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

FORM 10-K

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

For the fiscal year ended December 31, 2020

OR

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

Commission File Number 001-37449

ALPINE IMMUNE SCIENCES, INC.

(Exact name of Registrant as specified in its Charter)

Delaware	**20-8969493**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
188 East Blaine Street Suite 200 Seattle, WA	**98102**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: (206) 788-4545

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

Title of each class	Trading Symbol	Name of each exchange on which registered
Common Stock, par value $0.001 per share	ALPN	The Nasdaq Stock Market LLC

Securities registered pursuant to Section 12(g) of the Act: None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☐ No ☒

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 15(d) of the Act. Yes ☐ No ☒

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

Indicate by check mark whether the Registrant has submitted electronically every Interactive Data File required to be submitted 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 such files). Yes ☒ No ☐

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

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

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

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report.☐

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

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant, based on the closing price of the shares of common stock on the Nasdaq Stock Market on June 30, 2020, was approximately $49.6 million. Shares of common stock held by each executive officer and director and by each other person who may be deemed to be an affiliate of the registrant, have been excluded from this computation. The determination of affiliate status for this purpose is not necessarily a conclusive determination for other purposes.

The number of shares of the registrant's common stock outstanding as of March 10, 2021 was 23,882,138.

DOCUMENTS INCORPORATED BY REFERENCE

None.

Table of Contents

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.

Summary Risk Factors

Our business is subject to numerous risks and uncertainties, including those highlighted in the section of this report captioned "Risk Factors." The following is a summary of the principal risks we face:

- Our approach to the discovery and development of innovative therapeutic treatments based on our technology is unproven and may not result in marketable products.
- 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.
- Product development involves a lengthy and expensive process with an uncertain outcome, and results of earlier preclinical and clinical trials may not be predictive of future clinical trial results.
- 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.
- To date, our revenue has been primarily derived from our collaboration agreements, and our success will be dependent, in part, on our collaborators' efforts to develop our therapeutic candidates.
- If third parties on which we depend to conduct our clinical or preclinical studies, or any future clinical trials, do not perform as expected, fail to satisfy regulatory or legal requirements, or miss expected deadlines, our development program could be delayed, which may result in materially adverse effects on our business, financial condition, results of operations, and prospects.
- 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.
- The COVID-19 coronavirus could adversely impact our business, including our clinical trials.
- Our business and operations could suffer in the event of system failures.
- 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 are an early stage biopharmaceutical company with a history of losses, we expect to continue to incur significant loses for the foreseeable future, we may never achieve or maintain profitability, and we have a limited operating history that may make it difficult for investors to evaluate the potential success of our business.
- 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.
- We may license patent rights from third-party owners or licensees. If such owners or licensees do not properly or successfully obtain, maintain or enforce the patents underlying such licenses, or if they retain or license to others any competing rights, our competitive position and business prospects may be materially and adversely affected.
- We 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.
- 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.
- We may be unable to obtain U.S. or foreign regulatory approval and, as a result, may be unable to commercialize our therapeutic candidates.
- 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.
- 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.
- 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.

Forward-Looking Statements

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

- *our ability to identify, develop and commercialize additional products or product candidates;*
- *our estimates regarding our expenses, revenues, anticipated capital requirements and our needs for additional financing;*
- *our ability to obtain funding for our operations;*
- *the implementation of our business model and strategic plans for our business and technology;*
- *the timing of the commencement, progress and receipt of data from any of our preclinical and clinical trials;*
- *the expected results of any preclinical or clinical trial and the impact on the likelihood or timing of any regulatory approval;*
- *the scope of protection we are able to establish and maintain for intellectual property rights covering our technology and product candidates;*
- *the anticipated impact of the COVID-19 pandemic on our business, research and clinical development plans and timelines and results of operations;*
- *the timing or likelihood of regulatory filings and approvals;*
- *the therapeutic benefits, effectiveness and safety of our product candidates;*
- *the rate and degree of market acceptance and clinical utility of any future products;*
- *our ability to maintain and establish collaborations;*
- *our ability to achieve milestones in our current and any future collaborations;*
- *our expectations regarding market risk, including interest rate changes;*
- *our expectations regarding the sufficiency of our cash and cash equivalents to fund operations for at least the next 12 months;*
- *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 I, Item 1A. Risk Factors, and elsewhere in this report. Forward-looking statements are based on our management's beliefs and assumptions and on information currently available to our management. These statements, like all statements in this report, speak only as of their date, and we undertake no obligation to update or revise these statements in light of future developments, except as required by law.

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

PART I

Item 1. Business

Overview

We are a clinical-stage biopharmaceutical company dedicated to discovering and developing innovative, protein-based immunotherapies to treat cancer and autoimmune and inflammatory diseases. Our approach includes a proprietary scientific platform that converts native immune system proteins into differentiated, multi-targeted therapeutics. We believe our strategies are capable of meaningfully modulating the human immune system and significantly improving outcomes in patients with serious diseases.

Autoimmune/Inflammatory Diseases

ALPN-101 is a dual ICOS and CD28 antagonist intended for the treatment of autoimmune and inflammatory diseases. Preclinical studies have demonstrated efficacy in models of systemic lupus erythematosus, or SLE, Sjögren's syndrome, or SjS, arthritis, inflammatory bowel disease, multiple sclerosis, type 1 diabetes, uveitis, and graft versus host disease, or GVHD. In a presentation at the 2020 European League Against Rheumatism, or EULAR, E-Congress and in a peer reviewed publication in the journal *Clinical and Translational Science*, we presented data from our Phase 1 healthy volunteer study demonstrating that ALPN-101 was generally well-tolerated with no evidence of cytokine release, clinically significant immunogenicity, or severe adverse events. In June 2020, we entered into an Option and License Agreement, or the AbbVie Agreement, with AbbVie Ireland Unlimited Company, or AbbVie, which grants to AbbVie an exclusive option to take an exclusive license to ALPN-101. Under the terms of the agreement, we received an upfront payment of $60.0 million, and will also be eligible to receive up to an aggregate of $805.0 million for exercise of the option and success-based development, regulatory and commercial milestones. In addition, we are eligible to receive tiered royalties on net sales of ALPN-101. We intend to initiate a Phase 2 study of ALPN-101 in SLE in mid-2021. For additional information regarding the AbbVie Agreement, please see "—Partnerships—Collaboration with AbbVie (June 2020)."

ALPN-303 is a dual B cell cytokine antagonist being developed for B cell-mediated autoimmune/inflammatory diseases. Engineered using our proprietary directed evolution platform, ALPN-303 is a potent inhibitor of the pleiotropic B cell cytokines B cell activating factor, or BAFF, and a proliferation inducing ligand, or APRIL, which may play key roles in certain autoimmune/inflammatory disease through their regulation of B cell development, differentiation, and survival. Data presented at the 2020 EULAR E-Congress demonstrate that engineered proteins in the ALPN-303 series reduced important disease parameters such as proteinuria, serum autoantibodies, and nephritis in a preclinical efficacy model of lupus. We are targeting completion of activities to support initiation of a Phase 1 healthy volunteer study with ALPN-303 in the fourth quarter of 2021.

Immuno-oncology

Our lead oncology program is ALPN-202, a conditional CD28 costimulator and dual checkpoint inhibitor intended for the treatment of cancer. Preclinical *in vivo* data have demonstrated monotherapy efficacy in tumor models superior to approved therapies. In addition, ALPN-202 has a unique immuno-modulatory profile and has demonstrated evidence of anti-tumor immunity in preclinical models. Based on ALPN-202's efficacy in preclinical models and favorable nonclinical safety and development profile, we initiated NEON-1, a Phase 1 dose escalation and expansion study in patients with advanced malignancies, in 2020 and intend to continue enrolling patients throughout 2021. We plan to disclose interim data on NEON-1 at an upcoming medical conference and to determine expansion cohorts later this year. We also intend to initiate NEON-2, a Phase 1 combination study of ALPN-202 and a PD-1 inhibitor later this year.

Our scientific platform has also generated immune modulatory proteins with the potential of improving engineered cellular therapies, or ECT, such as chimeric antigen receptor T cells, or CAR-T, T cell receptor-engineered T cells, or TCR-T, and tumor infiltrating lymphocytes, or TILs. In May 2019, we signed a collaboration and license agreement with Adaptimmune Therapeutics plc, or Adaptimmune, to develop next-generation SPEAR™ T cell products which incorporate our secreted and transmembrane immunomodulatory protein (termed SIP™ and TIP™) technology. We intend to continue to leverage our existing pipeline and platform to actively explore and evaluate potential value-creating partnering opportunities.

Our Strategy

Our goal is to discover and develop modern therapies to treat patients with serious conditions such as cancer and autoimmune/inflammatory diseases. To achieve our goals, we intend to:

Aggressively move our lead autoimmune/inflammatory program ALPN-101 through clinical development as part of our Option and Licensing Agreement with AbbVie.

- We intend to conduct a Phase 2 clinical study of ALPN-101 for the treatment of SLE, including all non-clinical process development, and manufacturing activities required to support the development plan with AbbVie. We intend to initiate the Phase 2 study of ALPN-101 in SLE in mid-2021.

Aggressively move our second autoimmune/inflammatory program ALPN-303 through preclinical development and into the clinic.

- We are targeting completion of activities to support the initiation of a Phase 1 healthy volunteer study in the fourth quarter of 2021.

Aggressively move our lead oncology program ALPN-202 through clinical development for the treatment of cancer.

- We intend to continue enrolling patients in NEON-1, a Phase 1 dose escalation and expansion clinical study in patients with advanced malignancies, throughout 2021. We also intend to initiate NEON-2, a Phase 1 combination study of ALPN-202 and a PD-1 inhibitor later this year.

Maximize the value of our pipeline and platform via potential partnering activities.

- We intend to continue to leverage our existing pipeline and platform to actively explore and evaluate potential value-creating partnering opportunities.

Product Pipeline

We have a diverse pipeline of novel therapies, as shown in **Figure 1** below.

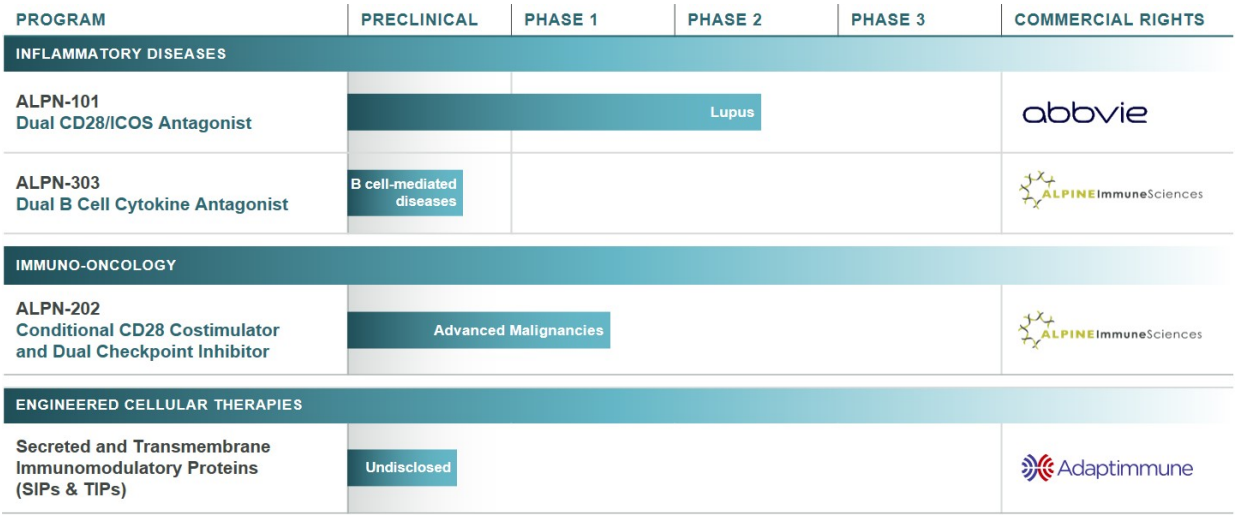

Figure 1

Our Scientific Platform

The human immune system is a complex network of biological processes and structures evolved to protect humans from external infections and harmful changes of internal cells. Within the immune system, proteins play a key role in a variety of

essential functions, including recognition of foreign and self-antigens, cell adhesion and trafficking, and modulation of cellular activity through costimulatory or inhibitory signaling. Our scientific platform seeks to develop novel therapeutics by engineering native, or so-called “wild-type,” proteins with unique properties that may benefit patients with cancer or inflammatory diseases. We have focused our efforts to-date on two major protein superfamilies that play critical roles in the regulation of immune cell signaling and activity: the immunoglobulin superfamily, or IgSF, and the tumor necrosis factor (receptor) superfamily, or TNFSF/TNFRSF.

The IgSF is the largest family of adhesion, costimulatory (activating), and inhibitory (blocking) proteins found on the surface of immunological, neurological, and other human cell types. These cell surface and soluble molecules are broadly involved with recognition of antigens, assisting in the formation of the immune synapse, and performing costimulatory, coinhibitory, and cytokine receptor signaling functions. This family includes many well-known targets, such as those seen in **Figure 2**. We believe the IgSF protein family members may be particularly valuable because many IgSF proteins naturally bind multiple binding partners, also referred to as “counterstructures.” ALPN-101 and ALPN-202 are both derived from members of the IgSF.

Group	Examples
Checkpoint	PD-1, PD-L1, CTLA-4, TIGIT, LAG-3, VISTA, CD47
Costimulatory	CD28, ICOS, CD80, CD86, CD2
Antigen Receptor-Related	CD3, TCR, BCR, MHC, CD19, CD4, CD8
Cytokine Receptors	IL-1R, IL-6R, CSF1R

Figure 2

TNFSF/TNFRSF proteins are expressed broadly in the immune system and play a critical role in immune cell signaling and proliferation. TNFSF/TNFRSF members are composed of 48 unique proteins that are structurally similar and are characterized by their ability to bind to trimeric tumor necrosis factors (**Figure 3**). Members of the TNFSF/TNFRSF include many clinically relevant targets with applications in both autoimmune disease and immuno-oncology (e.g., CD40, TACI, BCMA, 4-1BB, TNFα).

The TNF Superfamily

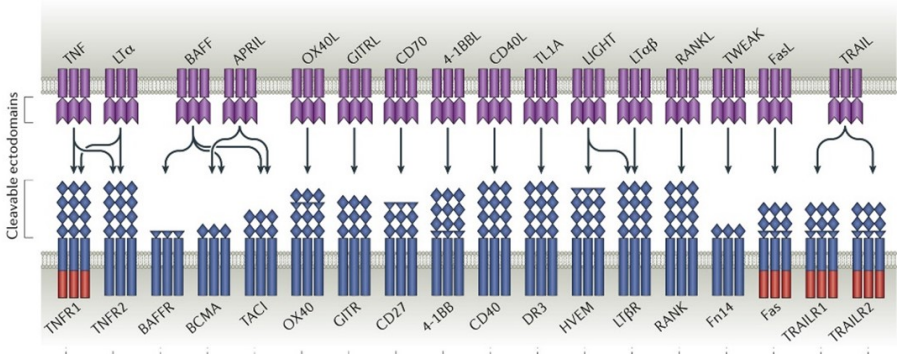

Figure 3

Our scientists create engineered proteins from IgSF members (variant immunoglobulin domains, or vIgDs) and TNFSF/TNFRSF members (variant TNF domains, or vTDs). We use directed evolution, which is an iterative scientific engineering process purposefully conducted to modify an IgSF and TNFSF/TNFRSF protein for a desired therapeutic function. The potential to create therapies capable of working within a formed immune synapse, forcing a synapse to occur, or preventing a synapse from occurring are important, novel attributes of our scientific platform.

Figure 4 illustrates the process of directed evolution in our scientific platform. Our scientists utilize yeast display protein library strategies to identify variants of wild-type proteins with desired binding characteristics. We start with a wild-type IgSF or TNFSF/TNFRSF protein and then enter a cycle of library generation and yeast display. Flow cytometry or other methods are used to sort for yeast clones displaying variants with desired binding characteristics. Biologic and biophysical assays of purified proteins assess biological function and manufacturing characteristics. The end product is an optimized vIgD or vTD. Additional cycles can be carried out by building next generation libraries from the output of prior libraries to result in further optimization.

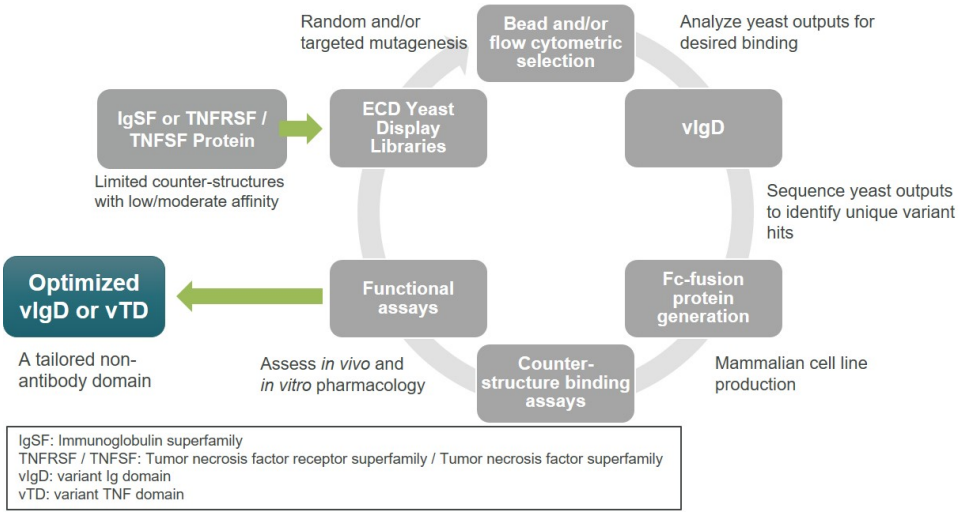

Figure 4

Our scientific platform is generally able to improve upon native IgSF or TNFSF/TNFRSF activity regardless of whether natural binding affinity is weak or strong. When starting affinity is very weak, techniques employed by our scientists have accomplished several thousand-fold increases in binding affinity with sometimes as few as two library generation cycles. Even when starting affinity is very high, our scientific platform can still improve binding affinities. The same general strategies can be used when the desired therapeutic profile requires reduced affinity compared to the wild-type protein. We have applied our scientific platform to several IgSF and TNFSF/TNFRSF protein targets.

We believe our vIgDs and vTDs are highly flexible. In many cases, a single affinity-maturation campaign can result in multiple domains suitable for use in the formats such as those illustrated in **Figure 5** and further described below.

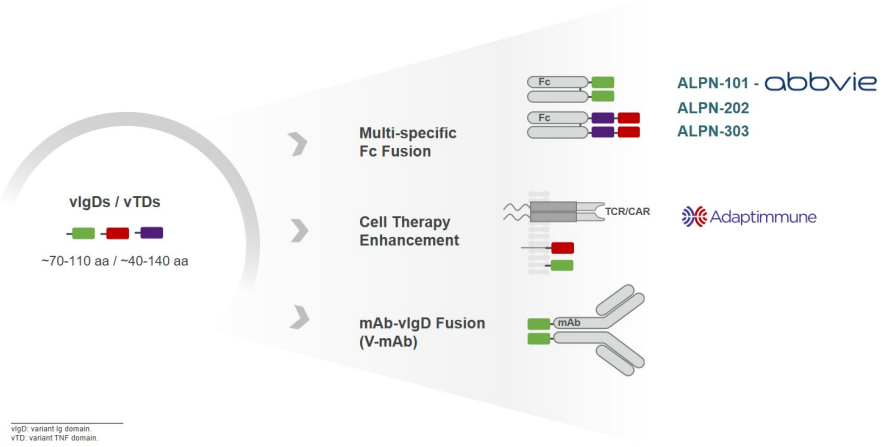

Figure 5

vIgD-Fc or vTD-Fc

A vIgD- or vTD-Fc fusion protein is the simplest format. Our lead autoimmune/inflammatory program, ALPN-101, and lead oncology program, ALPN-202, are both examples of vIgD-Fc formats. The engineered vIgD protein is fused to an Fc backbone. Combining vIgDs or vTDs with antibody Fc domains to make Fc fusion proteins potentially allows for better expression, facilitates purification, and improves pharmacokinetic (dosing) properties. Fc fusion proteins are a standard format in the industry, with examples such as etanercept, abatacept, and belatacept. A vIgD- or vTD-Fc could potentially be administered intravenously, subcutaneously, topically, or via other methods of delivery.

Cell Therapy Enhancement

Our scientific platform has also generated immune modulatory proteins with the potential of improving engineered cellular therapies, such as CAR-Ts, TCR-Ts, or TILs.

ALPN-101, a Dual ICOS/CD28 Antagonist for Autoimmune/Inflammatory Diseases

Our lead autoimmune/inflammatory disease program, ALPN-101, is an Fc fusion protein of a human inducible T cell costimulator ligand, or ICOSL, vIgD designed to inhibit simultaneously the CD28 and ICOS T cell costimulatory pathways (**Figure 6**). This vIgD is fused to an “effectorless” Fc backbone and is intended for the potential treatment of autoimmune/inflammatory diseases. Notably, ALPN-101 is not a bispecific antibody construct. A traditional bispecific might be constructed of one domain binding ICOS and one domain binding CD28. Instead, ALPN-101 makes use of a novel single vIgD domain capable of binding both ICOS and CD28 engineered by our scientists using our proprietary scientific platform.

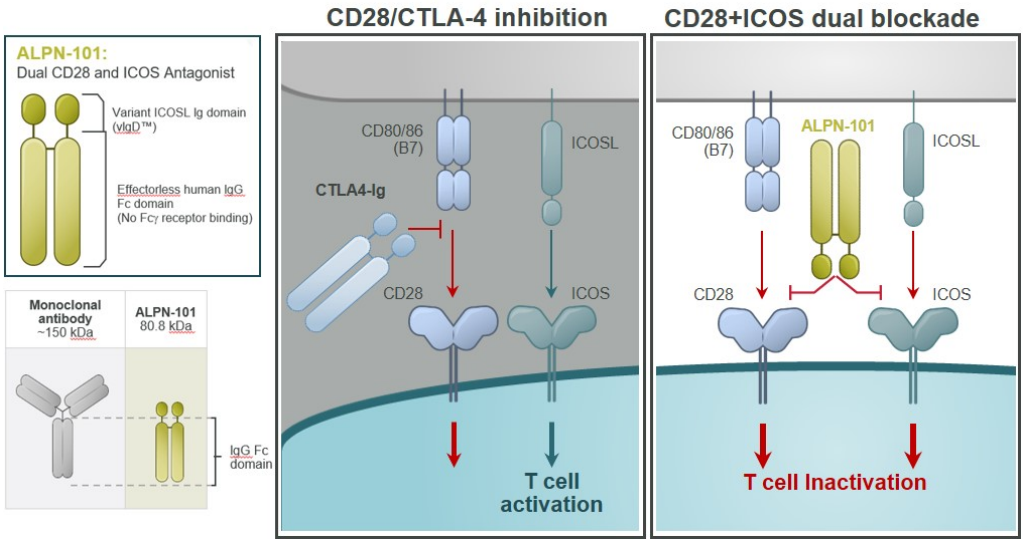

Figure 6

CD28 has been long recognized to be required for naïve T cell activation. The therapeutic inhibitors of the CD28 pathway (e.g., abatacept, CTLA4-Ig; and belatacept, a second generation CTLA4-Ig) have proven valuable for the treatment of some inflammatory arthritis conditions (rheumatoid arthritis, juvenile idiopathic arthritis, psoriatic arthritis) and for the prevention of renal allograft rejection. However, therapeutic blockade of the CD28 pathway, primarily as studied with abatacept, has not been successful in several other inflammatory diseases (e.g., Crohn's disease, lupus nephritis, multiple sclerosis) despite extensive evidence implicating T cells in disease pathogenesis and evidence of clinical biological activity. This suggests an additional pathogenic costimulatory pathway(s) remains unaddressed.

Inducible T cell Costimulator, or ICOS, is part of the CD28 costimulatory family of molecules, including PD-1, CD28, and CTLA-4. ICOS is related to CD28, but, in contrast, is poorly expressed in naïve T cells. ICOS is, however, rapidly induced upon T cell activation. It appears to be a dominant costimulatory pathway in at least some effector or pathogenic T cells, such as potentially in the absence of CD28. Elevated levels of ICOS-expressing T cells have been described in an increasing number of autoimmune/inflammatory diseases, correlating with disease activity. At the same time, inhibition of ICOS is effective in several preclinical inflammatory disease models. The ICOS pathway may therefore represent a major costimulatory pathway, nonredundant with CD28, and highly relevant to autoimmune/inflammatory diseases.

We have performed a number of preclinical experiments demonstrating ALPN-101 is active in both *in vitro* and *in vivo* models, several of which are described below.

A potent immunomodulator of diseased cells

ALPN-101 inhibits cytokine production from human peripheral blood mononuclear cells *in vitro* more potently than single CD28 (abatacept, or CTLAr-Ig) or ICOS (prezalumab, or anti-ICOSL mAB) pathway inhibitors alone or in combination (**Figure 7**).

