

**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 March 31, 2018

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

(State or other jurisdiction of
incorporation or organization)

20-8969493

(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)

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 and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted 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 and post 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	<input type="checkbox"/>	Accelerated filer	<input type="checkbox"/>
Non-accelerated filer	<input type="checkbox"/> (Do not check if a smaller reporting company)	Smaller reporting company	<input checked="" type="checkbox"/>
Emerging growth company	<input checked="" type="checkbox"/>		

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 May 4, 2018, the registrant had 13,849,562 shares of common stock, \$0.001 par value per share, outstanding.

ALPINE IMMUNE SCIENCES, INC.
FORM 10-Q
FOR THE QUARTER ENDED MARCH 31, 2018

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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

ALPINE IMMUNE SCIENCES, INC.
CONDENSED CONSOLIDATED BALANCE SHEETS
(in thousands, except share and per share amounts)

	<u>March 31, 2018</u>	<u>December 31, 2017</u>
	<u>(unaudited)</u>	
Assets		
Current assets:		
Cash and cash equivalents	\$ 7,446	\$ 8,000
Short-term investments	69,206	73,240
Prepaid expenses and other current assets	1,335	1,308
Total current assets	<u>77,987</u>	<u>82,548</u>
Restricted cash	132	132
Property and equipment, net	1,127	1,089
Intangible assets	1,453	1,453
Total assets	<u>\$ 80,699</u>	<u>\$ 85,222</u>
Liabilities, convertible preferred stock, and stockholders' equity		
Current liabilities:		
Accounts payable	\$ 528	\$ 193
Accrued liabilities	586	382
Deferred revenue	240	277
Deferred rent, current portion	66	48
Current portion of long-term debt	1,508	995
Total current liabilities	<u>2,928</u>	<u>1,895</u>
Deferred rent, long-term portion	67	66
Deferred tax liability	253	305
Long-term debt	3,570	4,039
Total liabilities	<u>6,818</u>	<u>6,305</u>
Commitments and contingencies		
Convertible preferred stock, \$0.001 par value per share; 10,000,000 shares authorized at March 31, 2018 and December 31, 2017; zero shares issued and outstanding at March 31, 2018 and December 31, 2017	—	—
Stockholders' equity:		
Common stock, \$0.001 par value per share; 200,000,000 shares authorized at March 31, 2018 and December 31, 2017; 13,896,551 shares issued and 13,846,084 shares outstanding at March 31, 2018; 13,881,645 shares issued and 13,831,178 shares outstanding at December 31, 2017	14	14
Treasury stock, at cost; 50,467 shares at March 31, 2018 and December 31, 2017	—	—
Additional paid-in capital	88,864	88,346
Accumulated other comprehensive loss	(105)	(59)
Accumulated deficit	(14,892)	(9,384)
Total stockholders' equity	<u>73,881</u>	<u>78,917</u>
Total liabilities, convertible preferred stock, and stockholders' equity	<u>\$ 80,699</u>	<u>\$ 85,222</u>

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 March 31,	
	2018	2017
	(unaudited)	
Collaboration revenue	\$ 315	\$ 737
Operating expenses:		
Research and development	3,792	1,858
General and administrative	2,108	873
Total operating expenses	5,900	2,731
Loss from operations	(5,585)	(1,994)
Other income (expense):		
Interest expense	(78)	—
Interest and other income	305	5
Loss before taxes	(5,358)	(1,989)
Income tax expense	52	—
Basic and diluted net loss attributable to common stockholders	\$ (5,306)	\$ (1,989)
Comprehensive loss:		
Unrealized loss on investments	(46)	—
Comprehensive loss	\$ (5,352)	\$ (1,989)
Weighted-average shares used to compute basic and diluted net loss per share attributable to common stockholders	13,844,731	615,844
Basic and diluted net loss per share attributable to common stockholders	\$ (0.38)	\$ (3.23)

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)

	Three Months Ended March 31,	
	2018	2017
	(unaudited)	
Operating activities		
Net loss	\$ (5,306)	\$ (1,989)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation expense	80	46
Non-cash interest expense	44	—
Deferred income tax	(52)	—
Stock-based compensation and warrant expense	511	52
Changes in operating assets and liabilities:		
Prepaid expenses	(27)	(134)
Accounts payable	335	199
Deferred revenue	(239)	(737)
Accrued liabilities	204	406
Deferred rent and other	19	(7)
Net cash used in operating activities	<u>(4,431)</u>	<u>(2,164)</u>
Investing activities		
Purchases of property and equipment	(118)	(108)
Purchase of short-term investments	(37,037)	—
Proceeds from the sale of short-term investments	41,025	—
Net cash provided by (used in) investing activities	<u>3,870</u>	<u>(108)</u>
Financing activities		
Proceeds from sale of preferred stock	—	4,000
Proceeds from exercise of stock options and common stock warrants	7	21
Net cash provided by financing activities	<u>7</u>	<u>4,021</u>
Net (decrease) increase in cash and cash equivalents and restricted cash	(554)	1,749
Cash and cash equivalents and restricted cash, beginning of period	8,132	11,819
Cash and cash equivalents and restricted cash, end of period	<u>\$ 7,578</u>	<u>\$ 13,568</u>
Supplemental Information		
Cash paid for interest	\$ 34	\$ —

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

ALPINE IMMUNE SCIENCES, INC.

NOTES TO CONDENSED CONSOLIDATED FINANCIAL STATEMENTS

(Information as of March 31, 2018 and for the three months ended March 31, 2018 and 2017 is unaudited)

1. Description of the Business

Alpine Immune Sciences, Inc. (the “Company”, “Alpine”, “we”, “us”, or “our”) is focused on discovering and developing modern, protein-based immunotherapies targeting the immune synapse to treat cancer, inflammation, and other diseases. Our proprietary scientific platform uses a process known as directed evolution, or an iterative scientific engineering process purposefully conducted to “evolve” a protein to create therapeutics potentially capable of modulating immune system interactions. In our pre-clinical animal studies, our platform has proven capable of identifying novel molecules, including single domains capable of modulating multiple targets. We were incorporated under the laws of the State of Delaware and are headquartered in Seattle, Washington.

Significant estimates inherent in the preparation of the accompanying condensed consolidated financial statements include recoverability and useful lives of intangible assets and the fair value of equity based awards.

Reverse Merger and Subscription Agreement

On April 18, 2017, we entered into a merger agreement with Nivalis Therapeutics, Inc. (“Nivalis”), a public biotechnology company, and one of its wholly-owned subsidiaries pursuant to which, the subsidiary merged with and into Alpine, with Alpine continuing as a wholly owned subsidiary of Nivalis and the surviving corporation of the merger (the “Merger Agreement”). Nivalis Therapeutics, Inc. was incorporated in Delaware in March 2007. Alpine Immune Sciences, Inc. (prior to its business combination with Nivalis Therapeutics, Inc.) was incorporated in Delaware on December 30, 2014.

The merger is intended to qualify for federal income tax purposes as a tax-free reorganization under the provisions of Section 368(a) of the Internal Revenue Code of 1986, as amended. At the closing of the merger, each outstanding share of our capital stock (common stock and preferred stock) was converted into the right to receive shares of Nivalis common stock (subject to the payment of cash in lieu of fractional shares and after giving effect to a 1:4 reverse stock split of Nivalis common stock) such that, immediately following the effective time of the merger, preexisting Nivalis stockholders, optionholders, and warrantholders owned, or held rights to acquire, approximately 26% of the fully-diluted common stock of Nivalis, which changed its name to “Alpine Immune Sciences, Inc.” following the completion of the merger and Alpine’s preexisting stockholders, optionholders, and warrantholders owned, or held rights to acquire approximately 74% of the fully-diluted common stock of Nivalis. The issuance of the shares to our pre-existing stockholders was registered under the Securities Act of 1933, as amended, pursuant to a registration statement on Form S-4 (No. 333-218134) (the “Registration Statement”) declared effective by the Securities and Exchange Commission (the “SEC”) on June 6, 2017.

Contemporaneously with the execution and delivery of the Merger Agreement, certain of our pre-existing stockholders entered into a subscription agreement with us pursuant to which such stockholders purchased, immediately prior to the closing of the merger, 1,335,118 shares of our capital stock at a purchase price of \$12.74 per share for an aggregate purchase price of approximately \$17.0 million.

