNE SCIENCES, INC.
CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Quarterly Report of Alpine Immune Sciences, Inc. (the "Company") on Form 10-Q for the quarter ended June 30, 2019, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Mitchell Gold, Executive Chairman and Chief Executive Officer *(Principal Executive Officer)* of the Company, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to my knowledge:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

/s/ Mitchell Gold

Mitchell Gold

Executive Chairman and Chief Executive Officer
(Principal Executive Officer)

August 13, 2019

A signed original of this written statement required by Section 906 of the Sarbanes-Oxley Act of 2002 has been provided to the Company and will be retained by the Company and furnished to the Securities and Exchange Commission or its staff upon request.

This certification accompanies the Report to which it relates, is not deemed filed with the Securities and Exchange Commission and is not to be incorporated by reference into any filing of Alpine Immune Sciences, Inc. under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended (whether made before or after the date of the Report), irrespective of any general incorporation language contained in such filing.

Exhibit 32.2

ALPINE IMMUNE SCIENCES, INC.
CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Quarterly Report of Alpine Immune Sciences, Inc. (the "Company") on Form 10-Q for the quarter ended June 30, 2019, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Paul Rickey, Senior Vice President and Chief Financial Officer *(Principal Accounting Officer and Principal Financial Officer)* of the Company, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to my knowledge:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

/s/ Paul Rickey

Paul Rickey

Senior Vice President and Chief Financial Officer
(Principal Accounting Officer and Principal Financial Officer)

August 13, 2019

A signed original of this written statement required by Section 906 of the Sarbanes-Oxley Act of 2002 has been provided to the Company and will be retained by the Company and furnished to the Securities and Exchange Commission or its staff upon request.

This certification accompanies the Report to which it relates, is not deemed filed with the Securities and Exchange Commission and is not to be incorporated by reference into any filing of Alpine Immune Sciences, Inc. under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended (whether made before or after the date of the Report), irrespective of any general incorporation language contained in such filing.