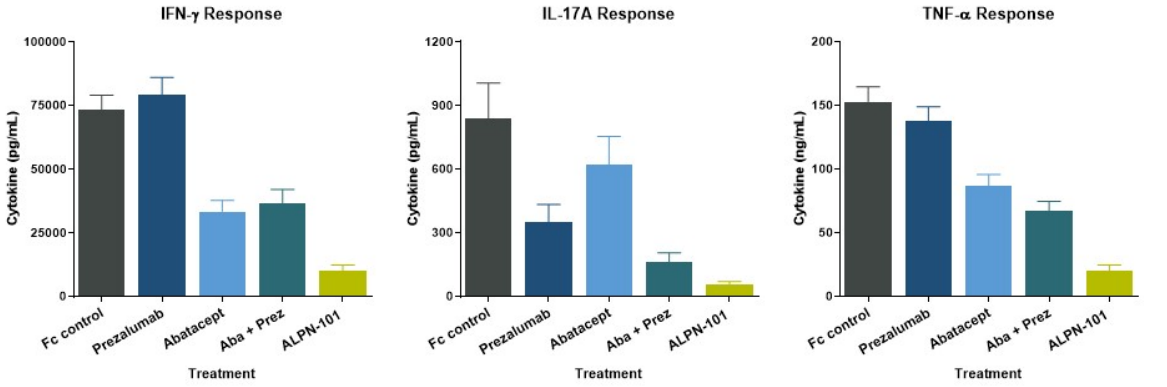

Figure 7

Sjögren's Syndrome Model

Sjögren's syndrome is an autoimmune disease in which immune cells attack the glands that produce saliva and tears. In an animal model of salivary gland inflammation (sialoadenitis), a key organ manifestation of Sjögren's syndrome, ALPN-101 appeared more efficacious in reducing the incidence and severity of sialadenitis as compared to abatacept or wild-type ICOSL-Fc alone or in combination. These data were presented at the 2019 annual meeting of the American College of Rheumatology. (**Figure 8)**

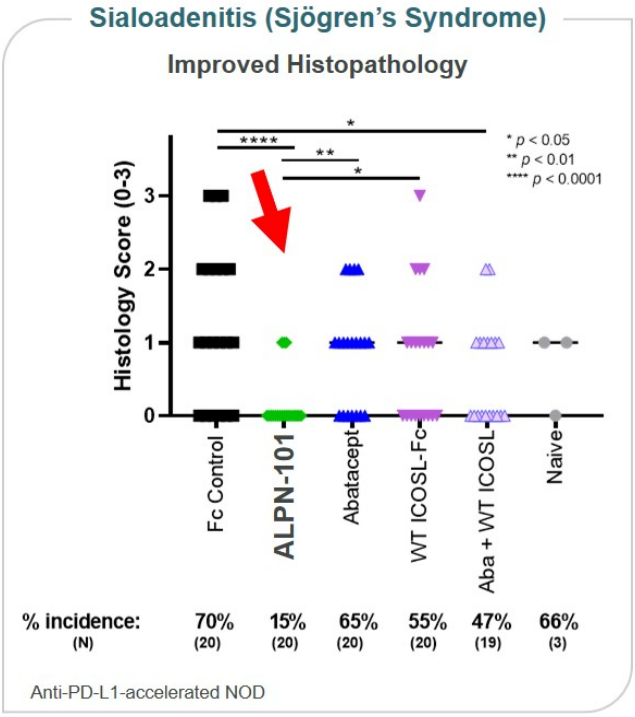

Figure 8

Systemic Lupus Erythematosus Model

ALPN-101 has demonstrated efficacy in a preclinical model of SLE, a multiorgan autoimmune disease that that can lead to serious organ complications and death. In **Figure 9**, which evaluated ALPN-101 in a bm12 inducible model of SLE, treatment with ALPN-101 reduced serum titers of anti-dsDNA autoantibodies throughout the study compared to Fc control treatment. These data were presented at the 2019 annual meeting of the American College of Rheumatology.

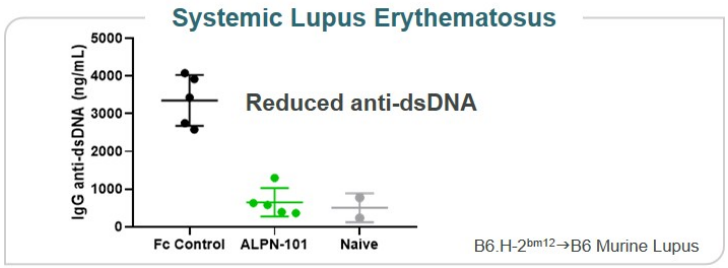

Figure 9

Arthritis Model

Figure 10 shows data from an *in vivo* collagen-induced arthritis model. This model is designed to test a drug's ability to reduce inflammatory signals thought to play a role in rheumatoid arthritis, psoriatic arthritis, and other types of inflammatory arthritis conditions. In the data presented at the 2019 annual meeting of the American College of Rheumatology, ALPN-101 was superior to abatacept, a drug approved by the FDA to treat rheumatoid, psoriatic, and juvenile idiopathic arthritis.

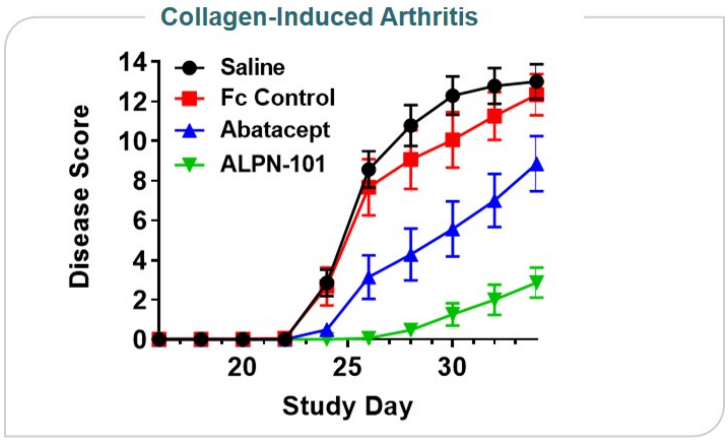

Figure 10

Human Xenograft GVHD Model

ALPN-101 has been studied in an *in vivo* mouse model of GVHD, a damaging and potentially fatal inflammatory disease frequently observed following allogeneic stem cell and/or bone marrow transplant treatments for cancer or other serious diseases. The results represented in **Figure 11** show ALPN-101 had superior survival when dosed three times per week for four weeks compared to belatacept (an FDA-approved drug for prevention of renal allograft rejection - a type of inflammation-related rejection process analogous to GVHD). In fact, 100% of ALPN-101 multi-dose treated animals across three different dose levels survived. Animals given only a single dose of ALPN-101 performed comparably to animals treated with belatacept dosed 3x/week for four weeks, demonstrating the potency and efficacy of ALPN-101 in this disease model.

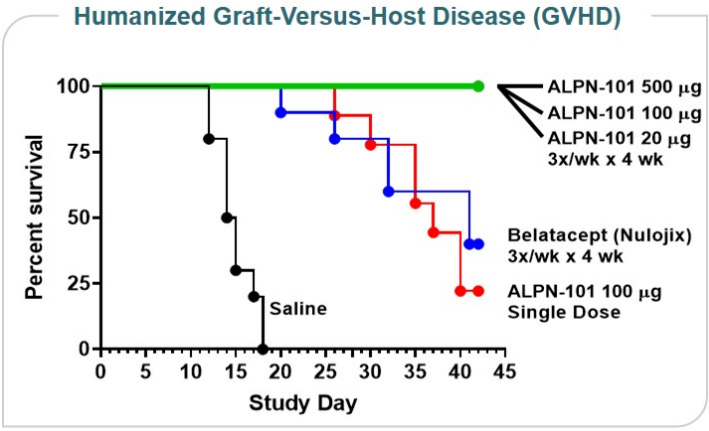

Figure 11

Summary of ALPN-101 Program Preclinical Data

Our scientists and collaborators have demonstrated in *in vivo* preclinical studies that ALPN-101:

- demonstrates a lower incidence and severity of sialadenitis, a model of Sjögren's syndrome, as compared to abatacept or wild-type ICOSL-Fc alone or in combination;
- shows reduced levels of anti-dsDNA autoantibodies compared to an Fc control in an animal model of SLE;
- reduces disease severity and delays disease onset time relative to control in an *in vivo* arthritis model with activity superior to abatacept, an FDA-approved drug for rheumatoid, psoriatic, and juvenile idiopathic arthritis;
- improves survival compared to belatacept in an *in vivo* animal GVHD model;
- demonstrates control of colitis in an animal model of inflammatory bowel disease, or IBD; and
- shows improved disease scores in an animal model of multiple sclerosis, or MS, compared to abatacept.

ALPN-101 Clinical Development

We have completed a Phase 1 study of ALPN-101 in healthy volunteers (NCT03748836). This study was designed to evaluate the safety and tolerability of single and multiple ascending intravenous and/or subcutaneous doses of ALPN-101. In addition, pharmacokinetics, pharmacodynamics and exploratory biomarkers were evaluated to help determine ALPN-101's potential for the treatment of autoimmune/inflammatory diseases. Results of the study were presented at the 2020 European League Against Rheumatism E-Congress and published in the peer-reviewed journal Clinical Translational Science (doi:10.1111/cts.12983). The first-in-human study randomized 96 healthy adults to receive single or multiple, intravenous or subcutaneous, placebo or ALPN-101 at doses ranging from 1 µg/kg to 10 mg/kg. At all dose levels, ALPN-101 was well-tolerated, with no severe adverse events, clinically-significant immunogenicity events, or evidence of cytokine release. Pharmacokinetics and pharmacodynamics (**Figure 12**) exhibited desirable dose dependence, with increasing doses corresponding to increasing duration of complete, or near-complete target saturation, as well as inhibition of antibody responses to keyhole limpet hemocyanin, or KLH, immunization.

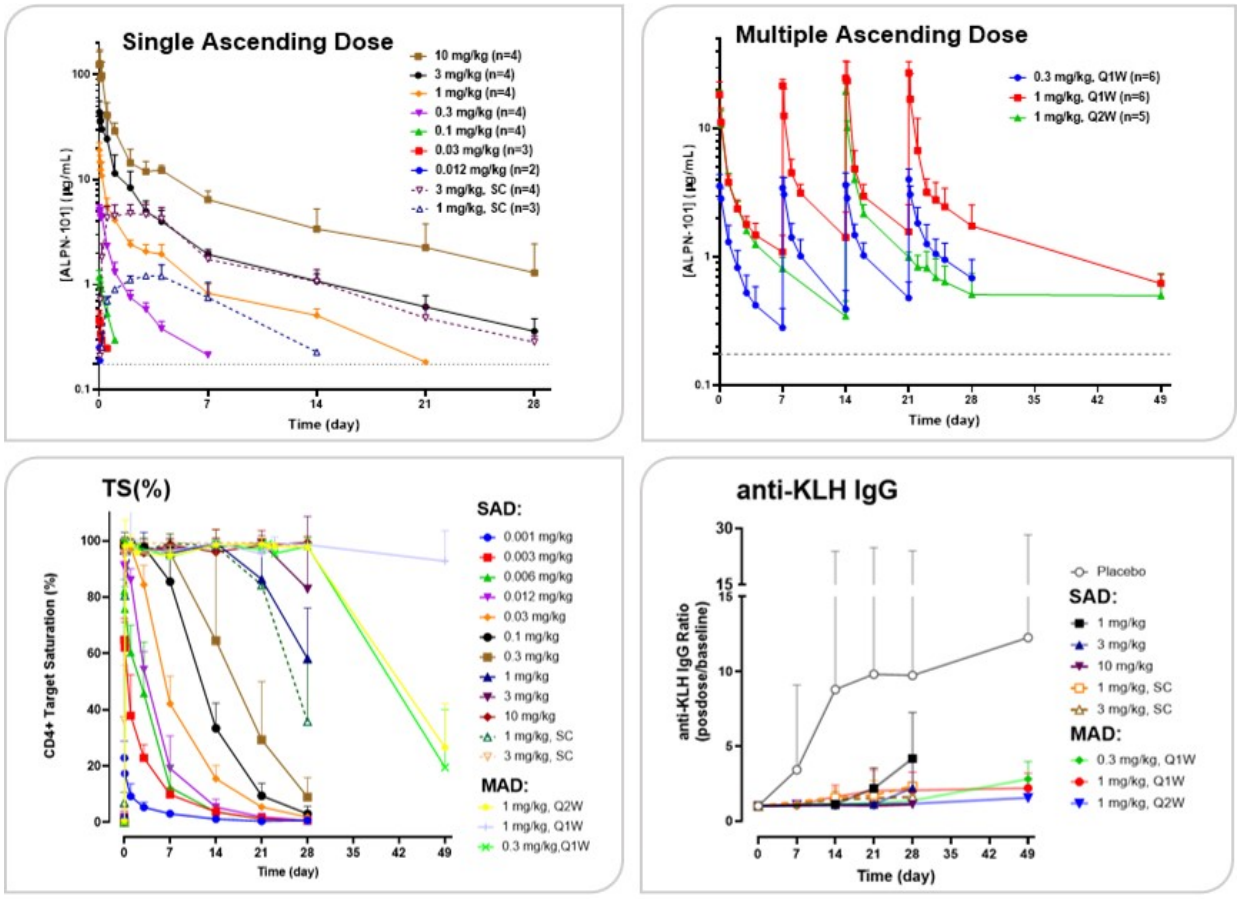

Figure 12

Supported by these results we plan to continue development of ALPN-101 in SLE. As part of the AbbVie Agreement, we intend to initiate a Phase 2 study of ALPN-101 in SLE in mid-2021.

ALPN-202, a Conditional CD28 Costimulator and Dual PD-L1/CTLA-4 Inhibitor for Oncology

Immune checkpoint blockade using inhibitors of the cytotoxic T-lymphocyte antigen 4, or CTLA-4, or programmed death 1, or PD-1, pathways have been therapeutically successful for a wide variety of malignancies, dramatically altering the treatment paradigm in oncology. However, the majority of patients treated with an inhibitor of CTLA-4, PD-1, or programmed death-ligand 1, or PD-L1, fail to respond or develop resistance, indicating that additional strategies to improve anti-tumor immunity and responses remain needed to improve outcomes. Because immune checkpoints like PD-1 and CTLA-4 appear to suppress anti-tumor immune responses in part by inhibiting the activating signals mediated by cluster of differentiation 28, or CD28 (**Figure 13a**), next generation immunotherapeutic strategies may substantially improve anti-tumor responses by

activating a T cell (co-)stimulatory pathway(s) while also inhibiting a checkpoint pathway(s). Preferably, such activity might be focused primarily within the tumor microenvironment to limit potential systemic immune activation and toxicity.

ALPN-202 is an Fc fusion protein of a modified human cluster of differentiation 80, or CD80, vIgD designed to block the inhibitory immune checkpoints PD-L1 and CTLA-4, and to provide PD-L1-dependent T cell activation via CD28 costimulatory receptor. As illustrated in **Figure 13b**, ALPN-202 binds PD-L1 expressed on the tumor, blocking PD-L1/PD-1 interactions. Localized to the tumor, ALPN-202 is able to provide a CD28 signal to T cells (PD-L1-dependent CD28 costimulation). Additionally, ALPN-202 binds CTLA-4 expressed on T cells and blocks CTLA4-CD80/CD86 interactions.

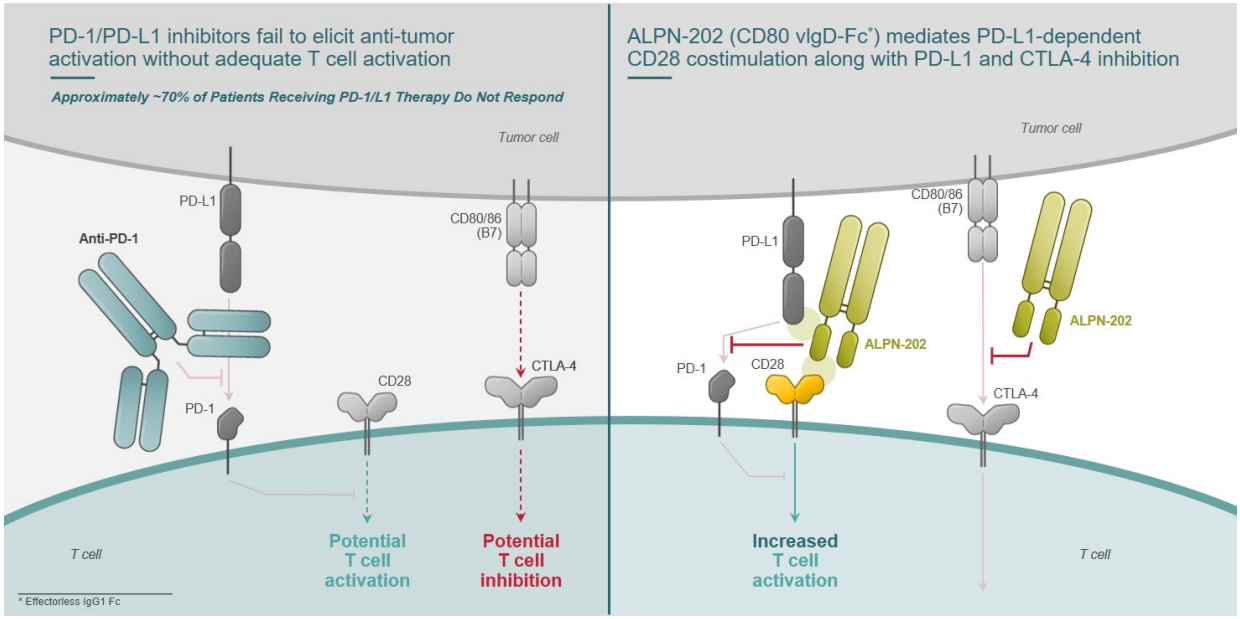

Figure 13a **Figure 13b**

Using *in vitro* assays, we have characterized and validated the three primary mechanisms of action of ALPN-202: conditional CD28 costimulation and dual PD-L1/CTLA-4 inhibition (**Figure 14**). Importantly, CD28 costimulation with ALPN-202 requires both T cell receptor, or TCR, signaling and expression of PD-L1 on the antigen presenting cell, or APC. PD-L1 dependent T cell costimulation is a unique and key attribute of ALPN-202 which we believe may limit the risk for systemic toxicity while providing potent anti-tumor activity.

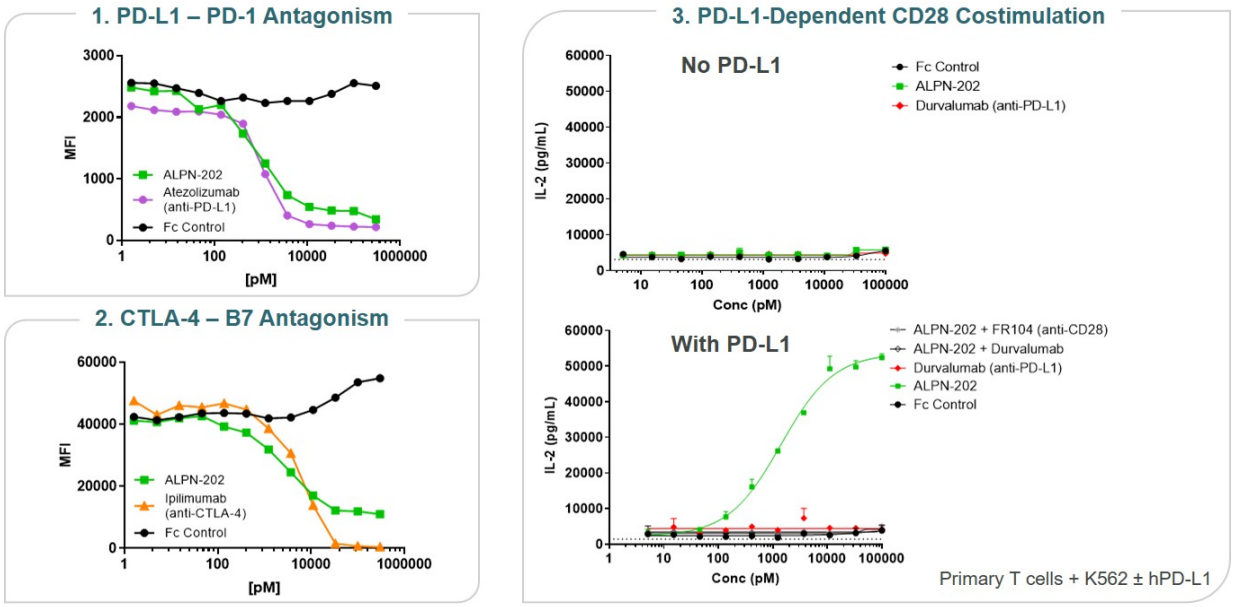

Figure 14

ALPN-202 has also been validated in *in vivo* tumor models. In a mouse model where mice were implanted with MC38 mouse colon cancer tumors transfected with human PD-L1, ALPN-202 as a monotherapy demonstrated superior tumor control compared to durvalumab, an FDA-approved anti-PD-L1 monoclonal antibody (**Figure 15**).

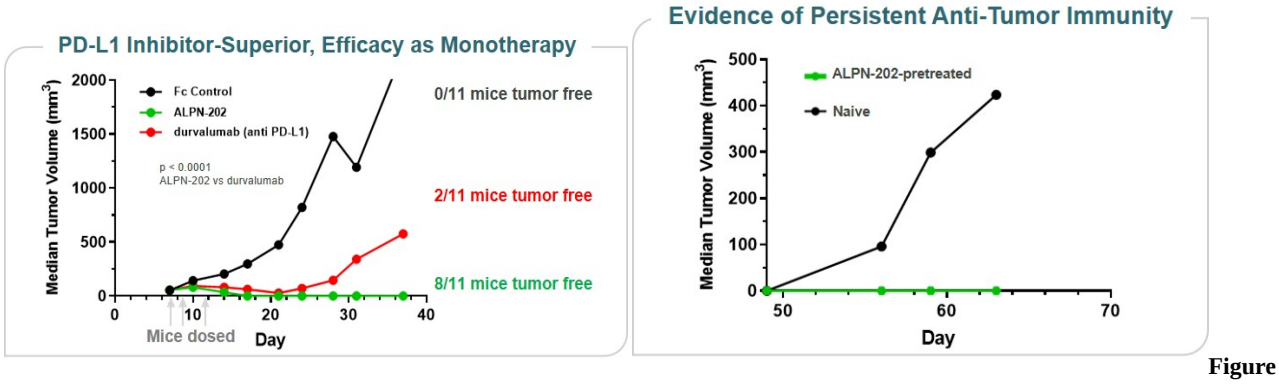

Figure 15 **Figure 16**

When tumor-free mice in the ALPN-202 arm were re-challenged with additional tumors, they continued to be tumor free despite no additional doses of ALPN-202. (**Figure 16**)

The effects of ALPN-202 or durvalumab on various components of the immune system were compared using a technique called RNA sequencing in the tumor model. This technique generates a display of inflammatory gene signatures where green represents lower or no upregulation of inflammatory genes and red represents higher upregulation of inflammatory genes. For the treatment of cancer, it is thought the more upregulation of the immune system - indicated by higher upregulation of inflammatory genes - potentially results in better outcomes for patients. As seen in **Figure 17** below, ALPN-202 upregulates a broader variety of different inflammatory genes connected with several different types of immune cells compared to durvalumab.

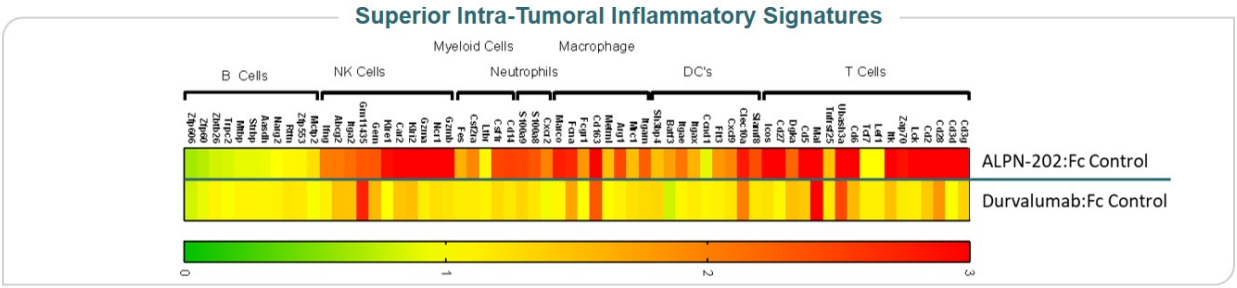

Figure 17

Summary of ALPN-202 Preclinical Data

We have demonstrated in preclinical studies that ALPN-202:

- exhibits three primary mechanisms of action: conditional CD28 costimulation and dual PD-L1/CTLA-4 inhibition;
- improves tumor control in a human PD-L1 transduced mouse model of colon cancer compared to the FDA approved anti PD-L1 therapeutic durvalumab;
- demonstrates a more robust intra-tumor inflammatory signature in the mouse colon cancer model than durvalumab, potentially indicating superior immune system upregulation to fight cancer; and
- has the potential to be used as a monotherapy or in combination with standard of care chemotherapy or checkpoint only inhibition.

ALPN-202 Clinical Development

We have initiated enrollment in NEON-1, our Phase 1 study in patients with advanced malignancies, and we intend to continue to enroll patients throughout 2021. NEON-1 includes two parts: dose escalation and expansion cohort(s). It will enroll adults with advanced solid tumors or lymphoma refractory or resistant to standard therapy, including checkpoint inhibitors when indicated. Measurable disease is required for most participants, as are an ECOG status of 0 to 2 and adequate hematological, renal, and hepatic function. Dose escalation begins with single-participant cohorts followed by standard 3 + 3 cohorts where two dose regimens, weekly versus every three weeks, will be studied in parallel. We plan to determine expansion cohorts later this year. Expansion cohorts will explore specific tumor types and/or biomarker-selected tumors, based upon the experience during dose escalation. Safety endpoints include dose-limiting toxicities, adverse events, and circulating cytokines. Objective responses will be assessed by RECIST v1.1 for solid tumors and Lugano criteria for lymphoma. Pharmacokinetics and pharmacodynamics will also be evaluated. More information is available at www.clinicaltrials.gov (NCT04186637). We also intend to initiate NEON-2, a Phase 1 combination study of ALPN-202 and a PD-1 inhibitor later this year.

ALPN-303, a Dual B Cell Cytokine Antagonist for B Cell-Mediated Autoimmune/Inflammatory Diseases

ALPN-303 is a dual B cell cytokine antagonist being developed for B cell-mediated autoimmune/inflammatory diseases. Engineered using our proprietary directed evolution platform, ALPN-303 is an Fc fusion protein of a human transmembrane activator and CAML interactor, or TACI, variant TNFR domain, or vTD, that inhibits the pleiotropic B cell cytokines B cell activating factor, or BAFF, and a proliferation inducing ligand, or APRIL. It mediates significantly improved combined BAFF and APRIL inhibition in vitro and enhanced pharmacokinetic and immunomodulatory properties *in vivo*, as compared to wild-type, or WT, TACI-Fc molecules. BAFF and APRIL are TNF superfamily members that bind TACI, BCMA, and/or BAFF-R on B cells and together support B cell development, differentiation, and survival. Their co-neutralization dramatically reduces B cell survival and function, including antibody production, whereas inhibition of either BAFF or APRIL alone mediates only modest effects (**Figure 18**). B cell targeting therapies like the WT TACI-Fc fusions atacicept and telitacicept have demonstrated

promising clinical potential in B cell-related diseases like SLE but have not yet clearly exhibited long-term and/or complete disease remissions. ALPN-303, with enhanced inhibitory activity against BAFF & APRIL, could further improve clinical outcomes.

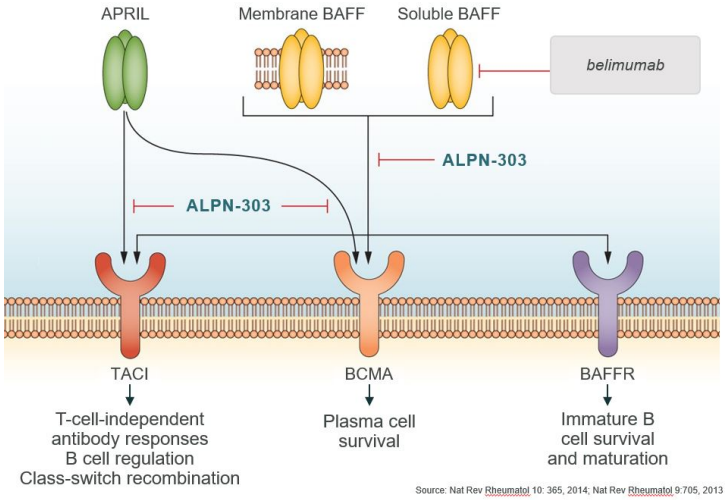

Figure 18

Data on the ALPN-303 series presented at the 2020 European League Against Rheumatism E-Congress demonstrate encouraging preclinical immunomodulatory activity and efficacy *in vitro* and *in vivo*, superior to anti-BAFF Abs and WT TACI-Fc. In **Figure 19**, ALPN-303 inhibits BAFF- and APRIL-mediated signaling *in vitro* with significantly lower IC50 values than WT TACI-Fc and belimumab comparators.