The merger and the subscription described above were consummated on July 24, 2017.

2. Summary of Significant Accounting Policies

Basis of Presentation and Use of Estimates

The accompanying unaudited condensed consolidated financial statements have been prepared in accordance with the rules and regulations of the 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. 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 results of our operations for the three months ended March 31, 2018 are not necessarily indicative of the results to be expected for the full year.

Principles of Consolidation

Our condensed consolidated financial statements include the financial position and results of operations of Alpine and AIS Operating Co., Inc., our wholly owned subsidiary and operating company. On July 24, 2017, we closed the merger on the

terms described in more detail in Note 1. In connection with the merger, Nivalis effected a 1:4 reverse stock split of its common stock. Upon the closing of the merger, (1) a wholly-owned subsidiary of Nivalis merged with and into Alpine, with Alpine (renamed as "AIS Operating Co., Inc.") remaining as the surviving entity; and (2) Nivalis was renamed as "Alpine Immune Sciences, Inc."

Unaudited Interim Financial Information

The accompanying unaudited condensed consolidated financial statements as of March 31, 2018, and for the three months ended March 31, 2018 and 2017 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, 2017 and 2016 included in our Annual Report on Form 10-K for the year ended December 31, 2017, filed with the Securities and Exchange Commission ("SEC") on March 28, 2017 ("Annual Report").

Unless indicated otherwise, all amounts presented in financial tables are presented in thousands, except for share, per share and par value amounts.

Restricted Cash

Restricted cash represents cash drawn on a line of credit used to establish collateral to support the security deposit on our operating lease 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.

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 revenue is primarily derived from our License and Research Agreement (the "Collaboration Agreement") with Kite Pharma, Inc. ("Kite"), which contains 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.

We allocate revenue to each performance obligation based on its relative standalone selling price. We generally determine standalone 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 the Collaboration Agreement based on employee hours contributed to each performance obligation.

The Collaboration Agreement provides 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 the Collaboration Agreement, 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.

Comprehensive Income (Loss)

Comprehensive income (loss) is comprised of net income (loss) and certain changes in equity excluded from net income (loss). For the three months ended March 31, 2018, other comprehensive loss consists of unrealized losses on our short-term investments. There was no difference between comprehensive income (loss) and net income (loss) for the three months ended March 31, 2017.

Recently Issued Accounting Pronouncements

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. ASU 2016-02 is effective for fiscal years beginning after December 15, 2018, including interim periods within those fiscal years, and is to be applied at the beginning of the earliest period presented using a modified retrospective approach. We are continuing to evaluate the effect the standard will have on our financial statements and related disclosures.

Recently Adopted Accounting Pronouncements

In May 2014, the Financial Accounting Standards Board ("FASB") issued Accounting Standards Update ("ASU") No. 2014-09, Revenue from Contracts with Customers, as amended ("new revenue standard" or "ASC 606"), which amends the guidance for revenue recognition to replace numerous industry specific requirements. ASC 606 implements a five-step process for customer contract revenue recognition focusing on transfer of control, as opposed to transfer of risk and rewards. ASC 606 also requires enhanced disclosures regarding the nature, amount, timing, and uncertainty of revenues and cash flows from contracts with customers. Other major provisions include ensuring the time value of money is considered in the transaction price, and allowing estimates of variable consideration to be recognized before contingencies are resolved in certain circumstances. ASC 606 is effective for reporting periods beginning after December 15, 2017. On January 1, 2018, we adopted the new accounting standard and all of the related amendments using the modified retrospective method. We recognized the cumulative effect of initially applying the new revenue standard as an adjustment to the opening balance of our accumulated deficit. The cumulative effect of the changes related to the adoption of the new revenue standard and increased our beginning balances in accumulated deficit and deferred revenue by \$203,000 within our condensed consolidated balance sheet. The comparative information has not been restated and continues to be reported under the accounting standards in effect for those periods.

Our Collaboration Agreement with Kite is the only contract that impacted the adoption of the new revenue standard. Prior to the adoption of the new revenue standard, we recognized revenue under the Collaboration Agreement based upon the estimated performance periods related to the non-refundable upfront payments we received from Kite. Under the new standard, we recognize revenue based on employee hours contributed to each performance obligation.

In accordance with the new revenue standard requirements, the disclosure of the impact of adoption on our condensed consolidated financial statements as of and for the three months ended March 31, 2018 is as follows (in thousands):

	As Reported	Adjustments	Balance without Adoption of ASC 606
Condensed Consolidated Balance Sheets			
Liabilities			
Deferred revenue	\$ 240	\$ (91)	\$ 149
Stockholders' equity			
Accumulated deficit	(14,892)	91	(14,801)
Condensed Consolidated Statements of Operations and Comprehensive Income (Loss)			
Collaboration revenue	\$ 315	\$ (112)	\$ 203
Net loss	(5,306)	(112)	(5,418)

In August 2016, the FASB issued ASU No. 2016-15 which provides new guidance on the classification of certain cash receipts and payments in the statement of cash flows. The new guidance is intended to reduce diversity in practice in how certain transactions are classified in the statement of cash flows. We adopted this new standard effective January 1, 2018. The adoption of this standard did not impact our financial statements.

In May 2017, the FASB issued ASU No. 2017-09 to provide clarity and reduce both diversity in practice and cost and complexity when applying the guidance in Compensation - Stock Compensation (Topic 718) about a change to the terms and conditions of a share-based payment award. The amendments in this update provide guidance about which changes to the terms or conditions of a share-based payment award require an entity to apply modification accounting in Topic 718. The amendments in this update are effective for annual periods, including interim periods within those annual periods, beginning after December 15, 2017. Early adoption is permitted, and applied prospectively to modifications occurring on or after the adoption date. We adopted this new standard effective January 1, 2018. The adoption of this standard did not have an impact on our financial statements. For the quarter ended March 31, 2018, there were no modifications to the terms or conditions of a share-based payment award.

3. Business Combination

On July 24, 2017, we closed the merger on the terms described in more detail in Note 1. In connection with the merger, Nivalis effected a 1:4 reverse stock split of its common stock. Upon the closing of the merger, (1) a wholly-owned subsidiary of Nivalis merged with and into Alpine, with Alpine (renamed as "AIS Operating Co., Inc.") remaining as the surviving entity; and (2) Nivalis was renamed as "Alpine Immune Sciences, Inc."

Under the terms of the Merger Agreement, Nivalis issued shares of its common stock to Alpine's stockholders, at an exchange rate of 0.4969 shares of Nivalis common stock, after taking into account the 1:4 reverse stock split, for each share of Alpine's common stock and preferred stock outstanding immediately prior to the merger. The exchange rate was determined through arms-length negotiations between Nivalis and Alpine. Nivalis also assumed all of the stock options outstanding under Alpine's Amended and Restated 2015 Stock Plan, as amended (the "Alpine Plan"), and stock warrants for Alpine's capital stock outstanding immediately prior to the merger, with such stock options and warrants henceforth representing the right to purchase a number of shares of the Nivalis common stock equal to 0.4969 multiplied by the number of shares of Alpine's common stock or preferred stock previously represented by such options and warrants. Nivalis also assumed the Alpine Plan. Immediately after the merger, there were 13,881,645 shares of common stock outstanding. Immediately after the merger, Alpine's former stockholders, warrant holders, and option holders owned, or held rights to acquire, approximately 74% of the fully-diluted common stock of Nivalis, which for these purposes is defined as the outstanding common stock of Nivalis, plus "in the money" options and warrants to purchase shares of Nivalis' common stock, assuming all "in the money" options and warrants of Nivalis outstanding immediately prior to the merger are exercised on a cashless basis immediately prior to the closing of the merger, with Nivalis' stockholders, option holders, and warrant holders immediately prior to the merger owning, or holding rights to acquire, approximately 26% of the fully diluted common stock of Nivalis. More than 74% of Nivalis' common stock outstanding immediately after the merger was held by stockholders party to lock-up agreements, pursuant to which such stockholders have agreed, except in limited circumstances, not to sell, transfer, or engage in swap or similar transactions with respect to shares of Nivalis' common stock, including, as applicable, shares received in the merger and issuable upon exercise of certain warrants and options, for a period of 180 days following the completion of the merger.