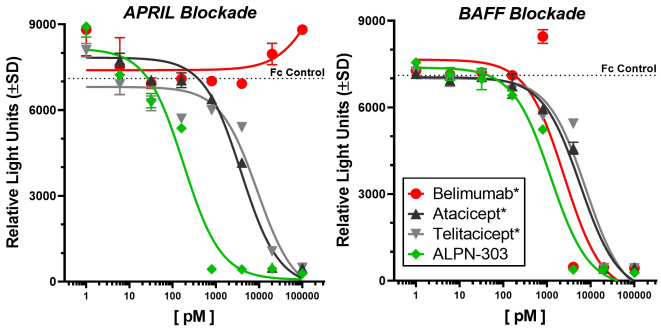

Figure 19

Administration of ALPN-303 rapidly and significantly reduced key B lymphocyte subsets including plasma cells, germinal center (**Figure 20**), and follicular B cells.

Developmental B Cell Blockade

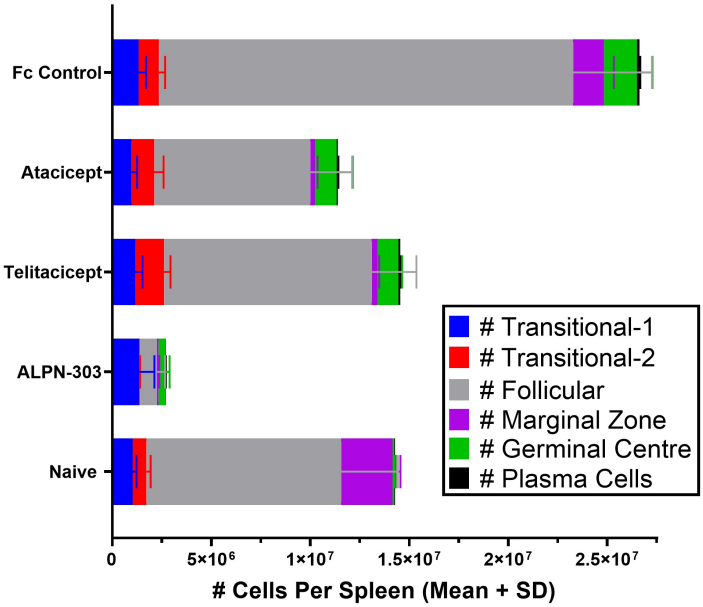

Figure 20

Furthermore, treatment with ALPN-303 potently suppressed anti-dsDNA auto antibodies, proteinuria, sialadenitis, kidney lesions, and renal immune complex deposition in the (NZBxNZW)F1 lupus model (**Figure 21**).

Encouraging Efficacy in Murine Connective Tissue Disease

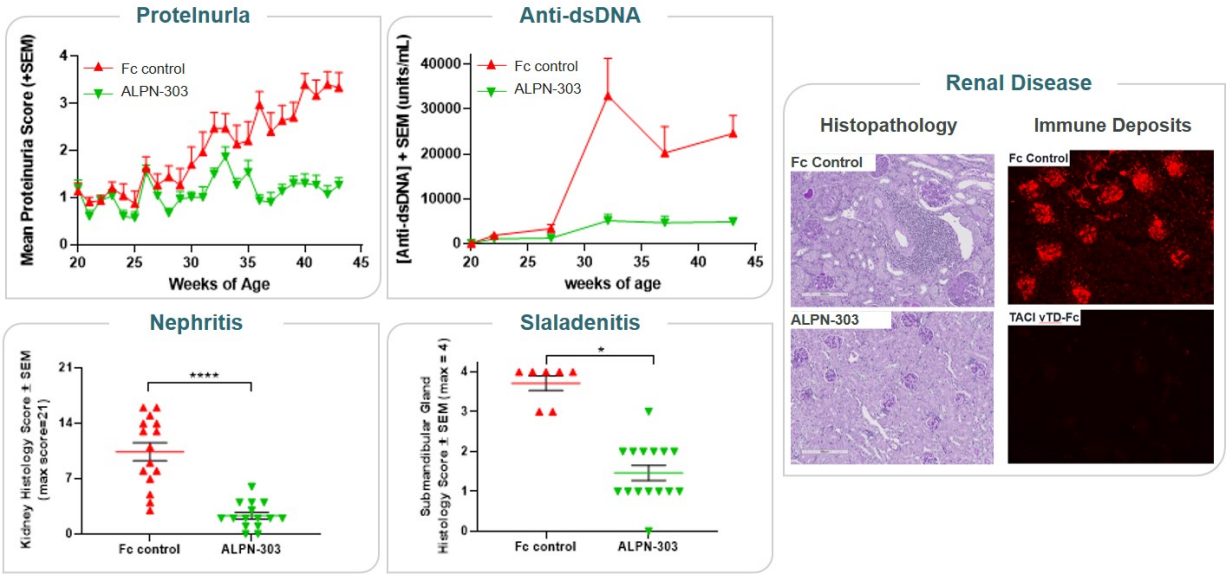

Figure 21

Based on these data, we believe that ALPN-303 represents an attractive development candidate for the treatment of multiple autoimmune and inflammatory diseases, particularly B cell-related diseases such as SLE, SjS, and other connective tissue diseases.

ALPN-303 Clinical Development

No clinical studies of ALPN-303 have been conducted to-date. We are targeting completion of activities to support initiation of a Phase 1 study for ALPN-303 in in the fourth quarter of 2021.

Other Research Programs

In addition to our ALPN-101, ALPN-202, and ALPN-303 programs, we have a number of other research efforts underway to address cancer and autoimmune/inflammatory diseases that we intend to continue to develop either internally or together with a partner.

Partnerships

In addition to advancing programs internally, we continue to seek partners who can bring therapeutic area experience, development expertise, commercialization capabilities, and funding allowing us to maximize the potential of vIgDs, vTDs, and our scientific platform.

Collaboration with AbbVie (June 2020)

In June 2020, we entered into the AbbVie Agreement, which grants to AbbVie an exclusive option to take an exclusive license to ALPN-101, or the License Option.

Under the terms of the AbbVie Agreement we granted to AbbVie an exclusive option to obtain an exclusive, royalty-bearing, sublicensable license to certain intellectual property rights for the research, development and commercialization of ALPN-101 and any other molecule owned or controlled by us that binds to or directly modulates or targets ICOS at certain agreed-upon levels, or the Compounds, on a worldwide basis for all human and non-human diagnostic, prophylactic and therapeutic uses, subject to certain exceptions set forth in the AbbVie Agreement. The License Option is immediately exercisable and will expire 90 days following our delivery of the data package described below to AbbVie, subject to certain exceptions, including clearance under the Hart-Scott-Rodino Antitrust Improvements Act of 1976, or the HSR Act, if required.

Financial Terms

In connection with the execution of the AbbVie Agreement, AbbVie paid us a nonrefundable upfront payment of $60.0 million in cash. If AbbVie exercises its License Option, they will pay a one-time cash payment of $75.0 million.

In addition to the upfront payment and License Option payment, AbbVie has agreed to make cash payments upon our achievement of certain development milestones prior to the exercise of the License Option as set forth in a written development plan, up to an aggregate amount of $75.0 million. Following the exercise of the License Option, AbbVie has agreed to make cash payments of up to $205.0 million upon AbbVie's achievement of certain development and commercial milestones and additional cash payments of up to $450.0 million upon AbbVie's achievement of certain sales-based cash milestones. AbbVie has further agreed to pay royalties from a high-single digit percentage to a low double-digit percentage of net sales of any pharmaceutical product that contains a Compound, or a Licensed Product, with the specific royalty rate depending on the aggregate net sales. AbbVie's obligations to pay royalties with respect to a Licensed Product and country will expire upon the latest of the expiration of the last to expire valid patent claim applicable to such Licensed Product in such country, 10 years from the first commercial sale of the Licensed Product in such country, and the expiration of regulatory exclusivity for such Licensed Product in such country. Royalty payments are subject to reduction in specified circumstances, including expiration of patent rights, if average net sales decrease by a certain percentage after the introduction of a generic product, or if AbbVie is required to pay amounts to a third party in order commercialize a Licensed Product in a particular country.

Development Activities

Prior to the exercise of the License Option, we will conduct ALPN-101 development efforts as per a development plan providing for, among other things, the generation of a data package in order for AbbVie to evaluate exercising the License Option and an itemized budget for such activities, including all activities reasonably necessary to conduct a Phase 2 clinical study of ALPN-101 for the treatment of systematic lupus erythematosus; all non-clinical activities; and all CMC activities agreed to under the development plan. We will be fully responsible for all costs incurred to conduct our activities, provided

that, AbbVie may be responsible for increased costs under the development plan in connection with certain material amendments agreed upon with AbbVie.

Prior to the exercise of the License Option, we will be solely responsible, at our sole cost and expense, for preparing, filing and maintaining regulatory documentation, which AbbVie will be entitled to access and review. We will also be responsible for any and all correspondence with the applicable regulatory authorities and for maintaining all data related to ALPN-101. We will be solely responsible, at our sole cost and expense, for manufacturing the Compounds necessary to complete the development activities consistent with the development plan.

Governance

The parties will establish a joint governance committee, or JGC, composed of an equal number of representatives from each of Alpine and AbbVie, which will, among other responsibilities, coordinate and oversee the development activities, approve amendments to the development plan and discuss interactions with regulatory authorities. The chairperson of the JGC will be appointed by AbbVie. AbbVie may disband the JGC, at its sole discretion, following the exercise of the License Option.

Commercialization

Upon AbbVie's exercise of the License Option, AbbVie and its affiliates will be solely responsible, at AbbVie's sole cost and expense, for the development, manufacture, commercialization, and regulatory compliance of any Licensed Product. Following exercise of the License Option, AbbVie shall use commercially reasonable efforts to develop and seek regulatory approval for one of the Compounds in one indication in each of the United States and one of the United Kingdom, Germany, France, Spain, or Italy, or the Major Markets, and, following receipt of any such regulatory approval, commercialize the compound in such country.

Changes in Control

We will notify AbbVie immediately upon the closing of any change in control (as defined in the AbbVie Agreement) during the term of the AbbVie Agreement. Following the delivery of such notice, AbbVie may, in its sole and absolute discretion, elect to continue the AbbVie Agreement subject to certain modifications as set forth in the AbbVie Agreement, including the assumption by AbbVie of responsibility to perform certain activities previously assigned to us.

Term and Termination

Unless earlier terminated, the AbbVie Agreement shall terminate either: (i) in the event that the License Option is not exercised by AbbVie, the first day following the last day of the License Option exercise period; or (ii) in the event that the License Option is exercised by AbbVie, the date of the expiration of the last Royalty Term for the last Licensed Product.

Both us and AbbVie may terminate the AbbVie Agreement upon written notice in the event of a material breach by the other party that has not been cured within a 90-day cure period. However, if the uncured material breach is with respect to AbbVie's obligation to use commercially reasonable efforts to obtain regulatory approval for and commercialize a Licensed Product with respect to any Major Market (but not all Major Markets), then we will only be entitled to terminate the AbbVie Agreement with respect to such Major Market(s). Both AbbVie and us may also terminate the AbbVie Agreement upon written notice if the other party voluntarily or involuntarily files for bankruptcy or insolvency, makes an assignment for the benefit of creditors, has a receiver or trustee appointed over substantially all of such other party's property, proposes or is party to any dissolution or liquidation, or admits in writing its inability generally to meet such other party's obligations as they fall due in the general course.

AbbVie may terminate the AbbVie Agreement in its entirety or on a country-by-country basis, for any or no reason, by providing at least 90 days' prior written notice to us. AbbVie may also terminate the AbbVie Agreement upon notice to us if (i) either we or AbbVie receives a second request for additional information under the HSR Act, provided AbbVie's notice of termination is delivered within ten business days after AbbVie becomes aware of such request or receives notice from us regarding such request or (ii) the License Option has not been exercised or clearance under the HSR Act, if required, has not occurred within 180 days of submission of the parties' request for such clearance, provided AbbVie's notice of termination is delivered within ten business days after the end of such 180-day period.

Upon the termination of the AbbVie Agreement in its entirety for any reason, all licenses and other rights granted (i) to AbbVie by us and (ii) to us by AbbVie shall terminate. Upon termination in certain circumstances, AbbVie has agreed to grant

to us licenses to certain intellectual property that is reasonably necessary, and that was actually used by AbbVie for the development, manufacturing or commercialization of the terminated products, to research, develop and commercialize the terminated products in the terminated countries.

In lieu of terminating the AbbVie Agreement in connection with an uncured material breach or the bankruptcy or insolvency of the Company, AbbVie may alternatively elect to continue the AbbVie Agreement subject to certain modifications, including that AbbVie will be entitled to conduct activities allocated to us under the Development Plan, subject to reimbursement by us for AbbVie's out-of-pocket expenses in connection with such activities. If AbbVie's right to terminate in connection with an uncured material breach or the bankruptcy or insolvency of the Company arises before exercise of the License Option, then the License Option exercise payment amount will be reduced by half and the amount of any then-unearned milestone payments will be reduced by half. If AbbVie's right to terminate arises after exercise of the License Option, then the amount of any then-unearned milestone payments will be reduced by 25%.

The AbbVie Agreement includes certain other customary terms and conditions, including mutual representations and warranties, indemnification and confidentiality provisions.

Collaboration with Adaptimmune Therapeutics (May 2019)

In May 2019, we entered into a collaboration and license agreement with Adaptimmune, or the Adaptimmune Agreement, to develop next-generation SPEAR™ T cell products which incorporate our secreted and transmembrane immunomodulatory protein (termed SIP™ and TIP™) technology. We and Adaptimmune will collaborate on a specified number of programs to develop SIP and TIP candidates with tailored affinities and modulatory activities that may enhance the anti-tumor responses seen with Adaptimmune's SPEAR™ T cells. For each program, Adaptimmune has an option to take a worldwide exclusive license for development and commercialization of SPEAR™ T cell products incorporating the developed SIP or TIP candidate for the treatment of cancer. Under the terms of the collaboration agreement, Adaptimmune provided an upfront payment and will provide research funding for ongoing programs. In addition, we may be eligible for downstream development and commercialization milestones up to $288.0 million, if all pre-specified milestones for each program are achieved. In addition, we are eligible to receive low-single digit royalties on worldwide net sales of the applicable products.

Manufacturing

We have established in-house non-cGMP recombinant protein generation capabilities enabling our scientific platform, including validation of new scientific discoveries *in vitro* and *in vivo*. Having protein production capabilities in-house allows more rapid progression for vIgDs and vTDs generated by our scientific platform.

We have chosen U.S.-based contract drug substance and U.S. and Australian drug product manufacturers for our initial cGMP clinical trial supplies of ALPN-101, ALPN-202 and ALPN-303. We believe these contract manufacturers' particular expertise in protein production, analytical development and fill/finish provide us with the capability to meet rapid timelines encompassing the development of production cell-lines to manufacturing of clinical trial quantities of the biopharmaceutical product.

We have successfully completed two cGMP manufacturing campaigns for ALPN-101 and one cGMP campaign for ALPN-202 and believe we have produced sufficient quantities of drug product necessary to execute our stated NEON-1 clinical trial and Phase 2 clinical trial in SLE. We have not yet manufactured any of our proteins at commercial scale.

Competition

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

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

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

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

Specifically, our competitors include companies developing therapies with the same target(s) as ALPN-101, ALPN-202 and ALPN-303 as well as companies building novel platforms to generate multi-specific antibody or non-antibody-based targeting proteins.

See the risk factor "*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.*" in Part I, Item 1A of this report for more discussion of the effects of competition and competitors on our business.

ALPN-101 Program Competitors (ICOSL/CD28)

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

- an anti-BAFF, anti-ICOSL bispecific antibody being developed by Amgen, Inc (rozibafusp alfa (AMG570/MEDI0700));
- an anti-CD28 monoclonal antibody fragment being developed by OSE ImmunoTherapeutics SA (FR104);
- an anti-CD28 peptide being developed by AtoxBio, Inc (reltecimod (AB-103));
- an anti-CD28 monoclonal antibody being development by TheraMAB (TAB08); and
- CTLA-4-Fc fusion proteins targeting CD80 and CD86 being marketed Bristol Myers Squibb (abatacept and belatacept).

ALPN-202 Program Competitors

There are numerous clinical trials for immuno-oncology products used as a single agent or in combination. One of the potentially novel attributes of the ALPN-202 program is it has exhibited conditional CD28 costimulation and dual checkpoint inhibition in a single molecule interacting with multiple immune targets.

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

- wild-type CD80-Fc being developed by Five Prime Therapeutics, Inc. (FPT155);
- bispecific antibodies being developed by Regeneron targeting tumor specific antigens and CD28 (REGN5678 anti-PSMAxCD28, REGN5668 anti-MUC16xCD28, and REGN7075 anti-EGFRxCD28);
- trispecific antibodies being developed by Sanofi (CD3xCD38xCD28) (SAR442257);
- bifunctional fusion protein composed of monoclonal antibody against PD-L1 fused to the extracellular domain of human transforming growth factor-ß, or TGF-ß, receptor II being developed by EMD Serono, Inc. and GlaxoSmithKline plc (bintrafusp alfa, or M7824);
- bifunctional fusion protein composed of PD-1 and OX40L developed by Shattuck Labs, Inc. (SL-279252);

- bispecific fusion protein targeting 4-1BB and PD-L1 being developed by Shattuck Labs, Inc. (SL-279137);
- bispecific fusion protein targeting 4-1BB and PD-L1 being developed by Pieris Pharmaceuticals, Inc. (PRS-344);
- bispecific monoclonal antibody targeting 4-1BB and PD-L1 being developed by Genmab A/S and BioNTech SE (GEN1046);
- trispecific monoclonal antibody/fusion targeting 4-1BB and PD-L1 being developed by Numab Therapeutics AG and CStone Pharmaceuticals Co., Ltd (NM021);
- bispecific monoclonal antibody targeting 4-1BB and PD-L1 being developed by Merus NV and Incyte Corporation (MCL-145);
- bispecific antibody 4-1BB and PD-L1 being developed by Inhibrx, Inc. and Elpiscience Biopharma Ltd. (INBRX-105);
- bispecific monoclonal antibody targeting 4-1BB and PD-L1 being developed by F-star Biotechnology Ltd. (FS-222);
- bispecific fusion protein targeting 4-1BB and PD-L1 being developed by Kahr Medical Ltd., (DSP105);
- bispecific monoclonal antibody/fusion protein targeting 4-1BB and PD-L1 being developed by ABL, Inc., and I-Mab Biopharma Co., Ltd. (ABL503);
- bispecific monoclonal antibody targeting PD-L1 and LAG-3 being developed by F-star Biotechnology, Ltd. (FS118);
- bispecific monoclonal antibodies being developed by Xencor, Inc. including XmAb20717 targeting CTLA-4 and PD-1, XmAb22841 targeting CTLA-4 and LAG-3, XmAb23104 targeting PD-1 and ICOS, and a CD28 bispecific antibody platform;
- bispecific constructs called “DARTs” being developed by Macrogenics Inc., including MGD013 targeting PD-1 and LAG-3 and MGD019 targeting PD-1 and CTLA-4;
- bispecific monoclonal antibody being developed by Tesaro, Inc., which was purchased by GlaxoSmithKline plc, targeting PD-1 and LAG-3;
- small molecule antagonists being developed by Aurigene Ltd and Curis, Inc., including CA-170 targeting PD-L1 and VISTA and CA-327 targeting PD-L1 and TIM-3;
- various combinations of separate anti PD-1/L1 and anti-CTLA-4 monoclonal antibodies; and
- various combinations of separate anti PD-1/L1 and costimulatory monoclonal antibodies such as OX-40, 4-1BB, and others.

ALPN-303 Program Competitors

The competitors listed below have programs targeting either the TACI, BCMA, or BAFF pathway for autoimmune disease.

- Anti-BAFF antibody marketed by GSK plc (belimumab);
- TACI-Fc being developed by Vera Therapeutics (atacicept);
- TACI-Fc being developed by RemeGen Ltd. (telitacicept (RC18));
- Anti-BAFFr IgG1 being developed by Novartis AG (Ianalumab (VAY736));
- Anti-APRIL antibody being developed by Visterra, Inc. (VIS649);
- an anti-BAFF, anti-ICOSL bispecific antibody being developed by Amgen, Inc. (rozibafusp alfa (AMG570/MEDI0700)); and
- an anti-APRIL antibody being developed by Chinook Therapeutics, Inc. (BION-1301).

Novel Platform Competitors

Multifunctional therapeutic protein platforms potentially competitive with our platform include:

- Amgen, Inc. (BiTE®): fusion proteins consisting of two single-chain variable fragments to link T cells to tumors;

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

Intellectual Property

Our scientific platform and substantially all our intellectual property have been developed internally. As of December 31, 2020, our patent portfolio consists of over 140 pending patent applications. Our initial patent application is directed to our scientific platform itself. Our second patent application is directed to the TIP program. We filed subsequent patent applications directed to our SIP program as well as to various target domains under development. Each of these patent applications is solely owned by us. As we continue the development of our scientific platform and target vIgDs, we intend to continue pursuing intellectual property protection for these technologies.

We have in-licensed some intellectual property and trade secret materials on a non-exclusive basis. To date, such non-exclusive in-licenses are solely related to commercially-available cell lines involved in the manufacture of our vIgD programs. To date, no other intellectual property related to our scientific platform has been in-licensed. We have out-licensed two programs under our TIP/SIP technology to Adaptimmune on an exclusive basis. Additionally, pursuant to the AbbVie Agreement, we have granted AbbVie an exclusive option to purchase an exclusive worldwide license to ALPN-101. If AbbVie exercises the License Option, AbbVie will take over the future development and commercialization. No other out-licenses have been made.

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

Government Regulation

The FDA and comparable regulatory authorities in state and local jurisdictions and in other countries impose substantial and burdensome requirements on the clinical development, manufacture, marketing, and distribution of therapeutic candidates. These agencies and other federal, state, and local entities regulate research and development activities and the testing, manufacture, quality control, safety, effectiveness, labeling, storage, record keeping, approval, advertising and promotion, and export and import of therapeutic candidates and products.

In the U.S., the FDA regulates drugs, medical devices, and biologic products under the Federal Food, Drug, and Cosmetic Act, or FFDCA, its implementing regulations and other laws, including, in the case of biologics, the Public Health Service Act. Our potential therapeutic candidates and products will be subject to regulation by the FDA as biologics. Biologics require the submission of a Biologics License Application, or BLA, and approval by the FDA before being marketed in the U.S.

None of our therapeutic candidates have been approved by the FDA for marketing in the U.S., and we currently have no BLAs pending. If we fail to comply with applicable FDA or other requirements at any time during the product development process, clinical testing, the approval process, or after approval, we may become subject to administrative or judicial sanctions. These sanctions could include the FDA's refusal to approve pending applications, license suspension or revocation, withdrawal of an approval, warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, civil penalties, or criminal prosecution. Any FDA enforcement action could have a material adverse effect on us. The process required by the FDA before biologic therapeutic candidates may be marketed in the U.S. generally involves the following:

- completion of extensive preclinical laboratory tests, preclinical animal studies, and formulation studies all performed in accordance with the FDA's current good laboratory practice, or cGLP, regulations;
- submission to the FDA of an IND application which must become effective before human clinical trials in the U.S. may begin;
- performance of adequate and well-controlled human clinical trials to establish the safety and efficacy of the drug candidate for each proposed indication;
- submission to the FDA of a BLA;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the product is produced to assess compliance with cGMP regulations; and
- FDA review and approval of the BLA prior to any commercial marketing, sale, or shipment of the therapeutic product.

The testing and approval process requires substantial time, effort, and financial resources, and we cannot be certain any approvals for our therapeutic candidates will be granted on a timely basis, if at all.

Once a therapeutic candidate is identified for development, it enters the preclinical testing stage. Preclinical studies include laboratory evaluations of protein chemistry, formulation, and stability, as well as studies to evaluate toxicity in animals. The results of the preclinical studies, together with manufacturing information and analytical data, are submitted to the FDA as part of an IND application. Currently, the IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day period, raises concerns or questions about the conduct of the clinical trial, including concerns that human research subjects will be exposed to unreasonable health risks. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. Submission of an IND may result in the FDA not allowing the clinical trials to commence or not allowing the clinical trials to commence on the terms originally specified in the IND. A separate submission to an existing IND must also be made for each successive clinical trial conducted during drug development, and the FDA must grant permission, either explicitly or implicitly by not objecting, before each clinical trial can begin.

Clinical trials involve the administration of the therapeutic candidate to human subjects under the supervision of qualified investigators. Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical trial, the parameters to be used in monitoring safety, and the effectiveness criteria to be used. Each protocol must be submitted to the FDA as part of the IND. For each medical center proposing to conduct a clinical trial, an institutional review board, or IRB, must also review and approve a plan for any clinical trial before it can begin at that center and the IRB must monitor the clinical trial until it is completed. The FDA, an IRB, or the sponsor may suspend or discontinue a clinical trial at any time on various grounds, including a finding that the subjects are being exposed to an unacceptable health risk. Clinical testing also must satisfy extensive Good Clinical Practice requirements, including the requirements for informed consent.

All clinical research performed in the U.S. in support of a BLA must be authorized in advance by the FDA under the IND regulations and procedures described above. However, a sponsor who wishes to conduct a clinical trial outside the U.S. may, but need not, obtain FDA authorization to conduct the clinical trial under an IND. If a foreign clinical trial is not conducted under an IND, the sponsor may submit data from the clinical trial to the FDA in support of a BLA so long as the clinical trial is conducted in compliance with an international guideline for the ethical conduct of clinical research known as the Declaration of Helsinki and/or the laws and regulations of the country or countries in which the clinical trial is performed, whichever provides the greater protection to the participants in the clinical trial.

Clinical Trials

For purposes of BLA submission and approval, clinical trials are typically conducted in three sequential phases, which may overlap or be combined.

- Phase 1 clinical trials are initially conducted in a limited population of subjects to test the therapeutic candidate for safety, dose tolerance, absorption, metabolism, distribution, and excretion in healthy humans or, on occasion, in patients with severe problems or life-threatening diseases to gain an early indication of its effectiveness.
- Phase 2 clinical trials are generally conducted in a limited patient population to evaluate preliminary efficacy of the therapeutic candidate for specific targeted indications in patients with the disease or condition under study, evaluate dosage tolerance and appropriate dosage, determine a dosage schedule, and identify possible adverse effects and safety risks.
- Phase 3 clinical trials are commonly definitive efficacy studies of the experimental medication. Phase 3 trials are typically conducted when Phase 2 clinical trials demonstrate a dose range of the therapeutic candidate is effective and has an acceptable safety profile. Phase 3 clinical trials are generally undertaken with large numbers of patients, such as groups of several hundred to several thousand, to provide substantial evidence of clinical efficacy and to further test for safety in an expanded patient population at multiple, geographically-dispersed clinical trial sites.