The issuance of shares of Nivalis' common stock to our pre-existing stockholders was registered with the SEC pursuant to the Registration Statement. Immediately prior to the merger, we issued and sold an aggregate of approximately \$17.0 million of shares of our capital stock to certain existing stockholders. For accounting purposes, our historical financial statements were not adjusted to reflect the merger, other than adjustments to the capital structure to reflect the historical capital structure of Nivalis. No other adjustments to our historical assets and liabilities were made as a result of the merger.

In addition to the operating assets and liabilities of Nivalis, we also acquired Nivalis' tax attributes, which primarily consisted of net operating losses which begin to expire in 2032. Our ability to utilize the tax attributes of Nivalis may be limited under Section 382 of the U.S. Internal Revenue Service and as such, have been reserved. We recorded a deferred tax liability related to future tax benefits arising from in-process research and development ("IPR&D") acquired in the Merger. The combined organization is focusing on the development and commercialization of our innovative immunotherapies. Following the merger, the increased cash resources and increased access to capital of the combined organization will help to support the clinical development of our products.

Consideration Transferred

The fair value of the consideration transferred was based on the most reliable measure, which was determined to be the market price of Nivalis shares of common stock as of the acquisition date. The fair value of the consideration transferred consisted of the following (in thousands except share and per share amounts):

Outstanding Nivalis common stock		3,914,058
Per share fair value of Nivalis common stock	\$	9.60
Outstanding Nivalis stock options		421,992
Weighted average per share fair value of Nivalis stock options	\$	1.25
Total fair value of consideration (in 000's)	\$	38,103

Pursuant to the Merger Agreement, unvested Nivalis stock options immediately vested as of the closing of the business combination and were adjusted to give effect to the recapitalization.

Purchase Price Allocation

As Alpine was the accounting acquirer in the merger, we allocated the purchase price to the acquired tangible and intangible assets and assumed liabilities of Nivalis based on their estimated fair values as of the acquisition date. The excess of the estimated fair values of net assets acquired over the acquisition consideration paid was recorded as a bargain purchase gain in the condensed consolidated statements of operations and comprehensive income (loss). The determination of the preliminary fair values of the assets acquired and liabilities assumed requires significant judgment, including third party valuation estimates relating to the value of the acquired IPR&D. The allocation of the purchase consideration to the assets acquired and liabilities assumed in our financial statements was finalized as of December 31, 2017.

Since the acquisition date, we have recorded adjustments to the allocation of the purchase consideration that included increases of \$77,000 and \$15,000 to other receivables and accrued liabilities, respectively, which resulted in a decrease of \$62,000 in our bargain purchase gain. These purchase price adjustments are reflected in the accompanying consolidated balance sheet as of December 31, 2017. The final allocation of the purchase consideration is as follows (in thousands):

	Fair Value
Assets:	
Cash and cash equivalents	\$ 31,130
Marketable securities	12,952
Other receivables	79
IPR&D	1,453
Total assets acquired	45,614
Liabilities:	
Accrued liabilities	(401)
Deferred tax liability	(509)
Total liabilities assumed	(910)
Bargain purchase gain	(6,601)
Total	\$ 38,103

We relied on significant Level 3 unobservable inputs to estimate the fair value of our acquired IPR&D using management's estimate of future royalties and expected earnings of the assets after taking into account an estimate of future expenses necessary to bring the products to completion. These projected cash flows were then discounted to their present values using a discount rate of 17%, which was considered commensurate with the risks and stages of development of the IPR&D.

The bargain purchase gain resulted from expenses incurred by Nivalis between the time the purchase price was negotiated and the close of the transaction, and changes in the Nivalis stock price during that period as the exchange ratio was fixed when the purchase price was negotiated.

We recognized acquisition-related costs of \$280,000 for the three months ended March 31, 2017. These costs are included within general and administrative expense in our condensed consolidated statements operations and of comprehensive income (loss).

Pro Forma Financial Information

The following pro forma consolidated results of net loss for the three months ended March 31, 2017 assume the business combination was completed as of January 1, 2017 (in thousands, except per share amounts):

	Three Months Ended March 31, 2017
Pro forma revenues	\$ 737
Pro forma net loss	(10,494)
Pro forma basic and diluted net loss per share	\$ (0.76)

For purposes of the pro forma disclosures above, the primary adjustments for the three months ended March 31, 2018 include the elimination of acquisition related costs and acceleration of stock compensation expense upon the change in control. There was no difference in our pro forma financial information for the three months ended March 31, 2018.

4. Net Loss Per Share

We compute net loss per share attributable to common stockholders using the two-class method required for participating securities. We consider our convertible preferred stock to be participating securities. In accordance with the two-class method, earnings allocated to these participating securities, which include participation rights in undistributed earnings,

are subtracted from net income to determine total undistributed earnings to be allocated to common stockholders. Net loss is not allocated to participating securities as there is no contractual obligation to share in net losses.

Basic net loss per share attributable to common stockholders is computed by dividing net income (loss) attributable to common stockholders by the weighted-average number of common shares outstanding during the period. All participating securities are excluded from basic weighted-average common shares outstanding. Because of net losses recognized in each period, potential common shares issuable upon the exercise of outstanding stock options and warrants and the conversion of preferred shares into common shares have not been reflected in the calculation of diluted net loss per share due to the anti-dilutive effect. Diluted net loss per share, therefore, does not differ from basic net loss per share.

The basic and diluted net loss per share for the three months ended March 31, 2018 was computed based on the weighted average shares of common stock outstanding during the respective periods. The net loss per share for the three months ended March 31, 2018 includes the conversion 9,301,433 shares of our convertible preferred stock into common stock, and 3,914,058 shares acquired in connection with the merger. 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 attributable to common stockholders calculation because their effect would have been anti-dilutive for the periods presented:

	March 31,	
	2018	2017
	(unaudited)	
Convertible preferred stock	—	5,019,000
Warrants to purchase common stock	24,123	—
Options to purchase common stock	1,942,712	857,819
Total	<u>1,966,835</u>	<u>5,876,819</u>

5. 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):

Assets:	March 31, 2018			
	(unaudited)			
	Amortized Cost	Gross unrealized gains	Gross unrealized losses	Fair market value
Money market funds	\$ 5,955	\$ —	\$ —	\$ 5,955
U.S. treasury bills	14,367	—	(26)	14,341
Corporate debt securities and commercial paper	54,944	—	(79)	54,865
Total	<u>\$ 75,266</u>	<u>\$ —</u>	<u>\$ (105)</u>	<u>\$ 75,161</u>

Assets:	December 31, 2017			
	Amortized Cost	Gross unrealized gains	Gross unrealized losses	Fair market value
Money market funds	\$ 5,680	\$ —	\$ —	\$ 5,680
U.S. treasury bills	19,909	—	(21)	19,888
Corporate debt securities and commercial paper	53,390	—	(38)	53,352
Total	<u>\$ 78,979</u>	<u>\$ —</u>	<u>\$ (59)</u>	<u>\$ 78,920</u>

All short-term investments held as of March 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.

6. Fair Value Measurements

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 March 31, 2018 and December 31, 2017, cash of \$1.5 million and \$2.3 million, respectively, is excluded from the following fair value table below. The following table summarizes our financial assets and liabilities measured at fair value on a recurring basis (in thousands):

	March 31, 2018			
	(unaudited)			
Assets:	Level 1	Level 2	Level 3	Total
Money market funds	\$ 5,955	\$ —	\$ —	\$ 5,955
U.S. treasury bills	14,341	—	—	14,341
Corporate debt securities and commercial paper	—	54,865	—	54,865
Total	\$ 20,296	\$ 54,865	\$ —	\$ 75,161

	December 31, 2017			
	Level 1	Level 2	Level 3	Total
Assets:				
Money market funds	\$ 5,680	\$ —	\$ —	\$ 5,680
U.S. treasury bills	19,888	—	—	19,888
Corporate debt securities and commercial paper	—	53,352	—	53,352
Total	\$ 25,568	\$ 53,352	\$ —	\$ 78,920

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.

7. Accrued Liabilities

Accrued expenses and other current liabilities consisted of the following (in thousands):

	March 31, 2018	December 31, 2017
	(unaudited)	
Accrued research and development	\$ 95	\$ 197
Accrued professional fees	395	112
Accrued taxes and licenses	17	30
Accrued other	79	43
Total	\$ 586	\$ 382

8. Long-term Debt

On June 30, 2017, we drew down a term loan of \$5.0 million from Silicon Valley Bank with whom we had entered into a long-term financing arrangement on December 16, 2016. The loan has an interest-only period that expires on July 1, 2018, at which point we will be 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 March 31, 2018, 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 March 31, 2018.

Also, in connection with the drawdown of the loan, we also granted the financial institution 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 on the accompanying condensed consolidated balance sheets. 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 \$44,000 for the three months ended March 31, 2018. The unamortized discount was \$298,000 as of March 31, 2018.

9. Commitments and Contingencies

Operating Lease

We lease laboratory and office space under an operating lease in Seattle, Washington. In January 2018, we entered into a lease amendment for approximately 6,184 square feet of additional office and laboratory space adjacent to our existing leased premises. The lease expires on December 31, 2019 and has two options to extend the lease term with each option enabling us to extend the lease term by twelve months. The annual base rent due under the amendment is \$295,000 for the first year and will increase by 3.0% each year thereafter.

10. License and Collaboration Agreement

In October 2015, we entered into a Collaboration and Licensing Agreement with Kite Pharma, Inc. to discover and develop protein-based immunotherapies targeting the immune synapse to treat cancer. Under our agreement, we are to perform certain research services and grant to Kite an exclusive license to two programs from our transmembrane immunomodulatory protein (TIP™) technology, which Kite is planning to further engineer into chimeric antigen receptor ("CAR") and T cell receptor ("TCR") product candidates.

Under the terms of the Collaboration Agreement, Kite made upfront payments to us of \$5.5 million, which were initially recorded as deferred revenue. As of March 31, 2018, we are eligible to receive milestone payments based upon the successful achievement of pre-specified research, clinical, and regulatory milestones totaling up to \$530.0 million plus royalty payments on product sales, if any. Kite will receive an exclusive, worldwide license to research, develop, and commercialize engineered autologous T cell therapies incorporating two programs coming from our platform.

In October 2017, we entered into an amendment with Kite to extend the research term of the Collaboration Agreement. Under the amended agreement, we are eligible to receive an additional \$450,000 in research support payments from Kite in two

tranches (instead of a single tranche as previously contemplated by the original Collaboration Agreement) (the “Amendment”). We recorded revenue of \$240,000 and \$737,000 for the three months ended March 31, 2018 and 2017, respectively.

On January 1, 2018, we adopted the new revenue standard using the modified retrospective method. We recognized the cumulative effect of initially applying the new revenue standard as an adjustment to the opening balance of our accumulated deficit. The cumulative effect of the changes related to the adoption of the new revenue standard increased our beginning balances in accumulated deficit and deferred revenue by \$203,000 within our condensed consolidated balance sheet. Prior to the adoption of the new revenue standard, we recognized revenue under the Collaboration Agreement based upon the estimated performance periods related to the non-refundable upfront payments we received from Kite. Under the new standard, we recognize revenue based on employee hours contributed to each performance obligation. We recognized \$112,000 in higher revenue for the three months ended March 31, 2018, as compared to what would have been recorded under previous accounting guidance.

11. Stockholders’ Deficit

Stock-Based Compensation Expense

We use the Black-Scholes option pricing model to estimate the fair value of stock options granted to employees 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. We also record stock options and other stock-based compensation issued to non-employees at fair value as of the date of grant using the Black-Scholes option pricing model. Non-employee awards are remeasured to reflect the current fair value at each reporting period and expense is recognized over the related vesting period. Assumptions used in valuing non-employee stock options are generally consistent with those used for employee stock options with the exception that the expected term is over the contractual life.

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 March 31,	
	2018	2017
	(unaudited)	
Employee:		
Research and development	\$ 197	\$ 13
General and administrative	308	27
Non-Employee:		
Research and development	1	12
General and administrative	5	—
Total stock-based compensation expense	\$ 511	\$ 52

12. Income Taxes

In December 2017, the SEC issued Staff Accounting Bulletin (SAB) 118 to address the application of U.S. GAAP in situations in which a registrant does not have the necessary information available, prepared, or analyzed (including computations) in reasonable detail to complete the accounting for certain income tax effects of the Tax Cuts and Jobs Act (the Tax Reform Act) which was signed into law on December 22, 2017. In March 2018, the FASB issued ASU 2018-05, which amended ASC 740 to incorporate the requirements of SAB 118. We recognized the provisional tax impacts of the Tax Reform Act in the fourth quarter of 2017. During the first quarter of 2018, we did not receive any additional information regarding these provisional calculations, except as disclosed in this footnote. As a result, we continue to anticipate finalizing our analysis in connection with the completion of our tax return for 2017 to be filed in 2018.

We are subject to income taxes in the United States 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. Our effective tax rate for the three-month period ended March 31, 2018 was 0.98%. The difference between the effective tax rate of 0.98% and the U.S. federal statutory rate of 21% for the three-month period ended March 31, 2018 was primarily due to recognizing a full valuation allowance on deferred tax assets.

As of March 31, 2018, we determined that, based on 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.

As part of the merger, we identified \$1.5 million of acquired IPR&D. IPR&D acquired in a business combination is an indefinite-lived intangible asset until the completion or abandonment of the associated R&D efforts. Once the research and development efforts are completed or abandoned, the IPR&D will either be impaired or amortized over the asset life as a finite-lived intangible.

As the acquired IPR&D is not completed, and has not been abandoned, it is considered indefinite-lived for accounting purposes. Any future reversal of a deferred tax liability resulting from IPR&D costs cannot be scheduled for tax purposes and therefore cannot be considered as a source of future taxable income. Thus, as of December 31, 2017, we had recorded a deferred tax liability of \$305,000 as a result of the acquired IPR&D having a financial reporting basis of \$1.5 million and a tax basis of \$0. However, we are projecting a large NOL for the 2018 tax year, and under the newly reformed U.S. corporate income tax laws, federal NOLs incurred during 2018 are carried forward indefinitely. As such, the indefinite nature of the estimated 2018 NOL is such that it can be scheduled against the indefinite lived intangible, thus eliminating the need to record a deferred tax liability outside of the valuation allowance. Accordingly, we have calculated an annual estimated tax rate of 0.98%, which represents the estimated annual benefit of the removal of the deferred tax liability, and have applied the rate to the quarterly results from continuing operations, arriving at a tax benefit for the quarter of \$52,000.

Current tax laws impose substantial restrictions on the utilization of R&D credit and net operating loss carryforwards in the event of an ownership change, as defined by the Internal Revenue Code Section 382 and 383. Such an event may limit our ability to utilize net operating losses and R&D tax credit carryforwards. Under Internal Revenue Code Section 382 and 383, the third quarter 2017 merger with Nivalis Therapeutics is likely considered an ownership change with respect to the potential limitation of the Nivalis Therapeutics federal tax credits and net operating losses. As such, it is likely that any future utilization of Nivalis Therapeutics federal tax credits and net operating losses is substantially limited. Therefore, all Nivalis Therapeutics tax credit and net operating loss carryforwards have been reduced to \$0.

Our net operating loss carry forward amounts expire starting in 2037, while our federal research and development tax credit carry forward amounts expire starting in 2035. As of December 31, 2017, we had accumulated approximately \$12.0 million of federal tax losses and \$0 (tax effected) of state tax losses, and \$600,000 in federal research and development tax credits.

Due to our operating loss carryforwards, all tax years remain open to examination by the major taxing jurisdictions to which we are subject. In the event we are assessed interest or penalties at some point in the future, it will be classified in the financial statements as tax expense.

Under ASC 740, the benefit of an uncertain tax position that is more likely than not of being sustained upon audit by the relevant taxing authority must be recognized at the largest amount that is more likely than not to be sustained. No portion of the benefit of an uncertain tax position may be recognized if the position has less than a 50% likelihood of being sustained. We have an uncertain tax position on our research and development credits as of the three month period ended March 31, 2018. However, no deferred asset is recorded for the credits due to the full valuation allowance.