In some cases, the FDA may condition approval of a BLA on the sponsor's agreement to conduct additional post-approval clinical trials to further assess the biologic's safety and effectiveness after BLA approval. Such post-approval clinical trials are typically referred to as Phase 4 clinical trials.

Concurrent with clinical trials, companies usually complete additional animal trials and must also develop additional information about the chemistry and physical characteristics of the biologic and finalize a process for manufacturing the biologic in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the therapeutic candidate and, among other things, the manufacturer must develop methods for testing the identity, strength, quality, and purity of the final biologic product. Additionally, appropriate packaging must be selected and tested, and stability studies must be conducted to demonstrate the therapeutic candidate does not undergo unacceptable deterioration over its shelf life.

Further, as a result of the COVID-19 pandemic, we may be required to develop and implement additional clinical trial policies and procedures designed to help protect subjects from the COVID-19 virus. For example, the FDA has issued guidance on conducting clinical trials during the pandemic, which describes a number of considerations for sponsors of clinical trials impacted by the pandemic, including certain reporting requirements, and additional guidance on the good manufacturing practice considerations for responding to COVID-19 infection and other topics. We may be required to make further adjustments to our clinical trials or business operations based on current or future guidance and regulatory requirements as a result of the COVID-19 pandemic.

Biologics License Applications

The results of preclinical studies and of the clinical trials, together with other detailed information, including extensive manufacturing information and information on the chemistry, pharmacology, clinical pharmacology, and the clinical effects of the biologic, are submitted to the FDA in the form of a BLA requesting approval to market the biologic for one or more specified indications. The FDA reviews a BLA to determine, among other things, whether a biologic is safe, pure, and potent and whether the facility in which the biological product is manufactured, processed, packed, or held meets standards designed to assure the biological product continues to be safe, pure, and potent.

Once a BLA has been accepted for filing, by law the FDA will review the application and respond to the applicant, but the review process may be significantly delayed by FDA's requests for additional information or clarification. Under the Prescription Drug User Fee Act, the FDA evaluates a standard original BLA submission within the first 60 days of its receipt to determine if it is sufficiently complete to conduct a full review, and the FDA has a goal of responding to the submission within ten months of the 60-day filing date, but this timeframe is often extended. The FDA may refer the application to an advisory committee for review, evaluation, and/or recommendation as to whether the application should be approved. The FDA is not bound by the recommendation of an advisory committee, but it generally follows such recommendations. The FDA may deny approval of a BLA if the applicable statutory and regulatory criteria are not satisfied, or for any reason, or it may require additional clinical data. Even if such data are submitted, the FDA may ultimately decide the BLA does not satisfy the criteria for approval. Data from clinical trials are not always conclusive and the FDA may interpret data differently than we interpret data. Once the FDA approves a BLA, or supplement thereto, the FDA may withdraw the approval if ongoing regulatory

requirements are not met or if safety problems are identified after the biologic reaches the market. Where a withdrawal may not be appropriate, the FDA still may seize existing inventory of such biologic or require a recall of any biologic already on the market. In addition, the FDA may require testing, including Phase 4 clinical trials and surveillance programs to monitor the effect of approved biologics which have been commercialized. The FDA has the authority to prevent or limit further marketing of a biologic based on the results of these post-marketing programs.

A sponsor may also seek approval of its therapeutic candidates under programs designed to accelerate FDA review and approval of BLAs. For instance, a sponsor may seek FDA designation of a therapeutic candidate as a "fast track product." Fast track products are those products intended for the treatment of a serious or life-threatening disease or condition and which demonstrate the potential to address unmet medical needs for such diseases or conditions. If fast track designation is obtained, the FDA may initiate review of sections of a BLA before the application is complete. This "rolling review" is available if the applicant provides, and the FDA approves, a schedule for the remaining information. In some cases, a fast track product may be approved on the basis of either a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments, under the FDA's accelerated approval program. Approvals of this kind typically include requirements for appropriate post-approval confirmatory clinical trials to validate the surrogate endpoint or otherwise confirm the effect of the clinical endpoint.

In addition, the Food and Drug Administration Safety and Innovation Act, or FDASIA, which was enacted and signed into law in 2012, established a new category of drugs referred to as "breakthrough therapies" that may be subject to accelerated approval. A sponsor may seek FDA designation of a drug candidate as a "breakthrough therapy" if the drug is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development.

Therapeutic candidates may also be eligible for "priority review," or review within a six-month timeframe from the 60-day filing date, if a sponsor provides sufficient clinical data demonstrating its therapeutic candidate provides a significant improvement compared to marketed products. Even if a therapeutic candidate qualifies for one or more of these programs, the FDA may later decide the therapeutic candidate no longer meets the conditions for qualification or that the period for FDA review or approval will be lengthened. When appropriate, we intend to seek fast track designation and/or accelerated approval for our biologics. We cannot predict whether any of our therapeutic candidates will obtain a fast track and/or accelerated approval designation and, if so, whether such designation will be maintained or rescinded by FDA, or the ultimate impact, if any, of the fast track or the accelerated approval process on the timing or likelihood of FDA approval of any of our proposed biologics.

Biologics may be marketed only for the FDA approved indications and in accordance with the provisions of the approved labeling. Further, if there are any modifications to the biologic, including changes in indications, labeling, or manufacturing processes, equipment, or facilities, the applicant may be required to submit and obtain FDA approval of a new BLA or BLA supplement, which may require us to develop additional data or conduct additional preclinical studies and clinical trials.

Before approving an application, the FDA will inspect the facility or the facilities at which the biologic product is manufactured and will not approve the product unless cGMP compliance is satisfactory. The FDA may also inspect the sites at which the clinical trials were conducted to assess their compliance and will not approve the biologic unless compliance with Good Clinical Practice requirements is satisfactory.

The testing and approval processes require substantial time, effort, and financial resources, and each may take several years to complete. The FDA may not grant approval on a timely basis, or at all. Even if we believe a clinical trial has demonstrated safety and efficacy of one of our therapeutic candidates for the treatment of a disease, the results may not be satisfactory to the FDA. Preclinical and clinical data may be interpreted by the FDA in different ways, which could delay, limit, or prevent regulatory approval. We may encounter difficulties or unanticipated costs in our efforts to secure necessary governmental approvals which could delay or preclude us from marketing our therapeutic candidates. The FDA may limit the indications for use or place other conditions on any approvals restricting the commercial application of the products. After approval, certain changes to the approved biologic, such as adding new indications, change in personnel, manufacturing changes, or additional labeling claims, are subject to further FDA review and approval. Depending on the nature of the change proposed, a BLA supplement which may require additional studies to evaluate the effect of such change on the identity, strength, quality, purity, or potency of the product as they may relate to the safety or effectiveness of the product—must be filed

and approved before the change may be implemented. As with new BLAs, the review process for BLA supplements may be delayed by the FDA through requests for additional information or clarification.

We believe any of our therapeutic products approved as a biological product under a BLA might qualify for a 12-year period of exclusivity currently permitted by the Biologics Price Competition and Innovation Act, or BPCIA. Specifically, the BPCIA established an abbreviated pathway for the approval of biosimilar and interchangeable biological products. The new abbreviated regulatory pathway establishes legal authority for the FDA to review and approve biosimilar biologics, including the possible designation of a biosimilar as "interchangeable" based on its similarity to an existing brand product. Under the BPCIA, an application for a biosimilar product cannot be submitted by an applicant until four years after the date the reference product was first licensed and cannot be approved by the FDA until 12 years after the original branded product was first licensed under a BLA. There is a risk the U.S. Congress could amend the BPCIA to significantly shorten this exclusivity period or the FDA will not consider our therapeutic candidates to be reference products for competing products, potentially creating the opportunity for competition sooner than anticipated. Moreover, the extent to which a biosimilar, once approved, will be substituted for any one of our reference products in a way similar to traditional generic substitution for non-biological products is not yet clear, and will depend on a number of marketplace and regulatory factors that are still developing. The BPCIA is complex and is only beginning to be interpreted and implemented by the FDA and the courts. As a result, its ultimate impact, implementation, and meaning are subject to uncertainty. While it is uncertain when any such processes may be fully adopted by the FDA, any such processes operating to limit the scope or length of exclusivity afforded by the BPCIA could have a material adverse effect on the future commercial prospects for our biological products. In addition, foreign regulatory authorities may also provide for exclusivity periods for approved biological products or for abbreviated pathways for follow on biological products. For example, biological products in Europe may be eligible for a 10-year period of exclusivity.

Under the Orphan Drug Act, the FDA may grant orphan drug designation to therapeutic candidates intended to treat a rare disease or condition, which is generally a disease or condition affecting fewer than 200,000 individuals in the U.S. or more than 200,000 individuals in the U.S. and for which there is no reasonable expectation the cost of developing and making available in the U.S. a therapeutic candidate for this type of disease or condition will be recovered from sales in the U.S. for that therapeutic candidate. Orphan drug designation must be requested before submitting a marketing application for the therapeutic for that particular rare disease or condition. After the FDA grants orphan drug designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process. The FDA may revoke orphan drug designation, and if it does, it will publicize the drug is no longer designated as an orphan drug. If a therapeutic candidate with orphan drug designation subsequently receives the first FDA approval for the disease for which it has such designation, the therapeutic candidate is entitled to orphan product exclusivity, which means the FDA may not approve any other applications to market the same therapeutic candidate 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 candidates for seven years if a competitor obtains approval of the same therapeutic candidate as defined by the FDA or if our therapeutic candidate is determined to be contained within the competitor's therapeutic candidate for the same indication or disease.

Under the Best Pharmaceuticals for Children Act, certain therapeutic candidates may obtain an additional six months of exclusivity if the sponsor submits information requested in writing by the FDA, referred to as a "Written Request," relating to the use of the active moiety of the therapeutic candidate in children. The FDA may not issue a Written Request for studies on unapproved or approved indications where it determines information relating to the use of a therapeutic candidate in a pediatric population, or part of the pediatric population, may not produce health benefits in that population. In addition, the Pediatric Research Equity Act, or PREA, requires a sponsor to conduct pediatric studies for most therapeutic candidates and biologics, for a new active ingredient, new indication, new dosage form, new dosing regimen, or new route of administration. Under PREA, original NDAs, BLAs and supplements thereto must contain a pediatric assessment unless the sponsor has received a deferral or waiver. The required assessment must assess the safety and effectiveness of the therapeutic candidate for the claimed indications in all relevant pediatric subpopulations and support dosing and administration for each pediatric subpopulation for which the therapeutic candidate is safe and effective. The sponsor or the FDA may request a deferral of pediatric studies for some or all of the pediatric subpopulations. A deferral may be granted for several reasons, including a finding that the drug or biologic is ready for approval for use in adults before pediatric studies are complete or additional safety or effectiveness data needs to be collected before the pediatric studies begin. The FDA must send a noncompliance letter to any sponsor that fails to submit the required assessment, keep a deferral current, or fails to submit a request for approval of a pediatric formulation.

Other Regulatory Requirements

Any biologics manufactured or distributed by us or our collaborators pursuant to FDA approvals would be subject to continuing regulation by the FDA, including recordkeeping requirements and reporting of adverse experiences associated with the product. Manufacturers and their subcontractors are required to register their establishments with the FDA and certain state

agencies and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with ongoing regulatory requirements, including cGMPs, which impose certain procedural and documentation requirements upon us and third-party manufacturers. Failure to comply with the statutory and regulatory requirements can subject a manufacturer to possible legal or regulatory action, such as warning letters, suspension of manufacturing, seizure of product, injunctive action or possible civil penalties. Our company cannot be certain it or its present or future third-party manufacturers or suppliers will be able to comply with the cGMP regulations and other ongoing FDA regulatory requirements. If our company or its present or future third-party manufacturers or suppliers are not able to comply with these requirements, the FDA may halt our clinical trials, require us to recall a drug from distribution, or withdraw approval of the BLA for the therapeutic product.

The FDA closely regulates the post-approval marketing and promotion of biologics, including standards and regulations for direct-to-consumer advertising, off-label promotion, industry-sponsored scientific and educational activities, and promotional activities involving the Internet. A company can make only those claims relating to safety and efficacy approved by the FDA. Failure to comply with these requirements can result in adverse publicity, warning letters, corrective advertising, and potential civil and criminal penalties. Physicians may prescribe legally available biologics for uses not described in the product's labeling and different from those tested by us and approved by the FDA. Such off-label uses are common across medical specialties. Physicians may believe such off-label uses are the best treatment for many patients in varied circumstances. The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, impose stringent restrictions on manufacturers' communications regarding off-label use.

Healthcare Reform

In 2010, Congress passed the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, which we refer to as the ACA, a sweeping law intended to broaden access to health insurance, reduce or constrain the growth of health spending, enhance remedies against fraud and abuse, add new transparency requirements for the healthcare and health insurance industries, impose new taxes and fees on the health industry, and impose additional policy reforms. The ACA contains a number of provisions, including those governing enrollment in federal healthcare programs, reimbursement changes, and fraud and abuse, impacting existing government healthcare programs and resulting in the development of new programs, including Medicare payment for performance initiatives, and improvements to the physician quality reporting system and feedback program. The Affordable Care Act also does, among other things, the following:

- Increases pharmaceutical manufacturer rebate liability under the Medicaid Drug Rebate Program due to an increase in the minimum basic Medicaid rebate on most branded prescription drugs, and the application of Medicaid rebate liability to drugs used in risk-based Medicaid managed care plans.
- Expands the 340B Drug Pricing Program to require discounts for "covered outpatient drugs" sold to certain children's hospitals, critical access hospitals, freestanding cancer hospitals, rural referral centers, and sole community hospital.
- Requires pharmaceutical companies to offer discounts on brand-name drugs to patients who fall within the Medicare Part D coverage gap, commonly referred to as the "Donut Hole."
- Requires pharmaceutical companies to pay an annual non-tax-deductible fee to the federal government based on each company's market share of prior year total sales of branded drugs to certain federal healthcare programs, such as Medicare, Medicaid, Department of Veterans Affairs, and Department of Defense.
- Establishes the Patient-Centered Outcomes Research Institute to identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research. The research conducted by the Patient-Centered Outcomes Research Institute may affect the market for certain pharmaceutical products.
- Establishes the Center for Medicare and Medicaid Innovation within the Centers for Medicare and Medicaid Services, or CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending.

From time to time, legislation is drafted, introduced, and passed in Congress that could significantly change the statutory provisions governing the sale, marketing, coverage, and reimbursement of products regulated by the CMS or other government agencies. In addition to new legislation, CMS regulations and policies are often revised or interpreted by the agency in ways significantly affecting our business and our products.

Since its enactment, there have been judicial and Congressional challenges to certain aspects of the ACA, and we expect there will be additional challenges and amendments to the ACA in the future. For example, in November 2020, the United States Supreme Court held oral arguments on the ACA case from the U.S. Court of Appeals for the 5th Circuit, which upheld the District Court ruling that the individual mandate is unconstitutional, and the Supreme Court is expected to issue a decision

by mid-2021. It is uncertain how the Supreme Court will rule on this case. We cannot predict how this decision or future litigation will impact our business, or what other healthcare measures and regulations will ultimately be implemented at the federal or state level.

Additionally, at the federal level, in 2020, the HHS and CMS issued various rules that are expected to impact, among others, price reductions from pharmaceutical manufacturers to plan sponsors under Part D, fee arrangements between pharmacy benefit managers and manufacturers, importation of prescription drugs from Canada and other countries, manufacturer price reporting requirements under the Medicaid Drug Rebate Program, including regulations that affect manufacturer-sponsored patient assistance programs subject to pharmacy benefit manager accumulator programs and Best Price reporting related to certain value-based purchasing arrangements. Multiple lawsuits have been brought against the HHS challenging various aspects of these new rules. In January 2021, the Biden administration issued a "regulatory freeze" memorandum that directs department and agency heads to review new or pending rules of the prior administration. In January 2021, President Biden also issued an executive order to initiate a special enrollment period for people to obtain health insurance coverage through the ACA marketplace, and instructs certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, among others. The impact of these lawsuits as well as legislative, executive, and administrative actions of the Biden administration on us and the biopharmaceutical industry as a whole is unclear. Certain healthcare 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 the impact of potential legislation on our company.

Furthermore, political, economic, and regulatory influences are subjecting the health care industry in the U.S. to fundamental change. Initiatives to reduce the federal budget and debt and to reform health care coverage are increasing cost-containment efforts. We anticipate federal agencies, Congress, state legislatures, and the private sector will continue to review and assess alternative health care benefits, controls on health care spending, and other fundamental changes to the healthcare delivery system. Any proposed or actual changes could limit coverage for, or the amounts federal and state governments will pay for, health care products and services, which could also result in reduced demand for our products or additional pricing pressures, and limit or eliminate our spending on development projects and affect our ultimate profitability.

Third-Party Payor Coverage and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any products for which we may obtain regulatory approval. In the U.S., sales of any products for which we may receive regulatory approval for commercial sale will depend in part on the availability of coverage and reimbursement from third-party payors. Third-party payors include government authorities such as Medicare, Medicaid, TRICARE, and the Veterans Administration, managed care providers, private health insurers and other organizations.

The Medicaid Drug Rebate Program, which is part of the federal Medicaid program, a program for financially needy patients, among others, requires pharmaceutical manufacturers to enter into and have in effect a national rebate agreement with the Secretary of the Department of Health and Human Services as a condition for states to receive federal matching funds for the manufacturer's outpatient drugs furnished to Medicaid patients.

In order for a pharmaceutical product to receive federal reimbursement under Medicare Part B, part of the federal Medicare program covering outpatient items and services for the aged and disabled, and Medicaid programs or to be sold directly to U.S. government agencies, the manufacturer must extend discounts to entities eligible to participate in the 340B drug pricing program, a federal program requiring manufacturers to provide discounts to certain safety-net providers. The required 340B discount on a given product is calculated based upon certain Medicaid Drug Rebate Program metrics reported by the manufacturer.

The process for determining whether a payor will provide coverage for a product is typically separate from the process for setting the reimbursement rate a payor will pay for the product. Third-party payors may limit coverage to specific products on an approved list or formulary which might not include all of the FDA-approved products for a particular indication. Also, third-party payors may refuse to include a particular branded product on their formularies or otherwise restrict patient access to a branded drug when a less costly generic equivalent or other alternative is available. However, under Medicare Part D - Medicare's outpatient prescription drug benefit - there are protections in place to ensure coverage and reimbursement for oncology products and all Part D prescription drug plans are required to cover substantially all anti-cancer agents. Furthermore, a payor's decision to provide coverage for a product does not imply an adequate reimbursement rate will be available. Adequate third-party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development.

Third-party payors are increasingly challenging the price and examining the medical necessity and cost-effectiveness of medical products and services, in addition to their safety and efficacy. In order to obtain coverage and reimbursement for any product approved for sale, we may need to pursue compendia listings or conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of any products, in addition to the costs required to obtain regulatory approvals. Our drug candidates may not be considered medically necessary or cost-effective. If third-party payors do not consider a product to be cost-effective compared to other available therapies, they may not cover an approved product as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow a company to sell its products at a profit.

Other Healthcare Laws and Regulations

If we obtain regulatory approval of our products, we may be subject to various federal and state laws targeting fraud and abuse in the healthcare industry. These laws may impact, among other things, our proposed sales and marketing strategies. In addition, we may be subject to patient privacy regulation by both the federal government and the states in which we conduct our business. The laws affecting our ability to operate include, but are not limited to:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, receiving, offering, or paying remuneration (a term interpreted broadly to include anything of value, including, for example, gifts, discounts, and credits), directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order, or recommendation of, an item or service reimbursable under a federal health care program, such as the Medicare and Medicaid programs;
- federal civil and criminal false claims laws and civil monetary penalty laws, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment to Medicare, Medicaid, or other third-party payors that are false or fraudulent, or making a false statement or record material to payment of a false claim or avoiding, decreasing, or concealing an obligation to pay money owed to the federal government;
- provisions of HIPAA, prohibiting knowingly and willfully executing a scheme to defraud any health care benefit program and making false statements relating to health care matters;
- provisions of HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act and its implementing regulations, which imposes certain requirements relating to the privacy, security, and transmission of individually identifiable health information;
- the federal transparency laws, including the federal Physician Payment Sunshine Act, which was part of the Affordable Care Act, requiring manufacturers of certain drugs and biologics, among other covered medical products, to track and report annually certain payments and other transfers of value they make to U.S. physicians and teaching hospitals, as defined by law, as well as physicians' and physicians' immediate family members' ownership and investment interests in the applicable manufacturer, which are subsequently made publicly available in a searchable format on the CMS Open Payments website; effective January 1, 2022, such reporting obligations with respect to covered recipients will be extended to include payments and transfers of value made during the previous year to certain non-physician providers, such as physician assistants and nurse practitioners, among others; and
- state law equivalents of each of the above federal laws, such as anti-kickback and false claims laws which may apply to items or services reimbursed by any third-party payor, including commercial insurers, state transparency reporting and compliance laws, 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 may not have the same effect, thus complicating compliance efforts.

The ACA broadened the reach of the fraud and abuse laws by, among other things, amending the intent requirement of the federal Anti-Kickback Statute and the applicable criminal healthcare fraud statutes contained within 42 U.S.C. § 1320a-7b. Pursuant to the statutory amendment, a person or entity no longer needs to have actual knowledge of this statute or specific intent to violate it in order to have committed a violation. In addition, the ACA provides the government may assert a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act or the civil monetary penalties statute. Many states have adopted laws similar to the federal Anti-Kickback Statute, some of which apply to the referral of patients for healthcare items or services reimbursed by any source, not only the Medicare and Medicaid programs.

Human Capital

Our employees share a passion for meaningful work and are committed to solving the most complex problems in creating immunotherapies to treat cancer and autoimmune and inflammatory diseases. Our culture is guided by our core values of innovative thinking, collaboration, flexibility, bias for action, and healthy debate. As of December 31, 2020, we had 57 employees, of which 44 are engaged in research and development activities and 13 in general and administrative. None of our employees are represented by labor unions or covered by collective bargaining agreements. We consider our relationship with our employees to be good.

We believe that we provide competitive compensation and benefits for our personnel and that our compensation and benefit packages are designed to attract and retain highly qualified personnel essential to our business. In addition to salary compensation, our compensation includes new equity grants, a 401(k) retirement plan, healthcare and insurance benefits and a flexible paid time off policy.

We are committed to diversity, equity and inclusion. We recruit the best qualified employees regardless of gender, ethnicity or other protected traits and it is our policy to comply with all applicable laws related to discrimination in the workplace.

Finally, in response to the COVID-19 pandemic, we continue to provide many employees with the ability to work from home and have implemented additional safety and infection prevention measures including enhanced cleaning, additional personal protective equipment, testing, and contact tracing protocols for employees who have transitioned back to critical work on site.

Corporate Information

On July 24, 2017, Alpine Immune Sciences, Inc., or Private Alpine, completed its business combination with Nivalis Therapeutics, Inc., a publicly held company. In connection with the merger, Nivalis Therapeutics, Inc. changed its name to Alpine Immune Sciences, Inc. 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.

Our principal executive office is located at 188 East Blaine Street, Suite 200, Seattle WA, 98102. Our telephone number is (206) 788-4545. Our website is www.alpineimmunesciences.com. Information contained in, or that can be accessed through, our website is not a part of, and is not incorporated into, this report.

Item 1A. Risk Factors

You should carefully consider the following risk factors, in addition to the other information contained in this Annual Report on Form 10-K, including Management's Discussion and Analysis of Financial Condition and Results of Operations included in Part II, Item 7, 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-K 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 Pipeline and Product Development

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 in part via our proprietary directed evolution platform 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 the majority of our approaches. 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 our platform is both preliminary and limited.

Relatively few therapeutic candidates based on immunoglobulin superfamily, or IgSF, domains, or tumor necrosis factor receptor super family, or TNFRSF, domains, have been tested in humans. We may discover the therapeutic candidates developed using our scientific platform do not possess certain properties required for the therapeutic candidate to be effective. We currently have only limited data to suggest we can introduce these necessary therapeutic properties into variant Ig domain, or vIgD or variant TNF(R) domain, or vTD, based therapeutic candidates. In addition, vIgDs or vTDs may demonstrate different chemical and pharmacological properties in human subjects or patients than they do in laboratory studies. Even if our programs 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. While we continue to evaluate our vIgDs and vTDs preclinically and clinically, the risk profile in humans is still being fully assessed. Undesirable side effects that may be caused by our therapeutic candidates could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or other comparable foreign authorities. Such side effects could also affect patient recruitment or the ability of enrolled patients to complete clinical trials or result in potential product liability claims. Any of these occurrences may harm our business, financial condition and prospects significantly. As a result, we may never succeed in developing a marketable therapeutic, we may not become profitable, and the value of our common stock may decline.

Further, we believe that the FDA has little prior experience with vIgDs or vTDs, which may increase the complexity, uncertainty, and length of the regulatory approval process for our therapeutic candidates. Our company and our current collaborators, or any future collaborators, may never receive approval to market and commercialize any therapeutic candidate. Even if our company or a collaborator obtains regulatory approval, the approval may be for disease indications or patient populations not as broad as we intended or desired or may require labeling, including significant use or distribution restrictions or safety warnings. Our company or a collaborator may be required to perform additional or unanticipated clinical trials to obtain approval or be subject to post-marketing testing requirements to maintain regulatory approval. If therapeutic candidates we develop using our scientific platform prove to be ineffective, unsafe, or commercially unviable, our entire platform and pipeline would have little, if any, value, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

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

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

our existing collaborator, or any future collaborators. Market acceptance of our therapeutic products will depend on, among other factors:

- the timing of our receipt of any marketing and commercialization approvals;
- the terms of any approvals and the countries in which approvals are obtained;
- the safety and efficacy of our therapeutic products;
- the prevalence and severity of any adverse side effects associated with our therapeutic products;
- the prevalence and severity of any adverse side effects associated with therapeutics of the same type or class as our therapeutic products;
- limitations or warnings contained in any labeling approved by the FDA or other regulatory authority;
- relative convenience and ease of administration of our therapeutic products;
- the willingness of patients to accept any new methods of administration;
- the success of our physician education programs;
- the availability of adequate government and third-party payor coverage and reimbursement;
- the pricing of our products, particularly as compared to alternative treatments;
- our ability to compliantly market and sell our products; and
- availability of alternative effective treatments for the disease indications our therapeutic products are intended to treat and the relative risks, benefits, and costs of those treatments.