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 operation for the year ended December 31, 2017, included in our Annual Report on Form 10-K, or the “Annual Report, filed with the SEC on March 28, 2018.

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 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 potential 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 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.

Overview

We are a development-stage immunotherapy company focused on developing treatments for autoimmune/inflammatory diseases and cancer. Our proprietary scientific platform produces Variant Immunoglobulin Domains, or vIgDs, using a process known as directed evolution to create 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 discovery platform to potentially treat patients with serious conditions such as cancer and inflammatory diseases. To achieve our goal, we currently plan to:

- advance our lead program ALPN-101 for the treatment of autoimmune/inflammatory diseases to clinical trials;
- advance our oncology program ALPN-202 for the treatment of cancer to clinical trials;
- develop our inhibitory (checkpoint) receptor agonist and V-mAb programs; 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 convertible preferred stock, funds received from a license and research agreement, debt, 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 March 31, 2018, we have raised an aggregate of \$103.8 million to fund operations, of which \$49.2 million was from the sale of convertible preferred stock, \$5.5 million was through a license and research agreement, \$5.0 million obtained from a long-term loan, and \$44.1 million in cash, cash equivalents, and marketable securities acquired through the merger with Nivalis. As of March 31, 2018, we had cash, cash equivalents, and short-term investments totaling \$76.7 million.

Our net loss was \$5.3 million and \$2.0 million for the three months ended March 31, 2018 and 2017, 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, or multi PD-1 inhibitor and CD28 costimulatory vIgD 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 support 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 public or private 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. Management's discussion and analysis of financial condition and results of operations is based upon the unaudited condensed consolidated financial statements included in this Quarterly Report on Form 10-Q, which we prepared in accordance with generally accepted accounting principles in the United States of America, or GAAP, for interim periods and with Regulation S-X promulgated under the Securities and Exchange Act of 1934, as amended, or the Exchange Act.

Business Combination with Nivalis

On April 18, 2017, we entered into a merger agreement, or the Merger Agreement, with Nivalis, a public biotechnology company. Upon the closing of the merger, (1) a wholly-owned subsidiary of Nivalis merged with and into Alpine, with Alpine (renamed continuing as "AIS Operating Co., Inc.") remaining as the surviving entity; and (2) Nivalis was renamed as "Alpine Immune Sciences, Inc.". On July 24, 2017, the business combination of Alpine and Nivalis was completed. Under the terms of the Merger Agreement, Alpine's preexisting stockholders, warrant holders and option holders received approximately 76% of the fully-diluted shares of common stock of the combined organization in exchange for the transfer of all of Alpine's common stock. This transaction was consummated to provide us with increased access to sources of capital and a broader range of investors to support the clinical development of our products. The acquired assets and liabilities of Nivalis are included in our condensed consolidated balance sheet as of March 31, 2018 and Nivalis' results of operations and cash flows for the period from July 25, 2017 through March 31, 2018 are included in our condensed consolidated statement of comprehensive income and cash flows for the period from July 25, 2017 through March 31, 2018. See notes to the condensed consolidated financial statements included in this Form 10-Q for further information regarding the business combination.

Financial Overview

Revenue

Collaboration and Licensing Revenue

We derive our revenue primarily from our License and Research Agreement (the "Collaboration Agreement"), with Kite Pharma, Inc., or Kite. In October 2015, we entered into the Collaboration Agreement providing Kite with access to two transmembrane immunomodulatory protein, or TIP, programs for use in Kite's engineered cellular therapy programs. We

received \$5.5 million in upfront cash and are eligible to receive up to \$530.0 million upon successful achievement of pre-specified research, clinical, and regulatory milestones in addition to royalties on any products containing our TIPs. In the collaboration, we provide the TIPs and perform *in vitro* testing, while Kite is responsible for *in vivo* testing, manufacturing, and clinical trials. Kite will receive an exclusive, worldwide license to research, develop, and commercialize engineered autologous T cell therapies incorporating two TIP programs coming from our platform.

On October 20, 2017, we entered into an amendment, or the Amendment, with Kite to extend the research term of the Collaboration Agreement. Under the Amendment, we are eligible to receive an additional \$450,000 in research support payments from Kite in two tranches (instead of a single tranche as previously contemplated by the Collaboration Agreement). The Amendment also amended and restated the original research plan. We have adjusted our expected recognition period of the remaining deferred upfront payments over the expected life of the amended research plan and will recognize the potential \$450,000 in additional research support only when the stated milestones have been completed.

We have recognized \$5.2 million in revenue from inception through March 31, 2018 related to the Collaboration Agreement. We may generate revenue in the future from milestone payments made pursuant to the Collaboration Agreement, or from payments from future license or collaboration agreements, product sales, or government contracts and grants. We expect any revenue we generate will fluctuate from quarter to quarter.

Research and Development Expenses

We focus our resources on research and development activities, including the conduct of preclinical 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; and
- allocation of facilities, depreciation, and amortization of laboratory equipment and other expenses.

We incurred \$3.8 million and \$1.9 million in research and development expenses for three months ended March 31, 2018 and 2017, 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 planned clinical trials that we may conduct;
- 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, and finance 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 to 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.

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.

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 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 three months ended March 31, 2018, as compared to those disclosed in our Annual Report except the following:

Recently Adopted Accounting Pronouncements

In May 2014, the Financial Accounting Standards Board, or FASB, issued Accounting Standards Update, or ASU, No. 2014-09, Revenue from Contracts with Customers, as amended ("new revenue standard" or "ASC 606"), which amends the guidance for revenue recognition to replace numerous industry specific requirements. ASC 606, implements a five-step process for customer contract revenue recognition focusing on transfer of control, as opposed to transfer of risk and rewards. ASC 606 also requires enhanced disclosures regarding the nature, amount, timing, and uncertainty of revenues and cash flows from contracts with customers. Other major provisions include ensuring the time value of money is considered in the transaction price, and allowing estimates of variable consideration to be recognized before contingencies are resolved in certain circumstances. On January 1, 2018, we adopted the new accounting standard and all of the related amendments, using the modified retrospective method. We recognized the cumulative effect of initially applying the new revenue standard as an adjustment to the opening balance of our accumulated deficit. The cumulative effect of the changes related to the adoption of the new revenue standard and increased our beginning balances in accumulated deficit and deferred revenue by \$203,000 within our condensed consolidated balance sheet. The comparative information has not been restated and continues to be reported under the accounting standards in effect for those periods. See Note 2 for additional discussion and the impact from the adoption of the new revenue standard.

In August 2016, the FASB issued ASU No. 2016-15 which provides new guidance on the classification of certain cash receipts and payments in the statement of cash flows. The new guidance is intended to reduce diversity in practice in how certain transactions are classified in the statement of cash flows. We adopted this new standard effective January 1, 2018. The adoption of this standard did not impact our financial statements.

In May 2017, the FASB issued ASU No. 2017-09 to provide clarity and reduce both diversity in practice and cost and complexity when applying the guidance in Compensation - Stock Compensation (Topic 718) about a change to the terms and conditions of a share-based payment award. The amendments in this update provide guidance about which changes to the terms or conditions of a share-based payment award require an entity to apply modification accounting in Topic 718. The amendments in this update are effective for annual periods, including interim periods within those annual periods, beginning after December 15, 2017. Early adoption is permitted, and applied prospectively to modifications occurring on or after the adoption date. We adopted this new standard effective January 1, 2018. The adoption of this standard did not have a material impact on our financial statements. For the quarter ended March 31, 2018, there were no modifications to the terms or conditions of a share-based payment award.