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

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

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

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

We have no products on the market and all of our therapeutic candidates are in early stages of development. Our ability to achieve and sustain profitability depends on obtaining regulatory approval and Institutional Review Board, or IRB, approval to conduct clinical trials at particular sites, obtaining regulatory approvals to market our therapeutic candidates and successfully commercializing our therapeutic candidates, either alone or with third parties, such as our collaborators. Before obtaining regulatory approval for the commercial distribution of our therapeutic candidates, we or a collaborator must conduct

extensive preclinical tests and clinical trials to demonstrate the safety and efficacy in humans of our therapeutic candidates. Preclinical testing and clinical trials are expensive, difficult to design and implement, can take many years to complete, and are uncertain as to outcome. For example, we are currently advancing the development of ALPN-101, ALPN-202 and ALPN-303; however, even with the significant investment of time and funding to advance these product candidates, we cannot guarantee that our clinical and preclinical development efforts will be successful. The start or end of a clinical study is often delayed or halted due to delays in or failure to obtain regulatory approval to commence the study, delays in or failure to reach agreement on acceptable terms with prospective contract research organizations or clinical trial sites, delays in or failure to obtain IRB approval at each site, changing regulatory requirements, manufacturing challenges, clinical sites or contract research organizations deviating from the trial protocol or failing to comply with regulatory requirements or meet contractual obligations, slower than anticipated patient enrollment, changing standards of care, availability or prevalence of use of a comparative therapeutic or required prior therapy, clinical outcomes, failure of patients to complete the trial or return for post-treatment follow-up, or financial constraints. For instance, delays or difficulties in patient enrollment or difficulties in retaining trial participants can result in increased costs, longer development times, or termination of a clinical trial. Clinical trials of a new therapeutic candidate require the enrollment of a sufficient number of patients, which may include patients who are suffering from the disease the therapeutic candidate is intended to treat and who meet other eligibility criteria. Rates of patient enrollment are affected by many factors, including the size of the patient population, the eligibility criteria for the clinical trial, the age and condition of the patients, the stage and severity of disease, the nature of the protocol, the proximity of patients to clinical sites, and the availability of effective treatments or competing academic and other clinical trials for the relevant disease.

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

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

- negative or inconclusive results from our clinical trials, or the clinical trials of others for therapeutic candidates similar to ours, leading to a decision or requirement to conduct additional preclinical testing or clinical trials or abandon a program;
- serious and unexpected drug-related side effects experienced by participants in our clinical trials or by individuals using therapeutics similar to our therapeutic candidates;
- serious drug-related side effects experienced in the past by individuals using therapeutics similar to our therapeutic candidates;
- delays in submitting Investigational New Drug, or IND, applications or clinical trial applications, or comparable foreign applications, or delays or failure in obtaining the necessary approvals from regulators or IRBs to commence a clinical trial, or a suspension or termination of a clinical trial once commenced;
- conditions imposed by the FDA or comparable foreign authorities, such as the European Medicines Agency, or EMA, regarding the scope or design of our clinical trials;
- delays in enrolling research subjects in clinical trials;
- high drop-out rates of research subjects;
- inadequate supply or quality of therapeutic candidate or therapeutic candidate components, or materials or other supplies necessary for the conduct of our clinical trials, including those owned, manufactured, or provided by companies other than ours;

- greater than anticipated clinical trial costs, including the cost of any approved drugs used in combination with our therapeutic candidates;
- poor effectiveness of our therapeutic candidates during clinical trials;
- unfavorable FDA or other regulatory agency inspection and review of a clinical trial site;
- failure of our third-party contractors or investigators to comply with regulatory requirements or otherwise meet their contractual obligations in a timely manner, or at all;
- delays and changes in regulatory requirements, policies, and guidelines, including the imposition of additional regulatory oversight around clinical testing generally or with respect to our technology in particular; or
- varying interpretations of data by the FDA and similar foreign regulatory agencies.

Product development involves a lengthy and expensive process with an uncertain outcome, and results of earlier preclinical 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 preclinical 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 evaluated ALPN-101 in a Phase 1 healthy volunteer trial and previously initiated a Phase 1b/2 study of ALPN-101 in patients with steroid-resistant or steroid-refractory active acute graft-versus-host disease, or SR-aGVHD. We terminated this Phase 1b/2 SR-aGVHD study in June 2020. The proposed Phase 2 study in SLE will materially increase our anticipated research and development spending. SLE is a challenging indication and a number of trials conducted by other companies have failed after significant investment of time and funding. We cannot predict whether our efforts in this indication will be successful. If we are unsuccessful, it is unlikely that AbbVie would exercise its option for ALPN-101 pursuant to our option and license agreement and, as a result, we would not receive the option payment pursuant to this agreement and we would not be eligible for future milestones and royalties. In addition, we have initiated our Phase 1 study of ALPN-202 and are conducting additional nonclinical studies and manufacturing activities for ALPN-303 to support initiation of a Phase 1 clinical trial in healthy volunteers in the fourth quarter of 2021. We will have to conduct additional preclinical studies and human trials in our proposed indications to verify the results obtained to date and to support any regulatory submissions for further clinical development. A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or adverse safety profiles despite promising results in earlier, smaller clinical trials. Moreover, clinical data are often susceptible to varying interpretations and analyses. We do not know whether Phase 1, Phase 2, Phase 3, or other clinical trials we may conduct will demonstrate consistent or adequate efficacy and safety with respect to the proposed indication for use sufficient to receive regulatory approval or market our therapeutic candidates.

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

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

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

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

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

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

Specifically, our competitors include companies developing therapies with the same target(s) as ALPN-101, ALPN-202 and ALPN-303 as well as companies building novel platforms to generate multi-specific antibody or non-antibody-based targeting proteins.

ALPN-101 Program Competitors (ICOSL/CD28)

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

- an anti-BAFF, anti-ICOSL bispecific antibody being developed by Amgen, Inc (rozibafusp alfa (AMG570/MEDI0700));
- an anti-CD28 monoclonal antibody fragment being developed by OSE ImmunoTherapeutics SA (FR104);
- an anti-CD28 peptide being developed by AtoxBio, Inc (reltecimod (AB-103));
- an anti-CD28 monoclonal antibody being development by TheraMAB (TAB08); and
- CTLA-4-Fc fusion proteins targeting CD80 and CD86 being marketed Bristol Myers Squibb (abatacept and belatacept).

ALPN-202 Program Competitors

There are numerous clinical trials for immuno-oncology products used as a single agent or in combination. One of the potentially novel attributes of the ALPN-202 program is that it has exhibited conditional CD28 costimulation and dual checkpoint inhibition in a single molecule interacting with multiple immune targets.

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

- wild-type CD80-Fc being developed by Five Prime Therapeutics, Inc. (FPT155);
- bispecific antibodies being developed by Regeneron targeting tumor specific antigens and CD28 (REGN5678 anti-PSMAxCD28, REGN5668 anti-MUC16xCD28, and REGN7075 anti-EGFRxCD28);
- trispecific antibodies being developed by Sanofi (CD3xCD38xCD28) (SAR442257);
- bifunctional fusion protein composed of monoclonal antibody against PD-L1 fused to the extracellular domain of human transforming growth factor-ß, or TGF-ß, receptor II being developed by EMD Serono, Inc. and GlaxoSmithKline plc (bintrafusp alfa, or M7824);
- bifunctional fusion protein composed of PD-1 and OX40L developed by Shattuck Labs, Inc. (SL-279252);
- bispecific fusion protein targeting 4-1BB and PD-L1 being developed by Shattuck Labs, Inc. (SL-279137);
- bispecific fusion protein targeting 4-1BB and PD-L1 being developed by Pieris Pharmaceuticals, Inc. (PRS-344);
- bispecific monoclonal antibody targeting 4-1BB and PD-L1 being developed by Genmab A/S and BioNTech SE (GEN1046);

- trispecific monoclonal antibody/fusion targeting 4-1BB and PD-L1 being developed by Numab Therapeutics AG and CStone Pharmaceuticals Co., Ltd (NM021);
- bispecific monoclonal antibody targeting 4-1BB and PD-L1 being developed by Merus NV and Incyte Corporation (MCL-145);
- bispecific antibody 4-1BB and PD-L1 being developed by Inhibrx, Inc. and Elpiscience Biopharma Ltd. (INBRX-105);
- bispecific monoclonal antibody targeting 4-1BB and PD-L1 being developed by F-star Biotechnology Ltd. (FS-222);
- bispecific fusion protein targeting 4-1BB and PD-L1 being developed by Kahr Medical Ltd., (DSP105);
- bispecific monoclonal antibody/fusion protein targeting 4-1BB and PD-L1 being developed by ABL, Inc., and I-Mab Biopharma Co., Ltd. (ABL503);
- bispecific monoclonal antibody targeting PD-L1 and LAG-3 being developed by F-star Biotechnology, Ltd. (FS118);
- bispecific monoclonal antibodies being developed by Xencor, Inc. including XmAb20717 targeting CTLA-4 and PD-1, XmAb22841 targeting CTLA-4 and LAG-3, XmAb23104 targeting PD-1 and ICOS, and a CD28 bispecific antibody platform;
- bispecific constructs called “DARTs” being developed by Macrogenics Inc., including MGD013 targeting PD-1 and LAG-3 and MGD019 targeting PD-1 and CTLA-4;
- bispecific monoclonal antibody being developed by Tesaro, Inc., which was purchased by GlaxoSmithKline plc, targeting PD-1 and LAG-3;
- small molecule antagonists being developed by Aurigene Ltd and Curis, Inc., including CA-170 targeting PD-L1 and VISTA and CA-327 targeting PD-L1 and TIM-3;
- various combinations of separate anti PD-1/L1 and anti-CTLA-4 monoclonal antibodies; and
- various combinations of separate anti PD-1/L1 and costimulatory monoclonal antibodies such as OX-40, 4-1BB, and others.

ALPN-303 Program Competitors

The competitors listed below have programs targeting either the TACI, BCMA, or BAFF pathway for autoimmune disease.

- Anti-BAFF antibody marketed by GSK plc (belimumab);
- TACI-Fc being developed by Vera Therapeutics (atacicept);
- TACI-Fc being developed by RemeGen Ltd. (telitacicept (RC18));
- Anti-BAFFr IgG1 being developed by Novartis AG (Ianalumab (VAY736));
- Anti-APRIL antibody being developed by Visterra, Inc. (VIS649);
- an anti-BAFF, anti-ICOSL bispecific antibody being developed by Amgen, Inc. (rozibafusp alfa (AMG570/MEDI0700)); and
- an anti-APRIL antibody being developed by Chinook Therapeutics, Inc. (BION-1301).

Novel Platform Competitors

Multifunctional therapeutic protein platforms potentially competitive with our platform include:

- Amgen, Inc. (BiTE®): fusion proteins consisting of two single-chain variable fragments to link T cells to tumors;

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

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.

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

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

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

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

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

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

Risks Related to Our Relationships with Third Parties

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

Our success is dependent, in part, on our collaborators' efforts to develop our therapeutic candidates and, historically, our revenue has been primarily derived from our agreements with collaborators. For example, in May 2019, we entered the Adaptimmune Agreement to develop next-generation SPEAR T cell products and in June 2020, we entered into the AbbVie Agreement for the development of ALPN-101. Pursuant to the terms of the AbbVie Agreement, we received an upfront payment of $60.0 million in cash and are eligible to receive up to $75.0 million in development milestones, an additional $75.0 million if AbbVie exercises its option with respect to ALPN-101 following our completion of certain development activities, additional development, commercial and sales-based milestones up to an aggregate of $655.0 million and royalties on any future net sales.

Pursuant to the AbbVie Agreement, we will conduct certain development activities under a development plan that provides for, among other things, the generation of a data package in order for AbbVie to evaluate exercising its option, including all activities reasonably necessary to complete our planned Phase 2 study of ALPN-101 in SLE. If we successfully complete these activities, AbbVie may not exercise its option, which would make achievement of future milestones and receipt of future royalties unattainable. If AbbVie exercises its option, our realization of additional milestones and royalty payments will depend upon the efforts of AbbVie. AbbVie will have discretion in determining and directing the efforts and resources for future development activities and, if approval is obtained, commercialization and marketing of the approved drug. AbbVie may not be effective in obtaining approvals for ALPN-101 or marketing or arranging for necessary supply, manufacturing, or distribution relationships for any approved products. AbbVie may also change its strategic focus or pursue alternative technologies in a manner resulting in reduced, delayed, or no additional payments to us. If AbbVie fails to develop, obtain regulatory approval for, or ultimately commercialize ALPN-101 or if AbbVie 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 AbbVie 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.

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

may occur, which could further delay development, distract management and generate substantial expenses, any of which could materially and negatively impact our business.

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

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

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

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

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

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

result in significant delay of our preclinical or clinical activities because there may be a limited number of qualified replacements.

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

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

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

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

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

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

- exposure to unknown liabilities;
- disruption of our business and diversion of our management's time and attention in order to manage a collaboration or develop acquired therapeutic candidates, or technologies;

- incurrence of substantial debt or dilutive issuances of equity securities to pay transaction consideration or costs;
- higher than expected collaboration, acquisition, or integration costs;
- write-downs of assets, or 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.

Risks Related to Our Ability to Commercialize Product Candidates

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

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

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

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

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

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

The FDA also has the authority to require a Risk Evaluation and Mitigation Strategies, or REMS, plan either before or after approval, which may impose further requirements or restrictions on the distribution or use of an approved therapeutic. The

EMA now routinely requires risk management plans, or RMPs, as part of the marketing authorization application process, and such plans must be continually modified and updated throughout the lifetime of the product as new information becomes available. In addition, the relevant governmental authority of any EU member state can request an RMP whenever there is a concern about the risk/benefit balance of the product.

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

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

Imposed price controls may adversely affect our future profitability.

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

Reference pricing used by various EU member states and parallel distribution, or arbitrage between low-priced and high-priced member states, can further reduce prices. In some countries, we or our collaborators may be required to conduct a clinical trial or other studies comparing the cost-effectiveness of our therapeutic candidates to other available therapies in order to obtain or maintain reimbursement or pricing approval. Publication of discounts by third-party payors or authorities may lead to further pressure on the prices or reimbursement levels within the country of publication and other countries. If reimbursement of any product candidate approved for marketing is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business, financial condition, results of operations, or prospects could be adversely affected.

Risks Related to Our Personnel and Operations

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 December 31, 2020, we had $131.4 million in cash and cash equivalents, restricted cash, and investments. Based on our current operating plan, we believe our available cash and cash equivalents, and investments 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, debt, and payments received under our collaboration agreements, including the AbbVie Agreement. We will be required to seek additional funding in the future and intend to do so through a combination of public or private equity offerings, debt financings, credit and loan facilities, research collaborations, and license agreements. Our ability to raise additional funds from these or other sources will depend on financial, economic, and other factors, many of which are beyond our control. Additional funds may not be available to us on acceptable terms or at all.

If we raise additional funds by issuing equity securities, our stockholders will suffer dilution, and the terms of any financing may adversely affect the rights of our stockholders. For example, in January 2019, we issued in a private placement 4,706,700 shares of common stock and warrants to purchase an additional 1,835,610 shares of common stock for gross proceeds of approximately $25.3 million. In July 2020, we issued in a private placement 5,139,610 shares of common stock, prefunded warrants to purchase 790,710 shares of common stock and warrants to purchase an additional 1,779,096 shares of common stock for gross proceeds of approximately $60.0 million.

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

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

We are a clinical-stage immunotherapy company, with a limited operating history, focused on developing treatments for autoimmune/inflammatory diseases and cancer. Since inception, we have devoted our resources to developing novel protein-based immunotherapies primarily using our proprietary directed evolution platform, which converts native immune system proteins into potential differentiated, multi-targeted therapeutics designed to modulate the immune system. We have had significant operating losses since inception. For the year ended December 31, 2020, our net loss was $27.9 million. Substantially all of our losses have resulted from expenses incurred in connection with our research programs and from general and administrative costs associated with our operations. Our technologies and therapeutic candidates are in early stages of development, and we are subject to the risks of failure inherent in the development of therapeutic candidates based on novel technologies.

We have historically generated revenue primarily from the receipt of research funding and upfront payments under our collaboration agreements, including the AbbVie Agreement. 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.

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

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

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

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

We have limited experience in therapeutic development and very limited experience with clinical trials of therapeutic candidates. As our therapeutic candidates enter and advance through preclinical studies and clinical trials, we will need to expand our development, regulatory, and manufacturing capabilities or contract with other organizations to provide these capabilities for us. For example, as we prepare to initiate our Phase 2 study in SLE, we will need to hire additional personnel in clinical operations. We also must manage 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.

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

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

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

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

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

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

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

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

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

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

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

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

treatment of animals used in research, we may be subject to fines and penalties and adverse publicity, and our operations could be adversely affected.

Our 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 man-made 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.

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.

Risks Related to Our Financial Position and Capital Needs

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 December 31, 2020, we had $131.4 million in cash and cash equivalents, restricted cash, and investments. We expect to invest our excess cash in marketable securities. These investments are subject to general credit, liquidity, market and interest rate risks. 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.

Our business may be materially affected by changes to fiscal and tax policies. Negative or unexpected tax consequences could adversely affect our results of operations.

New tax laws, statutes, rules, regulations or ordinances could be enacted at any time, which could adversely affect our business operations, and our business and financial performance. Further, existing tax laws, statutes, rules, regulations or ordinances could be interpreted, changed, modified or applied adversely to us. For example, the Tax Cuts and Jobs Act of 2017, or TCJA, enacted in December 2017, as modified by the Coronavirus Aid, Relief, and Economic Security Act, or the CARES Act, enacted in April 2020, significantly changed the U.S. Internal Revenue Code. Such changes include a reduction in the corporate tax rate and limitations on certain corporate deductions and credits, among other changes. We have generally accounted for changes related to the TCJA in accordance with our understanding of the legislation and guidance available as of the date of this filing as described in more detail in our financial statements and will continue to monitor and assess the impact of the federal legislation on our business and the extent to which various states conform to the newly enacted federal tax law. In addition, adverse changes in the financial outlook of our operations or further changes in tax laws or regulations could lead to changes in our valuation allowances against deferred tax assets on our consolidated balance sheets, which could materially affect our results of operations.

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 NOL carryforwards, 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 in 2017 likely resulted in an ownership change for Nivalis. It is likely that, due to the method by which limitations on the utilization of NOL carryforwards are calculated, we will not be able to utilize any of Nivalis' NOL carryforwards and certain other tax attributes. It is also possible that Alpine's NOL 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' NOL carryforwards and certain other tax attributes, which could have a material adverse effect on cash flow and results of operations.

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

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

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

These restrictions could inhibit our ability to pursue our business strategies. If we default under our term loan agreement, including a material adverse change in our business, operations or condition (financial or otherwise), 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.

Risks Related to COVID-19 and Other Health Epidemics

The COVID-19 coronavirus could adversely impact our business, including our clinical trials.

In December 2019, a novel strain of coronavirus, SARS-CoV-2, the causative agent of coronavirus disease 2019, or COVID-19, was first reported. Since then, SARS-CoV-2 has spread globally, including countries in which we have planned or active clinical trial sites. We have experienced and will likely continue to experience disruptions that could severely impact our business and clinical trials, including:

- delays or difficulties in enrolling patients in our clinical trials;
- delays or difficulties in clinical site initiation, including difficulties in recruiting clinical site investigators and clinical site staff;
- diversion of healthcare resources away from the conduct of clinical trials, including the diversion of hospitals serving as our clinical trial sites and hospital staff supporting the conduct of our clinical trials;
- interruption of key clinical trial activities, such as clinical trial site monitoring, due to limitations on travel imposed or recommended by federal or state governments, employers and others;

- limitations in employee resources that would otherwise be focused on the conduct of our clinical trials, including because of sickness of employees or their families or the desire of employees to avoid contact with large groups of people;
- delays in receiving approval from local regulatory authorities and ethics committees to initiate our planned clinical trials;
- delays in clinical sites receiving the supplies and materials needed to conduct our clinical trials;
- interruption in global shipping that may affect the transport of clinical trial materials, such as investigational drug product used in our clinical trials;
- changes in local regulations as part of a response to the COVID-19 coronavirus outbreak which may require us to change the ways in which our clinical trials are conducted, which may result in unexpected costs, or to discontinue the clinical trials altogether;
- delays in necessary interactions with local regulators, ethics committees and other important agencies and contractors due to limitations in employee resources or forced furlough of government employees; and
- refusal of the FDA to accept data from clinical trials whose conduct has been affected by the COVID-19 outbreak, such as due to missing data.

The global outbreak of the COVID-19 coronavirus continues to rapidly evolve. The extent to which the COVID-19 coronavirus may impact our business and clinical trials will depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the ultimate geographic spread of the disease, the duration of the outbreak, travel restrictions and social distancing in the United States and other countries, business closures or business disruptions and the effectiveness of actions taken in the United States and other countries to contain and treat the disease.

We face risks related to health epidemics and other outbreaks, which could significantly disrupt our operations and/or business.

Our business could be adversely impacted by the effects of the COVID-19 outbreak originating in China, or by other epidemics. Our supply chain for raw materials, drug substance or drug product is worldwide, including China, and accordingly could be subject to disruption. There may be restrictions on the export or shipment of raw materials, drug substance or drug product that could materially delay our business or clinical trials.

Certain of our research and development efforts are also conducted globally, for example the NEON-1 clinical trial includes investigative sites in Australia. A health epidemic or other outbreak, including the current COVID-19 outbreak, may materially and adversely affect our business, financial condition and results of operations. The extent to which the outbreak impacts our results will depend on future developments, which are highly uncertain and cannot be predicted, including new information which may emerge concerning the severity of the outbreak and the actions to contain the outbreak or treat its impact, among others.

Risks Related to Cybersecurity

Our business and operations could suffer in the event of system failures.

Computer system, network or telecommunications failures due to events such as damage from malware, unauthorized access, terrorism, war, or natural disasters could interrupt our internal or partner operations. For example, the loss of preclinical trial data, data from completed or ongoing clinical trials for our product candidates or other confidential information could result in delays in our regulatory filings and development efforts, significantly increase our costs and result in other adverse impacts to our business. To the extent that any disruption or cybersecurity breach was to result in a loss of or damage to our data, or inappropriate disclosure of confidential or proprietary information, we could incur liability and other remediation costs, and the development of our product candidates could be delayed. While we have implemented security measures, our internal computer systems and the external systems and services used by our third-party CMOs, third-party CROs, or other contractors, consultants, directors and partners remain potentially vulnerable to damage from these events.

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.

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 technology 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. Our scientific platform and substantially all of our intellectual property have been developed internally. As of December 31, 2020, our patent portfolio consists of over 140 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 platform technology and 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 platform technology and therapeutic candidates and products, are covered by valid and enforceable patents or are effectively maintained as trade secrets. If third parties disclose or misappropriate our proprietary rights, it may materially and adversely impact our competitive position in the market.

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

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

The issuance of a patent is not conclusive as to its inventorship, scope, validity, or enforceablity. Once granted, patents may remain open to opposition, interference, re-examination, post-grant review, inter partes review, nullification, or derivation action in court or before patent offices or similar proceedings before or after allowance or grant, during which time third parties can raise objections against such initial grant. In the course of such proceedings, which may continue for a protracted period of

time, the patent owner may be compelled to limit the scope of the pending, allowed or granted claims thus attacked or may lose the allowed or granted claims altogether. Our patent risks include that:

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

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

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

Patent terms may be inadequate to protect our competitive position on our platform technology and therapeutic candidates and products for an adequate amount of time.

Patents have a limited lifespan. In the United States and abroad, if all maintenance fees/annuity fees are timely paid, the natural expiration of a patent is generally 20 years from its earliest non-provisional filing date. The protection a patent affords is limited. Even if patents covering our products are obtained, once the patent life has expired, we may be open to competition from competitive products. Given the amount of time required for the development, testing and regulatory review of new products, patents protecting such products might expire before or shortly after such products are commercialized. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

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

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

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

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

sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could delay our research and development efforts and limit our ability to continue our operations.

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

If we were to initiate legal proceedings against a third party to enforce a patent covering our technology, including therapeutic candidates and products, the defendant could counterclaim that our patent is invalid or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, for example, patent ineligibility, lack of novelty, lack of written description, obviousness, or non-enablement. Grounds for an unenforceability assertion could be an allegation someone connected with prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during prosecution. The outcome following legal assertions of invalidity and unenforceability during patent litigation is unpredictable. With respect to the validity question, for example, we cannot be certain there is no invalidating prior art, of which we and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity or unenforceability, we would lose at least part, and perhaps all, of the patent protection on our technology, including our platform technology and 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 our platform technology and therapeutic candidates and products, if competitors design around our protected technology, including our platform technology and 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 our platform technology and 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 our platform technology and therapeutic candidates and products. Third party intellectual property rights holders may also actively bring infringement claims against us. We cannot guarantee we will be able to successfully settle or otherwise resolve such infringement claims. If we are unable to successfully settle future claims on terms acceptable to us, we may be required to engage in or continue costly, unpredictable, and time-consuming litigation and may be prevented from, or experience substantial delays in, marketing our technology, including therapeutic candidates and products. If we fail in any such dispute, in addition to being forced to pay damages, we may be temporarily or permanently prohibited from commercializing our technology, including a therapeutic product, held to be infringing. We might, if possible, also be forced to redesign therapeutic candidates or products so we no longer infringe the third-party intellectual property rights. Any of these events, even if we were ultimately to prevail, could require us to divert substantial financial and management resources we would otherwise be able to devote to our business.

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

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

If we do not obtain patent term extension and data exclusivity for any therapeutic candidate or product we may develop, our business may be materially harmed.

Depending upon the timing, duration, and specifics of any FDA marketing approval of any therapeutic candidate or product we may develop, one or more of our or in-licensed U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984 (Hatch-Waxman Act). The Hatch-Waxman Act permits a patent term extension of up to five years as compensation for patent term lost during the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent may be extended and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended. Similar extensions as compensation for patent term lost during regulatory review processes are also available in certain foreign countries and territories, such as in Europe under a Supplementary Patent Certificate. However, we may not be granted an extension in the United States and/or foreign countries and territories because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents, or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or the term of any such extension is shorter than what we request, our competitors may obtain approval of competing products following our patent expiration, and our business, financial condition, results of operations, and growth prospects could be materially harmed.

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

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

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

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

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

therapeutic candidates, which could severely harm our business. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to management.

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

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

Third parties may independently develop similar or superior technology.

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

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

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

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

Risks Related to Government Regulation

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

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

We have very limited experience in conducting and managing the clinical trials necessary to obtain regulatory approvals, including approval by the FDA as well as foreign regulatory authorities, such as the EMA. The time required to obtain FDA and foreign regulatory approvals is unpredictable but typically takes many years following the commencement of clinical trials, depending upon the type, complexity, and novelty of the therapeutic candidate, and at the substantial discretion of

the regulatory authorities. The standards the FDA and its foreign counterparts use when regulating us are not always applied predictably or uniformly and can change. Any analysis we perform of data from preclinical and clinical activities is subject to confirmation and interpretation by regulatory authorities, who could delay, limit, or prevent regulatory approval. We may also encounter unexpected delays or increased costs due to new government regulations, future legislation or administrative action, or from changes in the policy of FDA or foreign regulatory authorities during the period of product development, clinical trials, and regulatory review by the FDA or foreign regulatory authorities. It is impossible to predict whether legislative changes will be enacted, or whether FDA or foreign, regulations, guidance, or interpretations will be changed, or what the impact of such changes, if any, may be.