Results of Operations

Comparison of Three Months Ended March 31, 2018 and 2017

The following table summarizes our results of operations for the three months ended March 31, 2018 and 2017 (in thousands):

	Three Months Ended March 31,		Increase/ (Decrease)
	2018	2017 (unaudited)	
Collaboration revenue	\$ 315	\$ 737	\$ (422)
Operating expenses:			
Research and development	3,792	1,858	1,934
General and administrative	2,108	873	1,235
Total operating expenses	5,900	2,731	3,169
Loss from operations	(5,585)	(1,994)	(3,591)
Other income (expense):			
Interest expense	(78)	—	(78)
Interest and other income	305	5	300
Loss before taxes	(5,358)	(1,989)	(3,369)
Income tax expense	52	—	52
Basic and diluted net loss attributable to common stockholders	\$ (5,306)	\$ (1,989)	\$ (3,317)

Revenues

The \$0.4 million decrease in revenues was primarily attributable to the timing of revenue recognized under our Collaboration Agreement with Kite and the adoption of ASC 606, Revenue from Contracts with Customers. Under the terms of the Collaboration Agreement, we received upfront payments of \$5.5 million, which were initially recorded as deferred revenue and expensed over the period of the research term. The adoption of ASC 606 resulted in \$112,000 in higher revenue for the 2018 period, as compared to what would have been recorded under previous accounting guidance.

Research and Development Expenses

The \$1.9 million increase in research and development expenses was primarily attributable to an increase of \$1.2 million in direct research, contract manufacturing, and process development activities, an increase of \$0.5 million in personnel-related expenses as a result of growth in headcount to support ongoing discovery and development programs, and an increase of \$0.2 million in allocated overhead and facilities.

General and Administrative Expenses

The \$1.2 million increase in general and administrative expenses was primarily attributable to a \$0.4 million increase in professional and legal service fees to support operating as a public company, a \$0.7 million increase in personnel-related expenses primarily related to an increase in administrative headcount, and a \$0.1 million increase in insurance and facility costs to support the growth and expansion of our business.

Liquidity and Capital Resources

As of March 31, 2018, we had cash, cash equivalents, and short-term investments totaling \$76.7 million. We have raised an aggregate of \$103.8 million to fund operations, of which \$49.2 million was from the sale of convertible preferred stock, \$5.5 million was through a license and research agreement, \$5.0 million advanced from a long-term loan, and \$44.1 million in cash, cash equivalents, and marketable securities acquired through the merger with Nivalis. 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 the Collaboration Agreement. Our ability to earn these milestone and contingent

payments and the timing of achieving these milestones is primarily dependent upon the outcome Kite's research and development activities and 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 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 short-term investments as of the date of this report and research funding that we expect to receive under our existing collaboration, 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

Prior to execution and delivery of the Merger Agreement 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 July 2016, we entered into a sales agreement with a sales agent to sell shares of our common stock through an "at the market" equity offering program for up to \$30.0 million in gross cash proceeds. The sales agreement allows us to 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, limits on the number of shares that may be sold in any one trading day and a minimum price below which sales may not be made. Under the terms of the sales agreement, commission expenses to the sales agent will be 3% of the gross sales price per share sold through the sales agent. The sales agreement shall automatically terminate upon the issuance and sale of placement shares equaling sales proceeds of \$30.0 million and may be terminated earlier by either us, or the sales agent upon 10 days' notice. As of March 31, 2018, approximately 5,000 shares of common stock (as adjusted to reflect the impact of our one-for-four reverse stock split in July 2017), have been sold at an average sales price of \$32.00 per share (as adjusted to reflect the impact of our one-for-four reverse stock split in July 2017) under the sales agreement, net of offering costs of approximately \$140,000. Although the sales agreement is for sales of our common stock of up to \$30.0 million in the aggregate, the amount of shares that we may sell from time to time may be limited due to our status as a smaller reporting company and the market value of our voting and non-voting common equity held by non-affiliates.

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 has an interest-only period expiring on July 1, 2018, at which point we will 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 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 March 31, 2018.

Cash Flows

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

	Three Months Ended March 31,	
	2018	2017
	(unaudited)	
Net cash used in operating activities	\$ (4,431)	\$ (2,164)
Net cash provided by (used in) investing activities	3,870	(108)
Net cash provided by financing activities	7	4,021

Net Cash Used in Operating Activities:

Net cash used in operating activities was \$4.4 million during the three months ended March 31, 2018 compared to \$2.2 million during the three months ended March 31, 2017. The increase in cash used in operations in 2017 as compared to the 2016 period was primarily attributable to personnel-related expenses as a result of increased headcount, increased direct contract research costs to support product development, and cash used to support operating as a public company.

Net Cash Provided by (Used in) Investing Activities:

Net cash provided by investing activities was \$3.9 million during the three months ended March 31, 2018 and consisted primarily of our net purchases and sales of short-term investments in U.S. Treasury securities, commercial paper, and corporate debt securities. Net cash used in investing activities was \$0.1 million during the three months ended March 31, 2017 and related to the purchase of laboratory equipment.

Net Cash Provided by Financing Activities:

Net cash provided by financing activities was \$7,000 during the three months ended March 31, 2018 and consisted of proceeds for the exercise of stock options. Net cash provided by financing activities was \$4.0 million for the three months ended March 31, 2017 and consisted primarily of the sale of preferred stock.

Contractual Obligations and Contingent Liabilities

As of March 31, 2018, there have been no material changes to our contractual obligations and commitments from December 31, 2017 as those disclosed in our Annual Report except the following:

Operating leases

In January 2018, we entered into a lease amendment for approximately 6,184 square feet of additional office and laboratory space adjacent to our existing leased premises in Seattle, Washington. The lease expires on December 31, 2019 and has two options to extend the lease term with each option enabling us to extend the lease term by twelve months. The annual base rent due under the lease is \$295,000 for the first year and will increase by 3.0% each year thereafter.

Inflation

We do not believe that inflation has had a material effect on our business, financial condition or results of operations in the last three fiscal years.

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.

Recent Accounting Pronouncements

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.

Item 3. Quantitative and Qualitative Disclosures about Market Risk.

We are exposed to market risk related to changes in interest rates. As of March 31, 2018, we had cash, cash equivalents, and short-term investments of \$76.7 million, consisting of deposits with commercial banks in checking, 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. The primary objectives of our investment policy are to preserve principal and maintain liquidity to meet operating needs, while also maximizing total returns in a manner that complies with our primary two objectives.

Our investment policy specifies credit quality standards for our investments and limits the amount of credit exposure to any single issue, issuer, or type of investment. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates, particularly because our investments are in short-term securities. We believe that we do not have any material exposure to changes in the fair value of these assets as a result of changes in interest rates due to the short-term nature of our cash equivalents and short-term investments. Declines in interest rates, however, would reduce future investment income. Due to the short-term duration of our investment portfolio and the low risk profile of our investments, an immediate 10% change in interest rates during any of the periods presented would not have had a material effect on the fair market value of our portfolio, or on our financial statements.

We are subject to interest rate risk in connection with the borrowings under our term loan agreement. As of March 31, 2018, we had \$5.0 million outstanding principal amount under our term loan agreement. The term loan bears interest at a rate equal to the lender's prime rate minus 1.75%. A 10% change in interest rates during any of the periods presented would not have had a material effect on our interest obligations under the term loan agreement.

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 March 31, 2018, 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 report, including the section of this report captioned "Management's Discussion and Analysis of Financial Condition and Results of Operations" 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 March 31, 2018, we had \$76.7 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 license and research agreement with Kite, a Gilead company. 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 July 2016, we entered into a sales agreement with Cowen and Company, LLC, or Cowen, to sell up to \$30.0 million worth of shares of our common stock, from time to time, through an “at the market” equity offering program under which Cowen will act as sales agent. 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, and 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 development-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 three months ended March 31, 2018, our net loss was \$5.3 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 license and research agreement with Kite. 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 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 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 vIgDs. 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, the risk profile in humans has yet to be assessed. 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 vIgDs, 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 not 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 Institutional Review Board, or IRB, approval to conduct clinical trials at particular sites, regulatory approvals and successfully commercializing our therapeutic candidates, either alone or with third parties, such as our collaborator Kite. 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. The start or end of a clinical study is often delayed or halted due to changing regulatory requirements, manufacturing challenges, required clinical trial administrative

actions, slower than anticipated patient enrollment, changing standards of care, availability or prevalence of use of a comparative therapeutic or required prior therapy, clinical outcomes, 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, including 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 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. 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 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 product 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. We have conducted no clinical trials to date. 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.

To date, our revenue has been primarily derived from our license and research agreement with Kite, and we are dependent on Kite for the successful development of therapeutic candidates in the collaboration.

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 programs from our technology. Pursuant to the license and research agreement, we will be potentially eligible to receive up to \$530.0 million in total milestone payments upon the successful completion of research, clinical, and regulatory milestones. We will also potentially be eligible to receive a low single-digit percentage royalty for sales on a licensed product-by-licensed product and country-by-country basis.

Continued success of our collaboration with Kite, and our realization of the milestone and royalty payments under the agreement, depends upon the efforts of Kite. Kite has sole discretion in determining and directing the efforts and resources, including the ability to discontinue all efforts and resources, it applies to the development and, if approval is obtained, commercialization and marketing of the therapeutic candidates covered by the collaboration. Kite may not be effective in obtaining approvals for the therapeutic candidates developed under the collaboration arrangement or marketing or arranging for necessary supply, manufacturing, or distribution relationships for any approved products. Kite may change its strategic focus or pursue alternative technologies in a manner resulting in reduced, delayed, or no revenue to us. Kite has a variety of marketed products and its own corporate objectives and strategies may not be consistent with our best interests. If Kite fails to develop, obtain regulatory approval for, or ultimately commercialize any therapeutic candidate under the collaboration or if Kite terminates the collaboration, our business, financial condition, results of operations, and prospects could be materially and adversely affected. In addition, any dispute or litigation proceedings we may have with Kite in the future could delay development programs, create uncertainty as to ownership of intellectual property rights, distract management from other business activities and generate substantial expense.

If we are unable to secure intellectual property rights to programs covered under the license and research agreement, Kite may terminate the agreement and our business, financial condition, results of operations, and prospects could be materially and adversely affected. In addition, any dispute or litigation proceedings we may have with Kite related to intellectual property rights or other aspects of the agreement or the relationship could delay development programs, create uncertainty as to ownership of intellectual property rights, may distract management from other business activities and generate substantial expense.

In October 2017, Kite was acquired by Gilead Pharma, Inc., or Gilead. While the research term of the collaboration was extended after the closing of the acquisition, there is no guarantee Gilead will place the same emphasis on the collaboration or wish to continue the collaboration. If either of these occurs, our business, financial condition, results of operations, and prospects could be materially and adversely affected.

If third parties on which we depend to conduct our 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 preclinical studies of our therapeutic candidates and may do the same for any 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.

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. 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. Any such event could have a material adverse effect on our business, financial condition, results of operations, 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.

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 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. 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 regulatory standards, such as cGMPs. 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 does 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, in addition to our current arrangements with Kite, 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 candidate 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.

The development and commercialization of therapeutic candidates is highly competitive. We believe a significant number of products are currently under development, and may become commercially available in the future, for the treatment of conditions for which we may try to develop therapeutic candidates. There are also competitors to our proprietary therapeutic candidates currently in development, some of which may become commercially available before our therapeutic candidates.

We compete with a variety of multinational pharmaceutical companies and specialized biotechnology companies, as well as with technologies being developed at universities and other research institutions. Our competitors have developed, are developing, or may develop therapeutic candidates and processes competitive with our therapeutic candidates. Competitive therapeutic treatments include those already approved and accepted by the medical community and any new treatments entering or about to enter the market. We are aware of multiple companies developing therapies with the same target as at least one target of our lead program (ICOSL and/or CD28) as well as companies building novel platforms to generate multi-specific antibody or non-antibody-based targeting proteins. While it is still premature for us to determine which indications may be targeted by our lead program, potential competitors to our lead program include:

- an anti-ICOSL/B7RP-1 monoclonal antibody being developed by Amgen, Inc. (may be referred to as AMG557 or MEDI5872);
- an anti-CD28 monoclonal antibody fragment being developed by OSE ImmunoTherapeutics SA and Johnson & Johnson Inc. (FR104);
- a CTLA-4 Ig fusion selective for CD86 fusion protein being developed by Astellas Pharma Inc. (ASP 2408/09);
- a CD28 superagonist monoclonal antibody being developed by TheraMab LLC (TAB08); and
- an anti-BAFF, anti-ICOSL bispecific antibody being developed by Amgen, Inc (AMG/570/MEDI0700).

Platforms potentially competitive with our scientific platform include:

- Nanobody® (Ablynx NV): Platform technology of single-domain, heavy-chain antibody fragments derived from camelidae (e.g., camels and llamas);
- DART® (Macrogenics Inc): Dual-Affinity Re-Targeting and Trident technology platforms bind multiple targets with a single molecule;
- Anticalin® (Pieris Pharmaceuticals Inc): Engineered proteins derived from natural lipocalins found in blood plasma;
- Targeted Immunomodulation™ (Compass Therapeutics LLC): Antibody discovery targeting the tumor-immune synapse;
- Harpoon Therapeutics Inc: Trispecific antigen-binding proteins;
- Various bispecific antibody platforms (e.g., Amgen Inc (BiTE®—approved), Roche AG (RG7828), Zymeworks Inc (Azymetric™), Xencor Inc (XmAb Bispecific), Compass Therapeutics (StitchMabs™));
- Five Prime Therapeutics®: Proprietary protein library and rapid protein production and testing platform;
- Regeneron®: VEGF Trap and VelociSuite® antibody technology platforms; and
- Shattuck Labs® Agonist Redirected Antibody platform claimed to bind tumor-necrosis factor (“TNF”) and checkpoint targets.

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, Jay R. Venkatesan, M.D., our President and a member of our board of directors, Stanford Peng, M.D., Ph.D., our Executive Vice President of Research and Development and Chief Medical Officer, 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.

If four 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 any 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, 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. Any product promotion and advertising will also be subject to regulatory requirements and continuing regulatory review.

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 not have 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, 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 vIgD 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 ability 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 March 31, 2018, we had \$76.7 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.

Nivalis' pre-merger net operating loss carryforwards and certain other tax attributes are likely subject to limitations. The pre-merger net operating loss carryforwards and certain other tax attributes of Alpine and of the combined organization may also be subject to limitations as a result of ownership changes resulting from the merger.

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 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;

- compete 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 counterstructures 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, or approval for marketing, or interfere with our ability to market our product to patients and physicians or achieve reimbursement from payors.

Because we have no products currently in human clinical trials, 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 in peer-reviewed scientific publications or apply to present data related to our research and development 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 in peer-reviewed scientific publications or present data related to our research and development 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 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 March 31, 2018, our patent portfolio consists of over 30 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. 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 you 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, and the USPTO, 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 for a given period 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 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 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, and non-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 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 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 rely, and will continue to rely, upon intellectual property rights licensed from third parties to protect our technology, including platform technology and therapeutic candidates and products. We are a party to a number of licenses granting us rights to third-party intellectual property necessary or useful for our business. We may also license additional third-party intellectual property in the future. 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, the 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, substantially all of our existing licenses are non-exclusive and we may not be able to obtain exclusive rights in licenses obtained in the future, which would potentially allow third parties to develop competing products or technology. Without protection for, or exclusive right to, the intellectual property we license, other companies might be able to offer substantially identical products for sale, which could adversely affect our competitive business position and harm our business prospects. In addition, we may sublicense our rights under our 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. A U.S. utility application and international application under the Patent Cooperation Treaty, or PCT, are usually filed within twelve months after the priority filing. Based on the PCT filing, national and regional patent applications may be filed in various international jurisdictions, such as the European Union, Japan, Australia, and Canada. 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 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. 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 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, 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. 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. 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, for example, from 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 laws, regulations, guidance, or interpretations will be changed, or what the impact of such changes, if any, may be.

Because the therapeutics we are developing may represent a new class of therapeutics, the FDA and its foreign counterparts have not yet established any definitive policies, practices, or guidelines 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 reclassify them, namely 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. In addition, because there may be approved treatments for some of the diseases for which we may seek approval, in order to receive regulatory approval, we may need to demonstrate through clinical trials the therapeutic candidates we develop to treat these diseases, if any, are not only safe and effective, but safer or more effective than existing products.

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. 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 the labeling or 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 a Biologics License Application, or 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 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 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
- civil and criminal penalties and fines.

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 candidate, our ability to market and derive revenue from the therapeutic candidates 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 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 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 candidates 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.

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. This referendum has created political and economic uncertainty, particularly in the United Kingdom and the European Union, and this uncertainty may last for years. 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 referendum, and the likely withdrawal of the United Kingdom from the European Union it triggers, has caused and, along with events potentially occurring in the future as a consequence of the United Kingdom’s withdrawal, including the possible breakup of the United Kingdom, 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 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 following the merger 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;
- 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, own approximately 68% of our outstanding common stock as of March 31, 2018. 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.