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

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

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

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

We are also subject to numerous foreign regulatory requirements governing, among other things, the conduct of clinical trials, manufacturing, marketing authorization, pricing, and third-party reimbursement. The foreign regulatory approval process varies among countries and may include all of the risks associated with FDA approval described above as well as risks

attributable to the satisfaction of local regulations in foreign jurisdictions. Moreover, the time required to obtain approval may differ from that required to obtain FDA approval. Approval by the FDA does not ensure approval by regulatory authorities outside the U.S. and vice versa.

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

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

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

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

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

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

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

- the U.S. federal Anti-Kickback Statute, which prohibits, among other things, persons from soliciting, receiving, offering, or providing remuneration, directly or indirectly, to induce either the referral of an individual for a healthcare item or service, or the purchasing or ordering of an item or service, for which payment may be made, in whole or in part, under a federal healthcare program such as Medicare or Medicaid;
- the U.S. federal False Claims Act, which imposes criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, false or fraudulent claims for payment or making a false statement to avoid, decrease, or conceal an obligation to pay money to the federal government. In addition, the government may assert a claim including items and services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act;
- state all-payor fraud laws, which impose criminal and civil liability for executing a scheme to defraud any healthcare benefit program, or knowingly and willfully falsifying, concealing, or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services; similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- HIPAA, HITECH, and their implementing regulations, which impose obligations on certain covered entity healthcare providers, health plans, and healthcare clearinghouses as well as their business associates performing certain services involving the use or disclosure of individually identifiable health information, including mandatory contractual terms, with respect to safeguarding the privacy, security, and transmission of individually identifiable health information, and require notification to affected individuals and regulatory authorities of certain breaches of security of individually identifiable health information;
- the federal Physician Payment Sunshine Act and its implementing regulations, also referred to as "Open Payments," issued under the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or ACA, and any subsequent amending legislation or executive actions, which require manufacturers of pharmaceutical and biological drugs, among other covered medical products, reimbursable under Medicare, Medicaid, or Children's Health Insurance Programs to track and report to the CMC certain payments and transfers of value, including but not limited to, consulting fees, travel reimbursements, and research grants made to physicians, as defined by law, and teaching hospitals, as well as certain physicians' and their immediate family members' ownership and investment interests in the applicable manufacturer, with limited exceptions; effective January 1, 2022, such reporting obligations with respect to covered recipients will be extended to include payments and transfers of value made during the previous year to certain non-physician providers, such as physician assistants and nurse practitioners, among others; and
- analogous state laws and regulations, such as, state anti-kickback and false claims laws potentially applicable to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers; and some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring drug manufacturers to report information related to payments to physicians and other healthcare providers or marketing expenditures, and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Ensuring our future business arrangements with third-parties comply with applicable healthcare laws and regulations could involve substantial costs. If our operations are found to be in violation of any such requirements, we may be subject to penalties, including civil or criminal penalties, monetary damages, the curtailment or restructuring of our operations, or exclusion from participation in government contracting, healthcare reimbursement, or other government programs, including

Medicare and Medicaid, any of which could adversely affect our financial results. Although effective compliance programs can mitigate the risk of investigation and prosecution for violations of these laws, these risks cannot be entirely eliminated. Any action against us for an alleged or suspected violation could cause our company to incur significant legal expenses and could divert our management's attention from the operation of our business, even if our defense is successful. In addition, achieving and sustaining compliance with applicable laws and regulations may be costly to us in terms of money, time, and resources.

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

- adverse regulatory inspection findings;
- warning or untitled letters;
- voluntary product recalls with public notification or medical product safety alerts to healthcare professionals;
- restrictions on, or prohibitions against, marketing our therapeutics;
- restrictions on, or prohibitions against, importation or exportation of our therapeutics;
- suspension of review or refusal to approve pending applications or supplements to approved applications;
- exclusion from participation in government-funded healthcare programs;
- exclusion from eligibility for the award of government contracts for our therapeutics;
- FDA debarment;
- suspension or withdrawal of therapeutic approvals;
- seizures or administrative detention of therapeutics;
- injunctions; and
- restitution, disgorgement of profits, or civil and criminal penalties and fines.

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

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

We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or executive or administrative action, either in the United States or abroad. The FDA's and other regulatory authorities' policies may change, and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained, and we may not achieve or sustain profitability. It is difficult to predict how current and future legislation, executive actions, and litigation, including the executive orders, will be implemented, and the extent to which they will impact our business, our clinical development, and the FDA's and other agencies' ability to exercise their regulatory authority, including FDA's pre-approval inspections and timely review of any regulatory filings or applications we submit to the FDA. To the extent any legislative or executive actions impose constraints on FDA's ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted.

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

The regulations governing marketing approvals, pricing, coverage, and reimbursement for new drugs and biologics vary widely from country to country. Many countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is

granted. Although we intend to monitor these regulations, our programs are currently in the early stages of development and we will not be able to assess the impact of price regulations for a number of years. As a result, we might obtain regulatory approval for a product in a particular country but then be subject to price regulations delaying our commercial launch of the product and negatively impacting the revenues we are able to generate from the sale of the product in that country.

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

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

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

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

In addition, in recent years, the U.S. Congress has enacted various laws seeking to reduce the federal debt level and contain healthcare expenditures. For example, as a result of the Budget Control Act of 2011 and the Bipartisan Budget Act of 2015, an annual 2% reduction to Medicare payments that took effect in 2013 and will remain in effect through 2030, with the exception of a temporary suspension implemented under various COVID-19 relief legislation from May 1, 2020 through March 31, 2021, unless additional Congressional action is taken. These across-the-board spending cuts could adversely affect our future revenues, earnings, and cash flows.

There has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices. Specifically, there have been several recent U.S. Congressional inquiries and proposed federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. At the federal level, the Trump administration used several means to propose or implement drug pricing reform, including through federal budget proposals, executive orders and policy initiatives. For example, in 2020, HHS and CMS issued various rules that are expected to impact, among others, price reductions from pharmaceutical manufacturers to plan sponsors under Part D, fee arrangements between pharmacy benefit managers and manufacturers, manufacturer price reporting requirements under the Medicaid Drug Rebate Program, including regulations that

affect manufacturer-sponsored patient assistance programs subject to pharmacy benefit manager accumulator programs and Best Price reporting related to certain value-based purchasing arrangements. Multiple lawsuits have been brought against the HHS challenging various aspects of the rules. In January 2021, the Biden administration issued a "regulatory freeze" memorandum that directs department and agency heads to review new or pending rules of the prior administration. It is possible that additional governmental action will be taken to address the COVID-19 pandemic. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors.

The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our product candidates. It is unclear whether these new regulations will be withdrawn or when they will become fully effective under the Biden administration. The impact of lawsuits as well as legislative, executive, and administrative actions of the Biden administration on us and the biopharmaceutical industry as a whole is unclear. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

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, as defined by law, and teaching hospitals. Effective January 1, 2022, reporting obligations under the Sunshine Act with respect to covered recipients will be extended to include payments and transfers of value made during the previous year to certain non-physician providers, such as physician assistants and nurse practitioners, among others. 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. Complying with new regulatory requirements and changes in the laws and regulations will increase our compliance cost and exposure to potential liability.

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. We cannot predict the extent of legislative, executive, and administrative actions of the Biden administration will have on us and the biopharmaceutical industry as a whole. If federal spending is reduced, anticipated budgetary shortfalls may also impact the ability of relevant agencies such as the FDA or the National Institutes of Health to continue to function at current levels. Amounts allocated to federal grants and contracts may be reduced or eliminated. These reductions may also impact the ability of relevant agencies to timely review and approve drug research and development, manufacturing, and marketing activities, which may delay our ability to develop, market, and sell any therapeutics we may develop.

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

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

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

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

The Patient Protection and Affordable Care Act, signed into law in 2010, includes a subtitle called the Biologics Price Competition and Innovation Act of 2009, or BPCIA, which created an abbreviated approval pathway for biological products that are biosimilar to or interchangeable with an FDA-licensed reference biological product. Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date that the reference product was first licensed by the FDA. In addition, the approval of a biosimilar product may not be made effective by the FDA until 12 years from the date on which the reference product was first licensed. During this 12-year period of exclusivity, another company may still market a competing version of the reference product if the FDA approves a full BLA for the competing product containing the sponsor’s own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of their product. The law is complex and is still being interpreted and implemented by the FDA. As a result, its ultimate impact, implementation, and meaning are subject to uncertainty. While it is uncertain when such processes intended to implement BPCIA may be fully adopted by the FDA, any such processes could have a material adverse effect on the future commercial prospects for our biological products.

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

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

In June 2016, the United Kingdom held a referendum and voted in favor of leaving the European Union, and in January 2020, the United Kingdom officially left the European Union, with a transitional period that lasted until December 31, 2020. A trade and cooperation agreement that outlines the future trading relationship between the United Kingdom and the European Union was agreed in December 2020. The United Kingdom's withdrawal from the European Union and ongoing negotiations related to the United Kingdom's future trade and other relationships with the European Union have created political and economic uncertainty, particularly in the United Kingdom and the European Union. Any business we conduct, now and in the future, in the United Kingdom, the European Union, and worldwide could be affected during this period of uncertainty, and perhaps longer, by the impact of the United Kingdom's decision to withdraw from the European Union. There are many ways in which our business could be affected, only some of which we can identify as of the date of this filing.

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

It is currently unknown how regulations affecting clinical trials, the approval of our future products, and the sale of these products in the United Kingdom or elsewhere in Europe will be affected by the United Kingdom's withdrawal from the European Union.

These possible negative impacts, and others resulting from the United Kingdom's withdrawal from the European Union, 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 be sustained. The lack of an active market may impair the ability of our stockholders to sell their shares at the time they wish to sell them or at a price that they consider reasonable, which may reduce the fair market value of their shares. Further, an inactive market may also impair our ability to raise capital by selling our common stock should we determine additional funding is required.

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

- our and our collaborators' 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;
- our ability to achieve development milestones and receive associated milestone payments pursuant to the terms of our collaboration agreements;
- the entry into, or termination of, key agreements, including key licensing, collaboration or acquisition agreements;
- the initiation or material developments in, or conclusion of, litigation to enforce or defend any of our intellectual property rights or defend against the intellectual property rights of others;
- announcements by commercial partners or competitors of new commercial products, clinical progress (or the lack thereof), significant contracts, commercial relationships, or capital commitments;
- adverse publicity relating to our markets, including with respect to other products and potential products in such markets;

- adverse publicity about our company, employees, therapeutic candidates, and/or therapeutic products in the media or on social media;
- the impact of COVID-19 on our company or the economy generally;
- the introduction of technological innovations or new therapies competing with our potential products;
- the loss of key employees;
- changes in estimates or recommendations by securities analysts, if any, who cover our common stock;
- general and industry-specific economic conditions potentially affecting our research and development expenditures;
- changes in the structure of health care payment systems;
- unanticipated serious safety concerns related to the use of any of our product candidates;
- failure to meet or exceed financial and development projections we may provide to the public;
- failure to meet or exceed the financial and development projections of the investment community;
- the perception of the pharmaceutical industry by the public, legislators, regulators, and the investment community;
- adverse regulatory decisions;
- disputes or other developments relating to proprietary rights, including patents, litigation matters, and our ability to obtain patent protection for our technologies;
- commencement of, or our involvement in, litigation;
- sales of our common stock by us or our stockholders in the future;
- trading volume of our common stock;
- period-to-period fluctuations in our financial results; and
- the other factors described in this “Risk Factors” section.

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

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

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

Our executive officers and directors together with their respective affiliates, beneficially own approximately 58% of our common stock as of December 31, 2020. As a result, if some of these persons or entities act together, they will have the ability to exercise significant influence over matters submitted to the stockholders for approval, including the election of directors, amendments to the certificate of incorporation and bylaws and the approval of any strategic transaction requiring the approval of the stockholders. These actions may be taken even if they are opposed by other stockholders. This concentration of ownership may also have the effect of delaying or preventing a change of control of our company or discouraging others from making tender offers for our shares, which could prevent our stockholders from receiving a premium for their shares. Some of these persons or entities who make up our principal stockholders may have interests different from other stockholders. The significant concentration of stock ownership may adversely affect the trading price of our common stock due to investors’ perception that conflicts of interest may exist or arise.

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

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

For example, in connection with our July 2020 private placement, we entered into a registration rights agreement with the private placement investors that required us to prepare and file a resale registration statement, which was declared effective by the SEC on August 18, 2020 and permits the resale by the private placement investors of approximately 5.1 million shares of our common stock as well as approximately 2.6 million shares of common stock issuable upon the exercise of prefunded warrants and warrants issued in the July 2020 private placement. The shares subject to outstanding options and warrants, of which options and warrants (including prefunded warrants) to purchase 2.2 million shares and 4.5 million shares, respectively, were exercisable as of December 31, 2020, 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 could result in substantial dilution to our existing stockholders and could cause our stock price to decline.

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

We have broad discretion over the use of proceeds to us from our financing activities and our stockholders rely solely on the judgment of our board of directors and management regarding the application of these proceeds. Our use of proceeds may not improve our operating results or increase the value of our common stock. Any failure to apply these proceeds effectively could have a material adverse effect on our business, delay the development of our product candidates and cause the market price of our common stock to decline.

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. In addition, our amended and restated bylaws provide that the U.S. federal district courts will be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act.

These 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 these choice of forum provisions in our amended and restated certificate of incorporation and amended and restated bylaws 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.

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.

Risks Related to Our Financial Reporting and Disclosure

We are a smaller reporting company, and any decision on our part to comply only with reduced reporting and disclosure requirements applicable to such companies could make our common stock less attractive to investors.

We are a "smaller reporting company," as defined in the Securities Exchange Act of 1934, as amended, or the Exchange Act. For as long as we continue to be a smaller reporting company, we may choose to take advantage of exemptions from various reporting requirements applicable to other public companies that are not smaller reporting companies, including, but not limited to, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements.

We will remain a smaller reporting company so long as, as of June 30 of the preceding year, (i) the market value of our common shares held by non-affiliates, or our public float, is less than $250 million; or (ii) we have annual revenues less than $100 million and either we have no public float or our public float is less than $700 million.

If we take advantage of some or all of the reduced disclosure requirements available to smaller reporting companies, 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. For so long as we are a smaller reporting company and not classified as an "accelerated filer" or "large accelerated filer" pursuant to SEC rules, we will continue to be exempt from the auditor attestation requirements of Section 404(b) of Sarbanes-Oxley.

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

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

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

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

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

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

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

We will incur significant legal, accounting, and other expenses associated with public company reporting requirements. We will also incur costs associated with corporate governance requirements, including requirements under the Sarbanes-Oxley Act, as well as new rules implemented by the SEC and The Nasdaq Stock Market LLC. Although our status as a smaller reporting company may for a limited period of time somewhat lessen the cost of complying with these additional regulatory and other requirements, we nonetheless expect that these rules and regulations will increase our legal and financial compliance costs and to make some activities more time-consuming and costlier. Our executive officers and other personnel will need to devote substantial time to oversee our 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.

General Risk Factors

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.

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.

Item 1B. Unresolved Staff Comments.

None.

Item 2. Properties.

In March 2019, we entered into a lease for 27,164 square feet of office and laboratory space located at 188 East Blaine Street, Seattle, Washington. The term of the lease is 10.8 years with one option to extend the term by 5.0 years. The lease term commenced in June 2019. We believe that our existing facility is adequate for our current needs as the facility has sufficient space to house additional personnel as we expand.

Item 3. Legal Proceedings.

We are not engaged in any material legal proceedings. From time to time, we may become involved in litigation relating to claims arising from the ordinary course of business. We believe that there are no claims or actions pending against us currently, the ultimate disposition of which would have a material adverse effect on our consolidated results of operation, financial condition or cash flows.

Item 4. Mine Safety Disclosures.

Not applicable.

PART II

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities.

Market Information

From June 17, 2015 through July 24, 2017, our common stock was traded under the symbol "NVLS." On July 24, 2017, in connection with the business combination of Nivalis Therapeutics, Inc. and Alpine Immune Sciences, Inc., we completed a 1-for-4 reverse stock split. Commencing on July 25, 2017, our common stock began trading on The Nasdaq Global Market under the symbol "ALPN." As of March 10, 2021, we have approximately 24 stockholders of record for our common stock, which excludes stockholders whose shares were held in nominee or street name accounts through brokers.

Dividends

We have never declared or paid cash dividends on our capital stock. We currently intend to retain any future earnings for use in the operation of our business and do not intend to declare or pay any cash dividends in the foreseeable future. Any further determination to pay dividends on our capital stock will be at the discretion of our board of directors, subject to applicable laws, and will depend on our financial condition, results of operations, capital requirements, general business conditions and other factors that our board of directors considers relevant.

Stock Performance Graph

As a "smaller reporting company," as defined by Rule 12b-2 of the Exchange Act, and pursuant to Instruction 6 to Item 201(e) of Regulation S-K we are not required to provide the stock performance graph.

Item 6. Selected Financial Data.

As a "smaller reporting company," as defined by Rule 12b-2 of the Exchange Act, and pursuant to Item 301(c) of Regulation S-K we are not required to provide selected financial data.

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations.

You should read the following discussion and analysis of our financial condition and results of operations together with our consolidated financial statements and the related notes appearing elsewhere in this Annual Report on Form 10-K. In addition to historical information, some of the information contained in this discussion and analysis or set forth elsewhere in this report, including information with respect to our plans and strategy for our business, future financial performance, expense levels and liquidity sources, includes forward-looking statements that involve risks and uncertainties. You should read Risk Factors in Part I, Item 1A of this report for a discussion of important factors that could cause actual results to differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

Overview

We are a clinical-stage biopharmaceutical company dedicated to discovering and developing innovative, protein-based immunotherapies to treat cancer and autoimmune and inflammatory diseases. Our approach includes a proprietary scientific platform that converts native immune system proteins into differentiated, multi-targeted therapeutics. We believe our strategies are capable of meaningfully modulating the human immune system and significantly improving outcomes in patients with serious diseases.

In June 2020, we entered into the AbbVie Agreement, which grants AbbVie an exclusive option to take an exclusive license to our clinical candidate ALPN-101, a dual ICOS and CD28 antagonist intended for the treatment of autoimmune and inflammatory diseases. Preclinical studies with ALPN-101 have demonstrated efficacy in models of SLE, SjS, arthritis, inflammatory bowel disease, multiple sclerosis, type 1 diabetes, uveitis, and GVHD. We have evaluated ALPN-101 in a Phase 1 healthy volunteer trial and plan to initiate an international Phase 2 study in adults with SLE. We have successfully received U.S. FDA IND clearance, and anticipate that the study will commence enrollment in mid-2021.

ALPN-303 is a dual B cell cytokine antagonist, being developed for the treatment of B cell mediated inflammation and autoimmune diseases. We are targeting completion of activities to support initiation of a Phase 1 healthy volunteer study with ALPN-303 in the fourth quarter of 2021.

Our lead oncology program is ALPN-202, a conditional CD28 costimulator and dual checkpoint inhibitor intended for the treatment of cancer. Preclinical in vivo data have demonstrated monotherapy efficacy in tumor models superior to approved therapies. In addition, ALPN-202 has a unique immuno-modulatory profile and has demonstrated evidence of anti-tumor immunity in preclinical models. Based on ALPN-202's efficacy in preclinical models and favorable nonclinical safety and development profile, in June 2020, we initiated NEON-1, a Phase 1 dose escalation and expansion study in patients with advanced malignancies and intend to continue enrolling patients throughout 2021. We also intend to initiate NEON-2, a Phase 1 combination study of ALPN-202 and a PD-1 inhibitor later this year.

Our scientific platform has also generated immune modulatory proteins with the potential of improving engineered cellular therapies, or ECT, such as chimeric antigen receptor T cells, or CAR-T, T cell receptor-engineered T cells, or TCR-T, and tumor infiltrating lymphocytes, or TILs. In May 2019, we signed a collaboration and license agreement with Adaptimmune to develop next-generation SPEAR™ T cell products which incorporate our secreted and transmembrane immunomodulatory protein (termed SIP™ and TIP™) technology. We intend to continue to leverage our existing pipeline and platform to actively explore and evaluate potential value-creating partnering opportunities.

Our goal is to discover and develop modern therapies to treat patients with serious conditions such as cancer and autoimmune/inflammatory diseases. To achieve our goals, we intend to:

- aggressively move our lead autoimmune/inflammatory program ALPN-101 through clinical development as part of our Option and License Agreement with AbbVie, including conducting a Phase 2 study for the treatment of SLE;
- aggressively move our second autoimmune/inflammatory program ALPN-303 through preclinical development and into clinical studies for the treatment of B cell mediated autoimmune/inflammatory diseases;
- aggressively move our lead oncology program ALPN-202 through clinical development for the treatment of cancer; and
- maximize the value of our pipeline and platform via potential partnering activities.

Our operations to date have been limited to business planning, raising capital, developing our platform technology, identifying potential immunotherapy candidates, clinical studies, and other research and development activities. To date, we

have financed operations primarily through private placements of common stock and convertible preferred stock, funds received from license and research agreements, debt financing and assets acquired upon the close of our merger with Nivalis Therapeutics Inc., or Nivalis. We do not have any products approved for sale and have not generated any product sales. Since inception and through December 31, 2020, excluding amounts borrowed through debt financing, we have raised an aggregate of $242.4 million to fund operations, of which $79.9 million was from the sale of common stock and warrants, $49.2 million was from the sale of convertible preferred stock, $69.2 million was through our license and collaboration agreements, and $44.1 million in cash, cash equivalents, and marketable securities acquired through the merger with Nivalis. As of December 31, 2020, we had cash, cash equivalents, restricted cash, and investments totaling $131.4 million.

Our net loss was $27.9 million, $41.9 million, and $36.5 million for the years ended December 31, 2020, 2019, and 2018, respectively. We expect to continue incurring significant expenses and operating losses for at least the next several years as we:

- initiate and complete nonclinical studies and clinical trials for our product candidates, including ALPN-101, ALPN-202, and ALPN-303;
- contract to manufacture and perform additional process development for our product candidates;
- continue research and development efforts to build our pipeline beyond the current product candidates;
- maintain, expand, and protect our intellectual property portfolio;
- hire additional clinical, quality control, scientific, and management personnel; and
- add operational and financial personnel to support our product development efforts and operational capabilities applicable to operating as a public company.

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

Financial Overview

Collaboration Revenue

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

We adopted Accounting Standards Codification, or ASC, Topic 606, Revenue from Contracts with Customers , as amended, or the new revenue standard or ASC 606, on January 1, 2018, resulting in a change to our accounting policy for revenue recognition. We used the modified retrospective method transition option and recognized the cumulative effect of adopting the new revenue standard as a $203,000 decrease to the opening accumulated deficit balance at January 1, 2018. See Note 11 for additional information.

AbbVie Ireland Unlimited Company

In June 2020, we entered into the AbbVie Agreement for the development of ALPN-101. The AbbVie Agreement grants AbbVie the exclusive option to purchase an exclusive worldwide license to ALPN-101, or the License Option. The License Option is exercisable by AbbVie at any time and will expire 90 days from the achievement of certain development milestones. If AbbVie exercises the License Option, AbbVie will take over the future development and commercialization. Prior to the exercise of the License Option, we will perform research and development services, including conducting a Phase 2 study in SLE, based on an agreed-upon development plan. We will be fully responsible for all costs incurred to conduct the activities under the development plan, provided that, AbbVie may be responsible for increased costs under the development plan in connection with certain material amendments proposed by AbbVie. We will also be solely responsible, at our sole cost

and expense, for manufacturing and regulatory filings for ALPN-101 necessary to complete activities under the development plan.

In June 2020, in connection with the execution of the AbbVie Agreement, AbbVie paid us a nonrefundable upfront payment of $60.0 million. Prior to the exercise of the License Option, AbbVie has agreed to make cash payments upon our achievement of certain predefined pre-option development milestones, or the Alpine Development Milestones, up to an aggregate amount of $75.0 million. If AbbVie exercises the License Option, they will pay a one-time cash payment of $75.0 million. Following the exercise of the License Option, AbbVie has also agreed to make aggregate cash payments of up to $205.0 million upon AbbVie's achievement of certain development and commercial milestones and additional aggregate cash payments of up to $450.0 million upon AbbVie's achievement of certain sales-based cash milestones, collectively referred to as the AbbVie Milestones. Subsequent to commercialization, we are also eligible to receive high single-digit to low double-digit percentage royalties on worldwide net sales of licensed products.

For revenue recognition purposes, we determined that our contractual promises in the AbbVie Agreement are not distinct and are interdependent with our performance obligation to provide research and development services under the development plan. Thus, all contractual promises related to the upfront payment and Alpine's Development Milestones were combined into a single performance obligation. We determined the Alpine Development Milestone payments are probable of significant revenue reversal as the achievement is highly dependent on factors outside our control. Therefore, these milestone payments are fully constrained and were not included in the transaction price. We will re-evaluate the transaction price each reporting period and update as uncertain events are resolved or other changes in circumstances occur.

The License Option and the AbbVie Milestones were not determined to be performance obligations at the inception of the contract as they did not represent material rights. If exercised, the License Option and AbbVie Milestones will be accounted for as a separate contract and will be recognized as revenue if and when triggered. Any consideration related to sales-based royalties and profit-sharing payments will be recognized when the related sales occur.

We use a cost-based input method to measure progress toward completion of the performance obligation and to calculate the corresponding revenue to recognize each period. In applying the cost-based input, we use actual costs incurred relative to budgeted costs for the combined performance obligation. These costs consist primarily of internal personnel efforts and third-party contract costs relative to the level of patient enrollment in the study. Revenue will be recognized based on the level of costs incurred relative to the total budgeted costs for the performance obligation. A cost-based input method of revenue recognition requires management to make estimates of costs to complete our performance obligation. In making such estimates, significant judgment is required to evaluate assumptions related to cost estimates. The cumulative effect of revisions to estimated costs to complete our performance obligation will be recorded in the period in which changes are identified and amounts can be reasonably estimated. A significant change in these assumptions and estimates could have a material impact on the timing and amount of revenue recognized in future periods.

We recognized revenue from the AbbVie Agreement of $7.0 million for the year ended December 31, 2020. As of December 31, 2020 the remaining balance of the transaction price is $53.0 million and is recorded as current and noncurrent deferred revenue on our accompanying Consolidated Balance Sheets. We expect to recognize the remaining deferred revenue over the remainder of our development plan, which began in June 2020 and ends upon the later of the exercise or expiration of the option.