The resale of approximately 10.3 million shares was previously prohibited as a result of lock-up agreements entered into by certain of our stockholders in connection with our merger with Alpine Immune Sciences, Inc. in July 2017; however, subject to applicable securities law restrictions, these shares became eligible for sale in the public market beginning January 21, 2018. In addition, the shares subject to outstanding options and warrants, of which options and warrants to purchase 559,125 shares and 14,819 shares, respectively, were exercisable as of March 31, 2018, 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 under our sales agreement with Cowen, 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 “at the market” equity offering program 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 to us from our “at the market” equity offering program put into place in July 2016, 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 “at the market” equity offering program for general corporate purposes, 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. Our use of the proceeds may not improve our operating results or increase the value of the securities offered pursuant to the “at the market” equity offering program.

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 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 submit 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 Alpine did not incur as a private company, including costs 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 costly. For example, our management team will consist 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			Filing Date	Filed Herewith
		Form	File No.	Exhibit		
10.1+	Employment Agreement, dated as of January 1, 2018, by and between the Registrant and Mitchell H. Gold, M.D.	10-K	001-37449	10.33	3/28/2018	
10.2+	Employment Agreement, dated as of January 1, 2018, by and between the Registrant and Paul Rickey	10-K	001-37449	10.35	3/28/2018	
10.3+	Employment Agreement, dated as of January 1, 2018, by and between the Registrant and Stanford Peng, M.D., Ph.D.	10-K	001-37449	10.37	3/28/2018	
10.4+	Non-Employee Director Compensation Guidelines					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

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

* 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.

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: May 14, 2018

By: /s/ Mitchell Gold

Name: Mitchell Gold

Title: Executive Chairman and Chief Executive Officer

ALPINE IMMUNE SCIENCES, INC.

Date: May 14, 2018

By: /s/ Paul Rickey

Name: Paul Rickey

Title: Senior Vice President and Chief Financial Officer

Alpine Immune Sciences, Inc.

Non-Employee Director Compensation Guidelines

As of March 2018

The purpose of these Non-Employee Director Compensation Guidelines (the “*Guidelines*”) of Alpine Immune Sciences, Inc., a Delaware corporation the (the “*Company*”), is to provide a total compensation package that enables the Company to attract, retain and reward, on a long-term basis, directors who are not employees or officers of the Company or its subsidiaries (“*Outside Directors*”) to serve on the Company’s Board of Directors (the “*Board*”). A Board member who is also an officer or employee of the Company will not receive any Annual Cash Retainers or Equity Retainers for his or her service on the Board. In furtherance of the purpose stated above, all Outside Directors shall be paid compensation for services provided to the Company as set forth below:

I. Annual Cash Retainers

A. <u>Annual Retainer for Board Membership</u> : for general availability and participation in meetings and conference calls of our Board of Directors	\$ 35,000
B. <u>Additional Retainer for Board Chairman</u> :	\$ 25,000
C. <u>Additional Retainers for Committee Membership</u> :	
Audit Committee Chairperson:	\$ 15,000
Audit Committee member:	\$ 7,500
Compensation Committee Chairperson:	\$ 10,000
Compensation Committee member:	\$ 5,000
Nominating and Corporate Governance Committee Chairperson:	\$ 7,500
Nominating and Corporate Governance Committee member:	\$ 3,750

Annual Cash Retainers are paid quarterly in arrears. Any Outside Director that is appointed mid-fiscal year will receive his or her Annual Cash Retainer on a pro-rated basis.

II. Equity Retainers

All grants of equity retainer awards to Outside Directors pursuant to these Guidelines will be automatic and nondiscretionary and will be made in accordance with the following provisions:

A. Granting of Awards.

1. *Initial Award.* Each individual who is first elected or appointed as an Outside Director shall automatically be granted, on the date of such initial election or appointment, a nonqualified stock option (the “*Option*”) to purchase 7,650 shares of the Company’s common stock (the “*Initial Option*”), pursuant to the equity plan in effect at the time of grant (the “*Plan*”).

2. *Annual Award.* On the first trading day in January of each year, each Outside Director who is continuing to serve as such shall automatically be granted an Option to purchase 7,650 shares of the Company’s common stock (the “*Annual Option*”), pursuant to the Plan. There shall be no

limit on the number of Annual Options that an Outside Director may receive over his or her period of Board service.

3. *Award Agreement.* Each Option granted pursuant to these shall be evidenced by an agreement between the Outside Director and the Company in such form as the Board, the Committee or their respective authorized designee shall determine, which complies with the terms specified in these Guidelines (the “*Option Agreement*”).

4. *Exercise Price.* The exercise price per share of each Option shall be equal to one hundred percent (100%) of the Fair Market Value, as defined in the Plan, per share of the Company’s common stock on the grant date of the Option (the “*Grant Date*”).

5. *Option Term.* Each Option shall have a term of ten (10) years measured from the Grant Date.

6. *Vesting.* Subject to the other provisions of these Guidelines, the Plan and the Option Agreement:

(a) *Initial Options.* The shares subject to each Initial Option shall vest one thirty-sixth on each one-month anniversary of the Grant Date, such that the Option will be fully vested on the three-year anniversary of the Grant Date.

(b) *Annual Options.* The shares subject to each Annual Option shall vest one twelfth on each one-month anniversary of the Grant Date, such that the Option will be fully vested on the one-year anniversary of the Grant Date.

7. *Effect of Cessation of Board Service.* The following provisions shall govern the exercise of any Option held by an Outside Director at the time he or she ceases to serve as a Board member (the “*Optionee*”):

(a) The Optionee shall have a three-month period following the date of such cessation of Board service (the “*Termination Date*”) in which to exercise any vested but unexercised portion of the Option if Optionee’s service terminates for any reason other than death, disability or cause. If Optionee’s service terminates for cause, the Option will expire on the Termination Date. If Optionee’s service terminates due to death or disability, the Optionee (or, in the event of the Optionee’s death, the personal representative of the Optionee’s estate or the person or persons to whom the Option is transferred pursuant to the Optionee’s will or in accordance with the laws of descent and distribution) shall have a six-month period following the Termination Date in which to exercise any vested but unexercised portion of the Option.

(b) The unvested portion of the Option shall be cancelled as of the Termination Date. During the post-Termination Date exercise period, if any, the Option may not be exercised for more than the number of shares of common stock in which the Optionee is vested at the time of his or her Termination Date.

(c) In no event shall the Option remain exercisable after the expiration of the Option’s term.

B. Approval of Grants. The Board's approval of these Guidelines shall constitute pre-approval of each Option granted under these Guidelines, and the subsequent exercise of such Option in accordance with the terms and conditions of these Guidelines, the Plan and the Option Agreement.

C. Corporate Transaction or Change in Control. In the event of a Corporate Transaction or Change in Control, as defined in the Plan, awards granted to Outside Directors pursuant to these Guidelines will be fully vested and exercisable immediately prior to the consummation of such Corporate Transaction or Change in Control.

D. Revisions. The Board in its discretion may change and otherwise revise the terms of awards to be granted under these Guidelines, including, without limitation, the number of shares subject thereto, for awards of the same or different type granted on or after the date the Compensation Committee of the Board (the "*Compensation Committee*") makes a recommendation of any such change or revision.

All equity grants under these Guidelines will be made automatically in accordance with the terms of these Guidelines, the Plan and the Option Agreement, without the need for any additional corporate action by the Board or the Compensation Committee.

III. Expenses

The Company will reimburse all reasonable out-of-pocket expenses incurred by Outside Directors in the performance as their duties as members of the Board, in accordance with the Company's policy governing reimbursement of business expenses as in effect from time to time.

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: May 14, 2018

/s/ Mitchell Gold

Mitchell Gold

*Executive Chairman and Chief Executive Officer
(Principal Executive Officer)*

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: May 14, 2018

/s/ Paul Rickey

Paul Rickey

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

**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 March 31, 2018, 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)*

May 14, 2018

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.

**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 March 31, 2018, 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*)

May 14, 2018

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.