Adaptimmune Therapeutics plc

In May 2019, we entered into the Adaptimmune Agreement with Adaptimmune, a clinical-stage biopharmaceutical company primarily focused on providing novel cell therapies to patients, particularly for the treatment of solid tumors, to develop next-generation SPEAR T cell products which incorporate our secreted and transmembrane immunomodulatory protein (termed SIP™ and TIP™) technology. Under the Adaptimmune Agreement, we are to perform certain research services and grant Adaptimmune an exclusive license to programs from our SIP and TIP technologies. In June 2019, under the terms of the Adaptimmune Agreement, we received an upfront license payment of $2.0 million and through December 31, 2020 we have received an additional $1.6 million in research support payments to fund ongoing programs. These payments were recorded as deferred revenue upon receipt and were recognized as revenue based on employee hours contributed to each performance obligation. In the fourth quarter of 2020, based on the completion of our research and development efforts in connection with our performance obligations, we recognized the remaining balance in deferred revenue associated with Adaptimmune on our accompanying Consolidated Balance Sheets. Under the Adaptimmune Agreement, we have recognized revenue of $2.3 million and $1.3 million for the years ended December 31, 2020 and 2019, respectively. In addition, we are eligible for additional research support payments, one-time payments and downstream development and commercialization milestones of up to $288.0 million, if all pre-specified milestones for each program are achieved. We are also eligible to receive low-single digit royalties on worldwide net sales of the applicable products.

In October 2015, we entered into the Kite Collaboration Agreement, providing Kite with access to two transmembrane immunomodulatory protein, or TIP, programs for use in Kite's engineered cellular therapy programs. In May 2019, Kite provided us notice of termination of the Kite Collaboration Agreement following the expiration of the research term. Upon termination, the confidentiality and indemnity obligations of the parties survived and the licenses granted to Kite under the Kite Collaboration Agreement terminated. Pursuant to the terms of the Kite Collaboration Agreement, the termination was effective in June 2019, thirty days after the effectiveness of Kite's notice. We recognized a total of $630,000 for the year ended December 31, 2018 and $5.6 million over the life of the Kite Collaboration Agreement.

Research and Development Expenses

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

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

We incurred $27.2 million, $35.8 million, and $29.0 million in research and development expenses for the years ended December 31, 2020, 2019, and 2018, respectively. We expect our research and development expenses to increase for the foreseeable future as we continue to develop our platform and product candidates.

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

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

General and Administrative Expenses

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

We expect general and administrative expenses to increase as we expand infrastructure and continue to prosecute our patents and other intellectual property. Other increases could potentially include increased costs for director and officer liability insurance, costs related to the hiring of additional personnel, and increased fees for directors, outside consultants, lawyers, and accountants. We expect to incur significant costs to comply with corporate governance, internal controls, and similar requirements applicable to public companies.

Loss on Sale of Intangible Asset

Loss on sale of intangible asset relates solely to the sale of the GSNOR asset to Laurel Venture Capital Ltd., or Laurel, in June 2018. For additional information regarding the sale of the GSNOR asset, please see Note 7 to our consolidated financial statements contained elsewhere in this Annual Report on Form 10-K.

Interest Expense

Interest expense consists primarily of interest associated with our term loan with Silicon Valley Bank and the amortization of the related debt discount.

Interest Income

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

Other Income

Other income consists primarily of research and development tax credits received by our wholly-owned Australian subsidiary and an employee retention tax credit related to COVID-19 relief legislation.

Income Tax Benefit

Income tax benefit for 2018 relates to the sale of our in-process research and development, or IPR&D.

Results of Operations

Comparison of Years Ended December 31, 2020 and 2019

The following table summarizes our results of operations for the years ended December 31, 2020 and 2019 (in thousands):

	Years Ended December 31,		Increase/
	2020	2019	(Decrease)
Collaboration revenue	$ 9,335	$ 1,740	$ 7,595
Operating expenses:			
Research and development	27,185	35,847	(8,662)
General and administrative	10,899	9,467	1,432
Total operating expenses	38,084	45,314	(7,230)
Loss from operations	(28,749)	(43,574)	14,825
Other income (expense):			
Interest expense	(775)	(338)	(437)
Interest income	245	1,248	(1,003)
Other income	1,333	812	521
Loss before taxes	(27,946)	(41,852)	13,906
Income tax benefit	6	—	6
Net loss	$ (27,940)	$ (41,852)	$ 13,912

Collaboration Revenue

Revenue for the year ended December 31, 2020 consists of $7.0 million recognized under the AbbVie Agreement and $2.3 million recognized under the Adaptimmune Agreement. Revenue for the year ended December 31, 2019 consists of $1.3 million related to the Adaptimmune Agreement and $0.4 million related to the milestone payment from Laurel from the sale of our GSNOR assets.

Research and Development Expenses

The $8.7 million decrease in research and development expenses was primarily attributable to decreases of $5.7 million in contract manufacturing and process development of our product candidates and $4.1 million in other direct research activities. The decreases were partially offset by increases of $0.6 million in clinical trial activity and $0.5 million in stock-based compensation.

General and Administrative Expenses

The $1.4 million increase in general and administrative expenses was primarily attributable to increases of $0.8 million related to professional and legal services, $0.6 million in stock-based compensation and $0.4 million in insurance and facility costs to support the growth and expansion of our business. These increases were partially offset by a decrease of $0.4 million related primarily to personnel expenses.

Interest Expense

Interest expense relates primarily to interest paid on our term loan with Silicon Valley Bank, or SVB, and the related non-cash interest expense associated with the amortization of the debt discount. The $0.4 million increase in interest expense is due to additional interest related to the drawdown of the second tranche of our SVB loan in March 2020.

Interest Income

The $1.0 million decrease in interest income is due primarily to less interest earned on our investments as we maintained a lower average investment balance during the 2020 period.

Other Income

The $0.5 million increase in other income is attributable a $0.2 million increase in research and development tax credits received by our wholly-owned Australian subsidiary. Additionally, for the 2020 period, we recognized a $0.3 million employee retention tax credit related to COVID-19 relief legislation.

Comparison of Years Ended December 31, 2019 and 2018

The following table summarizes our results of operations for the years ended December 31, 2019 and 2018 (in thousands):

	Years Ended December 31,		Increase/
	2019	2018	(Decrease)
Collaboration revenue	$ 1,740	$ 705	$ 1,035
Operating expenses:			
Research and development	35,847	28,970	6,877
General and administrative	9,467	8,362	1,105
Loss on sale of intangible asset	—	1,203	(1,203)
Total operating expenses	45,314	38,535	6,779
Loss from operations	(43,574)	(37,830)	(5,744)
Other income (expense):			
Interest expense	(338)	(319)	(19)
Interest income	1,248	1,296	(48)
Other income	812	—	812
Loss before taxes	(41,852)	(36,853)	(4,999)
Income tax benefit	—	366	(366)
Net loss	$ (41,852)	$ (36,487)	$ (5,365)

Collaboration Revenue

Revenue for the year ended December 31, 2019 consists of $1.3 million related to the Adaptimmune Agreement and $0.4 million related to the milestone payment from Laurel from the sale of our GSNOR assets. Revenue for the year ended December 31, 2018 relates primarily to revenue recognized under the Kite Collaboration Agreement as well as an additional $0.2 million related to the adoption of ASC 606, which resulted in higher revenue for the 2018 period, as compared to what would have been recorded under previous accounting guidance.

Research and Development Expenses

The $6.9 million increase in research and development expenses was primarily attributable to an increase of $4.9 million in clinical trial activity, an increase of $0.3 million in direct research activities, an increase of $2.3 million in personnel-related expenses as a result of a growth in headcount to support ongoing discovery and development programs, an increase of $0.8 million in stock-based compensation, and an increase of $1.4 million in allocated overhead and facilities. These increases were partially offset by a decrease of $2.8 million in contract manufacturing and process development of our product candidates.

General and Administrative Expenses

The $1.1 million increase in general and administrative expenses was primarily attributable to o a $0.7 million increase in personnel-related expenses related to an increase in administrative headcount, a $0.3 million increase in professional and legal services, and an increase of $0.1 million in facility costs to support the growth and expansion of our business.

Loss on Sale of Intangible Asset

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

Interest Income

The $0.8 million increase in other income relates to income from the Australian tax credit from our wholly-owned Australian subsidiary.

Liquidity and Capital Resources

As of December 31, 2020, we had cash, cash equivalents, restricted cash, and investments totaling $131.4 million. Excluding amounts borrowed through debt financing, we have raised an aggregate of $242.4 million to fund operations, of which $79.9 million was from the sale of common stock, $49.2 million was from the sale of convertible preferred stock, $69.2 million was through our license and collaboration agreements, and $44.1 million in cash, cash equivalents, and marketable securities acquired through the merger with Nivalis. In June 2017, August 2019, and March 2020, we drew down term loans from Silicon Valley Bank, or SVB, as discussed below. In addition to our existing cash, cash equivalents, and marketable securities, we are eligible to receive research and development funding and to earn milestone and other contingent payments for the achievement of defined collaboration objectives and certain development and regulatory milestones and royalty payments under our collaborations with Adaptimmune and AbbVie; however, our ability to earn these milestone and contingent payments and the timing of achieving these milestones is uncertain.

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

Until such time as we can generate substantial product revenue, if ever, we expect to finance our cash needs through a combination of equity or debt financings and collaboration agreements. Except for any obligations of our collaborators to make milestone payments under our agreements 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 collaborations generate 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 collaborations 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.

We have considered that our long-term operations anticipate continuing net losses and the need for potential equity or debt financing. We have also considered that new collaborations or selectively partnering our technology or programs may provide other sources of capital. However, there can be no assurances that additional funding or other sources of capital will be available on terms acceptable to us, or at all. Based on our current operating plan, we believe our available cash and cash equivalents and investments, will be sufficient to fund our planned level of operations for at least the next 12 months. We have based this estimate on assumptions that may prove to be wrong, and we could use our capital resources sooner than we expect. Additionally, the process of testing drug candidates in preclinical and clinical studies is costly, and the timing of progress in these studies remains uncertain.

Financing Agreements

In July 2020, we entered into a securities purchase agreement, or the Securities Purchase Agreement, for a private placement with a select group of institutional investors, pursuant to which we sold 5,139,610 units, or the Common Units, and 790,710 units, or the Prefunded Warrant Units, for an aggregate purchase price of $60.0 million. Each Common Unit consists of one share of our common stock plus a warrant to purchase 0.3 shares of common stock, or the Common Stock Warrants, and each Prefunded Warrant Unit consists of one prefunded warrant to purchase one share of common stock, or the Prefunded Warrants, plus one Common Stock Warrant to purchase 0.3 shares of common stock. The Prefunded Warrant Units and the Common Units are collectively referred to as the Units and each Unit has a purchase price of $10.1175. The Common Stock Warrants have an exercise price of $12.74 and a term of 3.5 years. The Prefunded Warrants became fully exercisable upon the closing date and have an exercise price of $0.001 per share.

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

In June 2018, we entered into an equity distribution agreement, or the Equity Distribution Agreement, with Piper Jaffray & Co., or Piper Jaffray, pursuant to which we may sell shares of our common stock through an "at the market" equity offering program for up to $50.0 million in gross cash proceeds. As of December 31, 2020, we have made no sales under the Equity Distribution Agreement. On March 17, 2021, we provided written notice to Piper Jaffray terminating the Equity Distribution Agreement effective as of March 17, 2021.

Long-Term Financing

In December 2016, we entered into a Loan and Security Agreement, or the Original Agreement, with SVB under which we borrowed $5.0 million. The Original Agreement accrued interest at a floating per annum rate equal to the lender's prime rate minus 1.75%. The Original Agreement had an interest-only period through July 2018.

In August 2019, we entered into an Amended and Restated Loan and Security Agreement, or the Loan Agreement, with SVB, pursuant to which SVB agreed to extend term loans to us with an aggregate principal amount of up to $15.0 million, or the Term Loans. Borrowings under the Loan Agreement consist of up to three separate tranches. The initial tranche of $5.0 million was funded in August 2019, $3.0 million of which was used to repay amounts owing under our Original Agreement. In March 2020, the second tranche of $5.0 million was funded to us. We did not draw down the final tranche of $5.0 million, which expired on July 31, 2020. We intend to use the debt proceeds for working capital and other general corporate purposes, including the advancement of our development programs.

The Term Loans accrue interest at a floating per annum rate of 0.25% above the prime rate, subject to a floor of 5.75%, which interest is payable monthly commencing in September 2019. Upon the occurrence and during the continuance of an event of default, a default interest rate will apply that is 4.0% above the otherwise applicable interest rate. The Term Loans were interest only until September 30, 2020, however, under the Loan Agreement our interest only period automatically extends to June 30, 2021 if we receive aggregate new capital of at least $40.0 million no later than June 30, 2020. We met this milestone in June 2020 in conjunction with the execution of the AbbVie agreement, discussed in detail in Note 11. As a result of the

interest only extension, the Term Loans will be payable in 25 equal monthly installments of principal plus interest, with the final installment due and payable on July 1, 2023.

We may prepay all, but not less than all, of the Term Loans subject to a prepayment fee equal to $75,000, which represents the deferred portion of the final payment due under the Original Agreement, plus the outstanding principal balance under the Term Loans at the time of such prepayment multiplied by a prepayment fee of 2.0% in the first year, 1.0% in the second year, and 0.0% in the third year and thereafter. Additionally a final payment in the amount of 5.5% of the funded Term Loans is payable to SVB on the date on which the Term Loans are prepaid, paid or become due and payable in full.. The final payment fees are recorded in long-term debt with an offsetting reduction to debt discount on our accompanying Consolidated Balance Sheets.

The Loan Agreement contains customary representations and warranties, events of default and affirmative and negative covenants, including, among others, covenants that limit or restrict our ability to, among other things, incur additional indebtedness, grant liens, merge or consolidate, make acquisitions, pay dividends or other distributions or repurchase equity, make investments, dispose of assets, engage in any new lines of business, and enter into certain transactions with affiliates, in each case subject to certain exceptions. Among other events, a failure to make a required loan payment, an uncured covenant breach or a material adverse change in our business, operations or condition (financial or otherwise) could lead to an event of default, and in such case, all amounts then outstanding may become due and payable immediately. We were in compliance with our covenants as of December 31, 2020. As security for its obligations under the Loan Agreement, we granted SVB a first priority security interest on substantially all of our assets, except intellectual property, and subject to certain other exceptions. As of December 31, 2020, we had $10.6 million in outstanding principal and final fees due under our term loan agreement. See Note 9 for further discussion of our Term Loans.

Operating Lease

In March 2019, we entered into a lease with ARE-Seattle No. 28, LLC, or the Landlord, for 27,164 square feet of office and laboratory space located at 188 East Blaine Street, Seattle, Washington. The term of the lease is 10.8 years with one option to extend the term by 5 years. The lease term commenced in June 2019. The “Rent Commencement Date” began in March 2020, nine months after the commencement date. We were not required to pay base rent from the Rent Commencement Date through November 2020, the last day of the ninth month following the Rent Commencement Date. The annual base rent under the lease is $1.7 million for the first year and will increase by 3.0% each year thereafter. We received a tenant improvement allowance of $5.4 million, which is included in our base rent, and a maximum additional tenant improvement allowance of $1.8 million, which will result in additional rent amortized over the term of the lease at an annual rate of 8.0%. The lease also requires us to pay additional amounts for operating and maintenance expenses. In March 2019, in connection with the lease, we provided a $254,000 letter of credit as a security deposit, which is recorded as restricted cash in our accompanying Consolidated Balance Sheets.

Contingencies

Certain credits received related to our research and development expenditures and recorded within other income in our accompanying Consolidated Statements of Operations and Comprehensive Income (Loss) are subject to review by foreign taxing authorities. It is reasonably possible we may incur losses upon the completion of these reviews of up to approximately $1.8 million, which we would be required to repay to certain tax authorities.

Cash Flows

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

	Years Ended December 31,		
	2020	2019	2018
Net cash provided by (used in) operating activities	$ 30,084	$ (35,346)	$ (28,416)
Net cash (used in) provided by investing activities	(72,819)	16,763	32,118
Net cash provided by (used in) financing activities	61,381	24,255	(991)

Net cash provided by (used in) operating activities:

Net cash provided by operating activities was $30.1 million for the year ended December 31, 2020 and consisted primarily of our net loss of $27.9 million. This was offset by an increase of $52.9 million in our net operating assets and liabilities. This increase was primarily driven by the receipt of a $60.0 million upfront payment from AbbVie, which was recorded as current and noncurrent deferred revenue on our accompanying Consolidated Balance Sheets. Additionally, we had a $5.1 million increase in our net non-cash adjustments, which primarily relates to stock-based compensation, depreciation and amortization.

Net cash used in operating activities was $35.3 million for the year ended December 31, 2019 and consisted primarily of our net loss of $41.9 million. This was offset by increases of $3.2 million in our net operating assets and liabilities and $3.3 million in our net non-cash adjustments, which primarily relates to stock-based compensation, depreciation and amortization.

Net cash used in operating activities was $28.4 million for the year ended December 31, 2018 and consisted primarily of our net loss of $36.5 million. This was offset by increases of $5.0 million in our net operating assets and liabilities and $3.1 million in our net non-cash adjustments, which primarily relates to the loss on the sale of our intangible asset, stock-based compensation, the write-off of our deferred tax liability, depreciation and amortization.

Net cash (used in) provided by investing activities:

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

Net cash used in investing activities was $72.8 million for the year ended December 31, 2020 and consisted primarily of the purchases and maturities of investments in U.S. Treasury securities, commercial paper, and corporate debt securities, partially offset by purchases of property and equipment, primarily lab equipment, to support our research and development efforts.

Net cash provided by investing activities was $16.8 million for the year ended December 31, 2019 and consisted primarily of the maturities, sales and purchases of investments in U.S. Treasury securities, commercial paper, and corporate debt securities, partially offset by purchases of property and equipment, primarily lab equipment, to support our research and development efforts.

Net cash provided by investing activities was $32.1 million during the year ended December 31, 2018 and consisted primarily of the maturities and purchases of short-term investments in U.S. Treasury securities, commercial paper, and corporate debt securities, partially offset by purchases of property and equipment, primarily lab equipment, to support our research and development efforts.

Net cash provided by (used in) financing activities:

Net cash provided by financing activities was $61.4 million for the year ended December 31, 2020 and consisted primarily of the net proceeds of $56.3 million related to the sale of approximately 5.9 million Units under our July 2020 Securities Purchase Agreement, $5.0 million in proceeds received from the draw down of the second tranche of our Loan Agreement in March 2020, and $0.1 million related to the exercise of stock options.

Net cash provided by financing activities was $24.3 million for the year ended December 31, 2019 and consisted primarily of the net proceeds of $23.6 million related to the sale of approximately 4.7 million Units under our Purchase Agreement and $2.0 million in net proceeds from our debt refinancing, partially offset by $1.3 million in principal payments on our debt.

Net cash used in financing activities was $1.0 million for the year ended December 31, 2018 and consisted of principal payments on our debt, partially offset by the proceeds from stock option exercises.

Contractual Obligations and Contingent Liabilities

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

Off-Balance Sheet Arrangements

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

JOBS Act

We ceased to be an "emerging growth company" under the JOBS Act effective December 31, 2020. However, for so long as we are not classified as an "accelerated filer" or "large accelerated filer" pursuant to SEC rules, we will continue to be exempt from the auditor attestation requirements of Section 404(b) of Sarbanes-Oxley.

Critical Accounting Policies and Estimates

Our management's discussion and analysis of our financial condition and results of operations is based on our consolidated financial statements, which we have prepared in accordance with generally accepted accounting principles in the United States, or GAAP. The preparation of these 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 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.

While our significant accounting policies are more fully described in Note 2 to our consolidated financial statements, we believe that the following accounting policies are the most critical to fully understanding and evaluating our financial condition and results of operations.

Accrued Liabilities

As part of the process of preparing our consolidated financial statements, we are required to estimate accruals for professional services and research and development expenses. This process involves reviewing contracts and vendor agreements and communicating with applicable personnel to identify services that have been performed on our behalf. We estimate the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of the actual cost. We estimate accrued liabilities as of each balance sheet date based on known facts and circumstances.

Although we do not expect our estimates to be materially different from amounts actually incurred, if our estimates of the status and timing of services performed differ from the actual status and timing of services performed, we may report amounts that are too high or too low in any particular period. To date, we have not experienced any significant adjustments to our estimates.

Revenue Recognition

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

Our collaboration agreements principally contain multiple performance obligations, which may include (1) grants of, or options to obtain, intellectual property licenses; (2) research and development services; and/or (3) manufacturing or supply services. Payments typically received under these arrangements include one or more of the following: non-refundable upfront license fees, option exercise fees, payment for research and/or development efforts, amounts due upon the achievement of specified objectives, and/or royalties on future product sales. Our revenue is primarily derived from our collaboration agreements with AbbVie and Adaptimmune, as well as previously with Kite. See further discussion of our collaboration agreements in Note 11.

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

on employee hours contributed to each performance obligation, or by using a cost-based input method to measure progress toward completion of the performance obligation and to calculate the corresponding revenue to recognize each period.

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

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

Stock-based Compensation

Stock-based compensation is recognized for all share-based payments based on the estimated fair value as of the date of grant. The fair value of our stock options is calculated using the Black-Scholes option pricing model, which requires us to apply our judgment regarding certain key assumptions including risk-free interest rate, expected term, and volatility. For risk-free interest rate, we use the zero-coupon U.S. Treasury instruments security rate with a term equal to the expected life of the option. We use the “simplified method” for options to determine the expected term of stock option granted to employees. Under this approach, the weighted-average expected life is presumed to be the average of the vesting term and the contractual term of the option. For volatility, we analyzed the stock price volatility of companies at a similar stage of development to estimate expected volatility of our stock price. Our assumed dividend yield is zero as we have never paid cash dividends and have no present intention to pay cash dividends. Stock-based compensation expense is recognized over the requisite service period of the awards, usually the vesting period, on a straight-line basis. For performance-based awards where the vesting of the options may be accelerated upon the achievement of certain milestones, vesting and the related stock-based compensation is recognized as an expense when it is probable the milestone will be met. We recognize forfeiture of awards as they occur rather than estimating the expected forfeiture rate.

If factors change and we employ different assumptions for estimating stock-based compensation expense in future periods, or if we decide to use a different valuation model, the stock-based compensation expense we recognize in future periods may differ significantly from what we have recorded in the current period and could materially affect our financial statements.

Recently Issued Accounting Pronouncements

In December 2019, the Financial Accounting Standards Board, or FASB, issued Accounting Standards Update, or ASU, No. 2019-12, Simplifying the Accounting for Income Taxes. The objective of the standard is to improve areas of GAAP by removing certain exceptions permitted by ASC Topic 740, Income Taxes, and clarifying existing guidance to facilitate consistent application. The standard will become effective for us beginning on January 1, 2021. We are currently evaluating the new standard, but do not expect it to have a material impact on our financial condition, results of operations, cash flows, and financial statement disclosures.

Recently Adopted Accounting Pronouncements

In November 2018, the FASB issued ASU No. 2018-18, Collaborative Arrangements: Clarifying the Interaction between Topic 808 and Topic 606. This ASU clarifies that certain transactions between collaborative arrangement participants should be accounted for as revenue when the collaborative arrangement participant is a customer in the context of a unit of account and precludes recognizing as revenue consideration received from a collaborative arrangement participant if the participant is not a customer. We adopted this ASU effective January 1, 2020 and it did not have a material impact on our financial statements and related disclosures.

In August 2018, the FASB issued ASU No. 2018-13, Fair Value Measurement. ASU 2018-13 modifies the disclosure requirements for fair value measurements by removing, modifying, or adding certain disclosures. We adopted this ASU effective January 1, 2020 and it did not have a material impact on our financial statements or related disclosures.

In June 2016, the FASB issued ASU 2016-13, Financial Instruments: Credit Losses, as clarified in ASU 2019-04 and ASU 2019-05. The objective of the standard is to provide information about expected credit losses on financial instruments at each reporting date and to change how other-than-temporary impairments on investment securities are recorded. We adopted this ASU effective January 1, 2020 and it did not have a material impact on our financial statements and related disclosures.We will continue to monitor the impact of the COVID-19 outbreak on expected credit losses.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk.

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

Item 8. Financial Statements and Supplementary Data.

For information regarding our financial statements and supplementary data, please refer to the Notes to Consolidated Financial Statements included elsewhere in this report.

As a "smaller reporting company," as defined by Rule 12b-2 of the Exchange Act and pursuant to Article 8, Regulation X and Item 302 of Regulation S-K, we are permitted to provide scaled Item 8 disclosure.

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure.

None.

Item 9A. Controls and Procedures.

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer, evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2020. The term "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, or the Exchange Act, means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the Securities and Exchange Commission's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company's management, including its principal executive and principal financial officers, as appropriate to allow timely decisions regarding required disclosure. Our management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and our management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on the evaluation of our disclosure controls and procedures as of December 31, 2020, our Chief Executive Officer and Chief Financial Officer concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

Management's Annual Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting as defined in Rule 13a-15(f) and Rule 15d-15(f) of the Exchange Act. Our internal control over financial reporting is a process 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. Our internal control over financial reporting includes those policies and procedures that:

(i) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of our assets;

(ii) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that our receipts and expenditures are being made only in accordance with authorizations of our management and directors; and

(iii) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of our assets that could have a material effect on the financial statements.

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. Also, 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. Our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2020. In making this assessment, our management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission, or COSO, Internal Control-Integrated Framework (2013). Based on our assessment using those criteria, our management has concluded that, as of December 31, 2020, our internal control over financial reporting was effective.

Changes in Internal Control Over Financial Reporting

No significant changes in our internal control over financial reporting occurred during the fiscal quarter ended December 31, 2020, that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information.

Amended and Restated Bylaws

On March 16, 2021, our board of directors approved the amendment and restatement of our bylaws, or the Amended and Restated Bylaws, to designate the federal district courts of the United States as the sole and exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act of 1933, as amended, unless we consent in writing to the selection of an alternative forum. The foregoing description of the Amended and Restated Bylaws does not purport to be complete and is qualified in its entirety by reference to the full text of the Amended and Restated Bylaws, which are filed as Exhibit 3.2 to this Annual Report on Form 10-K and incorporated herein by reference.

Termination of Equity Distribution Agreement

On June 11, 2018, we entered into the Equity Distribution Agreement with Piper Jaffray, pertaining to the sale of shares of our common stock through an "at the market" equity offering program for up to $50.0 million in gross cash proceeds. On March 17, 2021, we provided written notice to Piper Jaffray terminating the Equity Distribution Agreement effective as of March 17, 2021. The foregoing description of the Equity Distribution Agreement is not complete and is qualified in its entirety by reference to the full text of the Equity Distribution Agreement, a copy of which is filed as Exhibit 1.1 to our Current Report on Form 8-K filed with the SEC on June 11, 2018.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

Executive Officers and Directors

The following table sets forth the names, ages and positions of our executive officers and directors as of March 18, 2021:

Name	Age	Position
Executive Officers		
Mitchell H. Gold, M.D.	53	Executive Chairman and Chief Executive Officer
Stanford Peng, M.D., Ph.D.	50	President and Head of Research and Development
Paul Rickey	42	Senior Vice President, Chief Financial Officer, Treasurer, and Secretary
Non-Employee Directors		
Robert Conway	67	
Min Cui, Ph.D.	52	
Natasha Hernday	49	
Christopher Peetz	42	
Peter Thompson, M.D.	61	
James Topper, M.D., Ph.D.	59	
Jay Venkatesan, M.D.	49	

Executive Officers

Mitchell H. Gold, M.D. has served as our executive chairman, chief executive officer and a member of our board of directors since the completion of the merger of Nivalis and Alpine in July 2017 and prior to the merger served as Alpine's chief executive officer since June 2016 and as Alpine's executive chairman and member of Alpine's board of directors since January 2015. Prior to co-founding Alpine, Dr. Gold was Chairman and Founder of Alpine Biosciences, a privately-held biotech company, from 2012 to 2014. From 2001 to 2012, Dr. Gold served in a variety of roles with Dendreon Corporation (which was acquired by Valeant Pharmaceuticals International, Inc. through an asset purchase agreement), including President, Chief Executive Officer, and Chairman of the board of directors. Earlier in his career, Dr. Gold served as Vice President of Business Development at Data Critical from 2000 to 2001. From 1995 to 2000, Dr. Gold was President and Chief Executive Officer of Elixis Corporation. Dr. Gold is currently a Managing Partner at Alpine BioVentures. Dr. Gold holds an M.D. from Rush Medical College of Rush University Medical Center and a B.S. in Biology from the University of Wisconsin. We believe that Dr. Gold possesses specific attributes that qualify him to serve as a member of our board of directors, including more than 20 years of experience in senior executive management roles with both early stage and public biopharmaceutical companies.

Stanford Peng has served as our president and head of research and development since April 2019, prior to which he served as our executive vice president of research and development and chief medical officer since the completion of the merger of Nivalis and Alpine in July 2017, as Alpine's chief medical officer from September 2016 to February 2017 and as Alpine's executive vice president of research and development and chief medical officer from February 2017 until completion of the merger. Prior to joining Alpine, Dr. Peng was chief medical officer and head of clinical development at Stemcentrx, providing strategic oversight of the company's clinical and translational programs from 2015 to 2016. Previously, Dr. Peng was executive medical director at Seattle Genetics where he developed multiple programs for antibody-drug conjugates from 2014 to 2015. Earlier in his career, he directed translational research and auto-immune related clinical trials as head of the Rheumatology Clinical Research Unit at the Benaroya Research Institute from 2009 to 2014 and served as senior director, clinical research and exploratory development at Roche from 2005 to 2008. Between 2009 and 2014, Dr. Peng also served as member physician at Virginia Mason Medical Center. Dr. Peng served as an assistant professor at the Washington University School of Medicine from 2002 to 2005. From 2008 to 2009, Dr. Peng served as senior director at ARYx Therapeutics, Inc. (Nasdaq: ARYX). Dr. Peng received an M.D. and Ph.D. in biology from the Yale University School of Medicine and a B.A. in music and B.S. in biological sciences from Stanford University.

Paul Rickey has served as our senior vice president and chief financial officer since the completion of the merger of Nivalis and Alpine in July 2017, and prior to the merger served as Alpine's senior vice president and chief financial officer

since April 2017. Mr. Rickey has served as our treasurer since December 2018, and our secretary since March 2019. Mr. Rickey previously served as chief financial officer of Sound Pharmaceuticals, overseeing finance, accounting and human resources from March 2016 to March 2017. Before joining Sound Pharmaceuticals, Mr. Rickey was vice president of finance and administration of Immune Design Corp. from 2009 to May 2015, which was a publicly traded biotechnology company for a portion of his time there, where he helped complete the company's private offerings, initial public offering, and follow-on financing, and also oversaw the corporate development, accounting and human resource functions. Before joining Immune Design in 2009, Mr. Rickey was corporate controller of Northstar Neuroscience, a publicly-traded medical device company, where he managed the company's finance and accounting groups following Northstar's initial public offering. Prior to his role at Northstar Neuroscience, Mr. Rickey was the accounting manager for Mobliss, Inc., a mobile technology company that was sold to Index Corp., of Japan. Mr. Rickey started his finance career at Ernst & Young LLP. Mr. Rickey graduated from the University of Washington with a B.A. and Masters in Professional Accounting and is a certified public accountant, inactive.

Our Directors

Robert Conway has served as a member of our board of directors since the completion of the merger of Nivalis and Alpine in July 2017 and previously served as a member of the board of directors of Nivalis since April 2015. From 1999 to 2012, Mr. Conway served as the chief executive officer and member of the board of directors of Array BioPharma (Nasdaq: ARRY), a publicly traded biopharmaceutical company. Prior to joining Array, Mr. Conway was the chief operating officer and executive vice president of Hill Top Research, from 1996 to 1999. From 1979 until 1996, Mr. Conway held various executive positions for Corning Inc. (NYSE: GLW), including corporate vice president and general manager of Corning Hazleton, a contract research organization. Since 2013, Mr. Conway has served on the board of directors of ARCA BioPharma (Nasdaq: ABIO), a publicly traded biopharmaceutical company, and was elected Chairman in June 2014. From 2004 to 2013, Mr. Conway served on the board of directors of PRA International (Nasdaq: PRAH), which was a public company for a portion of his tenure there. Mr. Conway is also a member of the board of directors of Signant Health and Advarra, Inc., private clinical technology companies. In addition, Mr. Conway is a member of the strategic advisory committee of Genstar Capital. Mr. Conway received a B.S. in accounting from Marquette University in 1976. We believe that Mr. Conway's experience and expertise in the pharmaceutical industry, pharmaceutical development and clinical trials, and corporate finance, governance, accounting and public company compliance give him the qualifications and skills to serve on our board of directors.

Min Cui, Ph.D. has served as a member of our board of directors since January 2019. Dr. Cui has served as managing director of Decheng Capital, an investment firm focused on life sciences companies, since he founded the firm in 2011. Prior to founding Decheng, Dr. Cui was an investment partner at Bay City Capital, an international life science venture capital firm in San Francisco. Dr. Cui was previously director of strategic investment for the Southern Research Institute, a not-for-profit research organization. Prior to that, Dr. Cui co-founded Pan Pacific Pharmaceuticals and Hucon Biopharmaceuticals, where he led efforts in discovery and development of several key technologies in the fields of oncology, cardiology, infectious and inflammatory diseases. Dr. Cui has served as a member of the board of directors of ARMO BioSciences, Inc., a publicly-traded immuno-oncology company acquired by Eli Lilly and Company in May 2018, from August 2017 to May 2018, and also currently serves on the boards of directors of several private companies. Dr. Cui holds a Ph.D. in Cancer Biology from Stanford University and a BS and MS in Molecular Biology from Peking University. We believe that Dr. Cui's venture capital and management experience in the pharmaceuticals industry provides him with the qualifications and skills necessary to serve as a member of our board of directors. Dr. Cui was appointed to the Board pursuant to the terms of the Purchase Agreement.

Natasha Hernday has served as a member of our board of directors since December 2020. Ms. Hernday has served as Executive Vice President, Corporate Development and as a member of the Executive Committee for the publicly traded biotechnology company Seagen, Inc. (Nasdaq: SGEN), since October 2020, where she previously served as Senior Vice President of Corporate Development from September 2017 to October 2020 and as Vice President, Corporate Development from January 2011 to September 2017. Since joining Seagen in 2011, Ms. Hernday has built and led the business development team responsible for licensing deals, acquisitions and strategic alliances. From 1994 through 2010, after starting her career in molecular and mammalian cell biology, Ms. Hernday served in various roles of increasing responsibility at Amgen Inc., including as Director, Mergers & Acquisitions and as Director, Out-Partnering. She also serves on the board of directors of Xoma Corp. (Nasdaq: XOMA) and PDL BioPharma, Inc. (Nasdaq: PDLI), and on the Knight Campus External Advisory Board for the University of Oregon. Ms. Hernday received her BA in microbiology from the University of California at Santa Barbara and MBA from Pepperdine University. We believe that Ms. Hernday's experience and expertise in the pharmaceuticals industry provides her with the qualifications necessary to serve as a member of our board of directors.

Christopher Peetz has served as a member of our board of directors since April 2018. Mr. Peetz has been the president and chief executive officer of Mirum Pharmaceuticals, Inc. since March 2019 and president since November 2018. He has served as an entrepreneur-in-residence at Frazier Healthcare Partners since May 2017. He served as the chief executive officer

of Flashlight Therapeutics, Inc. from May 2017 until December 2019 and served as chief financial officer and head of corporate development at Tobira Therapeutics, Inc., a publicly-traded biotechnology company acquired by Allergan plc in November 2016, from May 2014 to December 2016. Prior to joining Tobira Therapeutics, Mr. Peetz served as vice president, finance & corporate development of Jennerex Biotherapeutics, a private biopharmaceutical company. Prior to Jennerex, Mr. Peetz held various positions at Onyx Pharmaceuticals, Inc. (now Amgen), including oversight of financial planning and analysis, corporate strategy, product lifecycle management and commercial roles. Prior to Onyx, Mr. Peetz provided merger and acquisition advisory services at LaSalle Corporate Finance, a part of ABN AMRO, and held positions at Abgenix Inc. and Solazyme Inc. Mr. Peetz received an MBA from Stanford Graduate School of Business and a B.S.B.A. in Finance, International Business and French from Washington University in St. Louis. We believe Mr. Peetz' experience in senior management positions in both business and finance and his experience supporting various corporate and financing transactions provide him with the qualifications and skills to serve on our board of directors.

Peter Thompson, M.D. has served as a member of our board of directors since the completion of the merger of Nivalis and Private Alpine in July 2017 and previously served as a member of the board of directors of Private Alpine since June 2016. Dr. Thompson currently serves as a private equity partner for OrbiMed Advisors LLC, an investment firm focused on the healthcare sector, where he has also served as venture partner since joining in September 2010. Dr. Thompson is a co-founder of and has served as a member of the board of directors of Corvus Pharmaceuticals, Inc. (Nasdaq: CRVS) since December 2014. Dr. Thompson has served as a director of Decibel Therapeutics, Inc. (Nasdaq: DBTX) since November 2020, as director of PMV Pharmaceuticals, Inc. (Nasdaq; PMVP) since November 2014, and as a director of Silverback Therapeutics, Inc. (Nasdaq: SBTX) since April 2016. Dr. Thompson also served as a director of Adaptimmune Therapeutics plc (Nasdaq: ADAP), a biopharmaceutical company, from 2014 until June 2018, as a member of the board of directors of Prevail Therapeutics Inc. (Nasdaq: PRVL) from October 2017 until January 2021, and as a member of the board of directors of Synthorx, Inc. (Nasdaq: THOR) from April 2018 to January 2020. He also currently serves on the boards of directors of several private companies. Dr. Thompson is a board-certified internist and oncologist and has served as Affiliate Professor of Neurosurgery at the University of Washington since 2010. Dr. Thompson co-founded and served as the chief executive officer of Trubion Pharmaceuticals, Inc., a biopharmaceutical company, from 2002 to 2009. Dr. Thompson previously held executive positions at Chiron Corporation and Becton Dickinson and served on the faculty of the National Cancer Institute following his medical staff fellowship there. Dr. Thompson holds a Sc. B. in Molecular Biology and Mathematics from Brown University and an M.D. from Brown University Medical School. We believe that Dr. Thompson's venture capital and management experience in the pharmaceuticals industry provides him with the qualifications and skills necessary to serve as a member of our board of directors.

James N. Topper, M.D., Ph.D. has served as a member of our board of directors since the completion of the merger of Nivalis and Alpine in July 2017 and prior to the merger served as a member of the board of directors of Alpine since June 2016. Dr. Topper has been a partner with Frazier Healthcare Partners since August 2003, serving as general partner since 2005. Before joining Frazier Healthcare Partners, Dr. Topper served as head of the cardiovascular research and development division of Millennium Pharmaceuticals, Inc. and ran Millennium San Francisco (formerly COR Therapeutics, Inc.) from 2002 to 2003. Before the merger of COR and Millennium in 2002, Dr. Topper served as the vice president of biology at COR from 1999 to 2002. Dr. Topper currently serves as a member of the board of directors of AnaptysBio, Inc. (Nasdaq: ANAB), Allena Pharmaceuticals (Nasdaq: ALNA), Phanthom Pharmaceuticals, Inc. (Nasdaq: PHAT), and Frazier Life Sciences Acquisition Corporation (Nasdaq: FLAC), and has served on numerous other boards of directors, including Aptinyx, Inc. (Nasdaq: APTX), Entasis Therapeutics Holdings Inc. (Nasdaq: ETTX), Sierra Oncology, Inc. (formerly ProNai) (Nasdaq: SRRA), Amicus Therapeutics, Inc. (Nasdaq: FOLD), Portola Pharmaceuticals, Inc. (Nasdaq: PTLA), and La Jolla Pharmaceutical Company (Nasdaq: LJPC). Dr. Topper received his M.D. and Ph.D. in biophysics from Stanford University and his B.S. in biology from the University of Michigan. We believe that Dr. Topper's experience overseeing Frazier Healthcare Partners' investments in biotechnology, his experience in senior management positions, and his significant knowledge of industry, medical and scientific matters, provide Dr. Topper with the qualifications and skills to serve on our board of directors.

Jay Venkatesan, M.D. has served as a member of our board of directors since the completion of the merger of Nivalis and Alpine in July 2017, served as our president from July 2017 to August 2018 and previously served as Alpine's chief executive officer from November 2015 to June 2016 and Alpine's president from June 2016 to July 2017. Dr. Venkatesan also served as a member of Alpine's board of directors since November 2015. Since May 2018, Dr. Venkatesan has served as chief executive officer and a member of the board of directors of Angion Biomedica, Inc., a private pharmaceutical company. Prior to joining Alpine, Dr. Venkatesan was the executive vice president and general manager of Oncothyreon, Inc. (now Cascadian Therapeutics, which was acquired by Seattle Genetics, Inc. in March 2018) from August 2014 to May 2015 following Oncothyreon's acquisition of Alpine Biosciences, where he served as co-founder and chief executive officer. Previously, Dr. Venkatesan was the founder, portfolio manager, and managing director of Ayer Capital Management, a global healthcare equity fund from 2008 to 2013. Prior to that, he was a director at Brookside Capital Partners from 2002 to 2007. Earlier in his career, Dr. Venkatesan was involved in healthcare investing at Partricof & Co. Ventures from 1995 to 1996 and consulting at

McKinsey & Company from 1993 to 1995. Dr. Venkatesan is currently a managing partner at Alpine BioVentures. In addition, Dr. Venkatesan currently serves on the board of directors of CellBioTherapy and served on the board of directors of Exicure Therapeutics (Nasdaq: XCUR) until December 2020. Dr. Venkatesan received an M.D. from the University of Pennsylvania School of Medicine, an M.B.A. from the Wharton School of the University of Pennsylvania, and a B.A. in Chemistry from Williams College. We believe that Dr. Venkatesan possesses specific attributes that qualify him to serve as a member of our board of directors, including his experience on the boards of and in management positions with biopharmaceutical companies, including publicly-traded companies.

Code of Business Conduct and Ethics

We are committed to the highest standards of integrity and ethics in the way we conduct our business. Our board of directors has adopted a Code of Business Conduct and Ethics, which applies to all of our employees, officers and directors, including our chief executive officer, chief financial officer, and other executive and senior financial officers. Our Code of Business Conduct and Ethics establishes our policies and expectations with respect to a wide range of business conduct, including preparation and maintenance of financial and accounting information, compliance with laws and conflicts of interest. In accordance with our code of conduct, each of our employees, officers and directors is required to report suspected or actual violations to the extent permitted by law. In addition, our board of directors has adopted separate policies and procedures concerning the receipt and investigation of complaints relating to accounting, internal accounting controls or auditing matters, which are administered by our audit committee. Our Code of Business Conduct and Ethics is posted on the Corporate Governance portion of our website at https://ir.alpineimmunesciences.com/governance. We will post amendments to our Code of Business Conduct and Ethics or waivers of our Code of Business Conduct and Ethics for directors and executive officers on the same website.

Audit Committee

The responsibilities of the audit committee include, but are not limited to, the following:

- meeting with our independent auditors, our management team and such other personnel as it deems appropriate to conduct and assist with certain audit committee functions;
- overseeing our accounting and financial reporting processes and audits of its financial statements;
- deciding whether to appoint, retain or terminate our independent auditors, including the sole authority to approve all audit engagement fees and terms and to pre-approve all audit and permitted non-audit and tax services to be provided by the independent auditors;
- reviewing and discussing with management and our independent auditors our financial statements, including certain disclosures, addressing any issues encountered in the course of the audit work, and evaluating the performance of our independent auditors;
- discussing with management our earnings press releases, financial information and any earnings guidance provided to analysts and ratings agencies;
- discussing with us and the internal auditors (if any) our disclosure controls, internal accounting and financial controls and accounting policies and practices;
- discussing with management any outsourcing of the internal audit function (if any), including selection of vendor, fees paid and areas to be audited;
- establishing procedures for the receipt, retention and treatment of complaints received by us regarding certain accounting or audit matters;
- establishing policies governing the hiring by us of any current or former employee of our independent auditors;
- reviewing our compliance with applicable laws and regulations and to review and oversee our policies and procedures designed to promote and monitor regulatory compliance;
- obtaining assurance from the independent auditors that the audit of the financial statements was conducted in a manner consistent with Section 10A of the Exchange Act;
- reviewing, approving and overseeing transactions between us and any related person and any other potential conflict of interest situation;
- administering our Whistleblower and Non-Retaliation Policy and responding to and resolving related complaints or concerns;
- overseeing portions of our Code of Business Conduct and Ethics as designated by our board of directors;
- providing our board of directors with the results of its monitoring and recommendations derived from its responsibilities;
- reviewing and approving our investment policy;
- providing the independent and internal auditors with access to the board of directors; and
- producing the report required to be prepared for inclusion in our annual proxy statement.

From April 2018 to December 2020 the audit committee was composed of three directors: Messrs. Conway (chairman), Peetz and Sekhri. In December 2020, Mr. Sekhri resigned from our board of directors and, in connection with her appointment to the board of directors, Ms. Hernday was appointed to the audit committee. Our board of directors has determined that Mr. Conway is an "audit committee financial expert" as defined in the SEC rules and made a qualitative assessment of Mr. Conway's level of knowledge and experience based on several factors, including his prior experience, business acumen and independence. Our board of directors has concluded that the composition of the audit committee meets the requirements for independence under the rules and regulations of Nasdaq and the SEC.

The audit committee met four times during 2020. The audit committee also meets periodically with our outside auditors without management present, at such times as it deems appropriate. Our board of directors has adopted a written charter for the audit committee in compliance with the applicable rules of the SEC and the Nasdaq listing standards and which is available on our website at https://ir.alpineimmunesciences.com/governance.

Item 11. Executive Compensation.

Summary Compensation Table

The following table provides information regarding the compensation of our named executive officers:

Name and Principal Position	Year	Salary ($)	Option Awards ($)(1)		Nonequity Incentive Plan Compensation ($)(2)	Total ($)(3)
Mitchell H. Gold, M.D.	2020	$ 500,000	$ 566,512		317,500	$ 1,384,012
Executive Chairman and Chief Executive Officer	2019	485,000	852,681		218,250	1,555,931
Stanford Peng, M.D., Ph.D.	2020	464,000	226,605	(4)	294,640	985,245
President and Head of Research and Development	2019	442,708	319,757	(5)	208,126	970,591
Paul Rickey	2020	382,000	214,016		169,799	765,815
Senior Vice President and Chief Financial Officer	2019	370,000	319,757		119,788	809,545

(1) Amounts shown in this column do not reflect dollar amounts actually received by our named executive officers. Instead, these amounts reflect the aggregate grant date fair value of the stock options granted, computed in accordance with the provisions of FASB ASC Topic 718. For additional details regarding the assumptions and methodologies used to calculate the amounts reported, please see the discussion of equity awards contained in Note 12 to our consolidated financial statements contained elsewhere in this Annual Report on Form 10-K.

(2) 2020 amounts represent cash bonuses earned by the named executive officers pursuant to our Executive Incentive Compensation Plan, or Incentive Plan, for 2020 performance, paid in 2021. 2019 amounts represent cash bonuses earned by the named executive officers pursuant to our Incentive Plan for 2019 performance, paid in 2020. For 2019 bonuses, in January of 2020 in lieu of 100% of such cash bonus amount, Dr. Gold was granted a restricted stock unit, or RSU, award for 67,569 shares of our common stock, representing an aggregate grant date value of $218,250. In 2019, in lieu of 50% of such cash bonus amounts, Dr. Peng and Mr. Rickey were each granted an RSU award for 32,217 shares of our common stock and 18,543 shares of our common stock, respectively, representing an aggregate grant date value of $104,063 and $59,894, respectively, with the remaining amounts of the bonuses earned paid in cash in 2020.

(3) Perquisites and personal benefits are excluded as the total value of all perquisites and personal benefits for each named executive officer is less than $10,000.

(4) Reflects the probable value of $0 for Dr. Peng's September 15, 2020 performance-based option award. The maximum value of such award is $462,921.

(5) Reflects the probable value of $0 for Dr. Peng's April 22, 2019 performance-based option award. The performance factor on this award was met in July 2020, at which point 100% of the underlying options vested. Had we determined that as of the date of grant the probably outcome was 100% achievement, we would have assigned a probable value of $231,160.

Executive Employment Arrangements

We entered into amended and restated executive employment agreements with each of Drs. Gold and Peng and Mr. Rickey effective January 1, 2018. Pursuant to these agreements, the annual base salaries for Drs. Gold and Peng and Mr. Rickey were $400,000, $400,000, and $335,000 respectively. In February 2019, the compensation committee approved adjusted salaries for Drs. Gold and Peng and Mr. Rickey of $485,000, $425,000 and $370,000, respectively. Dr. Peng's salary was increased to $450,000 effective April 16, 2019, in connection with his appointment as our President and Head of Research and Development. In January 2020, the compensation committee approved adjusted salaries for Drs. Gold and Peng and Mr. Rickey of $500,000, $464,000, and $382,000 respectively. In January 2021, the compensation committee approved adjusted salaries for Drs. Gold and Peng and Mr. Rickey of $523,000, $485,000, and $400,000 respectively. In March 2021, the compensation committee approved an adjusted salary for Dr. Peng of $500,000. Additionally, Drs. Gold and Peng and Mr. Rickey are eligible to earn cash bonuses of up to 50%, 50% and 40%, respectively, of their base salary under our Executive Incentive Compensation Plan described below. These agreements also provide for certain severance benefits upon the termination of employment or a change in control of the company pursuant to our Change in Control and Severance Policy, or the Severance Policy.

Pursuant to the Severance Policy, if we terminate the employment of any of Dr. Gold, Dr. Peng or Mr. Rickey, each an Eligible Employee, other than for cause, death or disability, or the Eligible Employee resigns for good reason on or within 12 months following a change of control, then, subject to the Eligible Employee signing and not revoking a separation agreement

and release of claims and continuing to adhere to the Eligible Employee's non-competition, non-disclosure and invention assignment agreement, such Eligible Employee will be eligible to receive the following severance benefits, less applicable tax withholdings:

- A lump-sum payment totaling 100% (or, in case of Dr. Gold, 150%) of the Eligible Employee's applicable annual base salary.
- A lump-sum payment equal to (1) 100% of the Eligible Employee's applicable target annual bonus plus (2) a payment equal to the Eligible Employee's pro-rated applicable target annual bonus.
- 100% of the Eligible Employee's then-outstanding and unvested time-based equity awards will become vested and exercisable.
- Payment or reimbursement of continued health coverage for the Eligible Employee and the Eligible Employee's dependents under COBRA for a period of up to 12 months (or, in Dr. Gold's case, 18 months).

Further, under the Severance Policy, if we terminate an Eligible Employee's employment other than for cause, death or disability or such Eligible Employee resigns for good reason at any time other than during the period lasting from the date of a change of control or within 12 months thereafter, then, subject to the Severance Conditions, such Eligible Employee will be eligible to receive the following severance benefits, less applicable tax withholdings:

- Continued payments totaling 75% (or, in Dr. Gold's case, 100%) of the Eligible Employee's applicable annual base salary over a period of 9 months (or in Dr. Gold's case, 12 months).
- 100% of the Eligible Employee's then-outstanding and unvested time-based equity awards granted prior to the closing of the merger by and between Alpine Immune Sciences, Inc. and Nivalis Therapeutics, Inc. that would have otherwise vested during the 12-month period following the date of the Eligible Employee's termination, and 0% in all other cases.
- Payment or reimbursement of continued health coverage for the Eligible Employee and the Eligible Employee's dependents under COBRA for a period of up to 9 months (or, in Dr. Gold's case, 12 months).

Executive Incentive Compensation Plan

Each of our executive officers is eligible for bonuses under our Executive Incentive Compensation Plan, which plan was approved by our board of directors in March 2019, and has an established target bonus amount as set forth in the section titled "—Executive Employment Arrangements." The actual amount of such bonuses is tied to the achievement of various objectives for each year. For 2020, the compensation committee of our board of directors determined that Dr. Gold's bonus would be based solely on achievement of corporate objectives (including advancement of our ALPN-101, ALPN-202 and ALPN-303 development programs, enhancement of our discovery portfolio and achievement of other corporate objectives such as extension of our cash runway), and that the bonuses for Dr. Peng and Mr. Rickey are based 75% on achievement of the previously noted corporate objectives and 25% individual objectives developed in consultation with Dr. Gold.

In January 2021, our compensation committee determined that the 2020 corporate objectives had been achieved at the 127% level and that Dr. Peng's and Mr. Rickey's individual goals had been achieved at the 127% level. The amounts earned in fiscal 2020 were paid in 2021 and Dr. Gold received a payment of $317,500, Dr. Peng received a payment of $294,640, and Mr. Rickey received a payment of $169,799.

Outstanding Equity Awards at Year-End

The following table provides information regarding the equity awards outstanding at December 31, 2020 held by each of our named executive officers:

			Option Awards					
Name	Vesting Commencement Date	Grant Date	Number of Securities Underlying Unexercised Options (#) Exercisable	Number of Securities Underlying Unexercised Options (#) Unexercisable	Equity Incentive Plan Awards: Number of Securities Underlying Unexercised Unearned Options (#)		Option Exercise Price ($)	Option Expiration Date
Mitchell H. Gold	01/16/2015	12/16/2015	51,242	—	—		$ 0.45	12/15/2025
	01/20/2017	03/14/2017	294,361	6,263	—	(1)	0.65	03/13/2027
	01/20/2017	04/12/2017	204,564	4,352	—	(1)	5.02	04/11/2027
	01/02/2018	01/02/2018	51,041	18,959	—	(1)	11.31	01/01/2028
	02/06/2019	02/06/2019	91,666	108,334	—	(1)	6.51	02/05/2029
	01/23/2020	01/23/2020	—	270,000	—	(1)	3.23	01/22/2030
Paul Rickey	04/01/2017	04/12/2017	68,327	6,208	—	(1)	5.02	04/11/2027
	01/02/2018	01/02/2018	32,812	12,188	—	(1)	11.31	01/01/2028
	02/06/2019	02/06/2019	34,375	40,625	—	(1)	6.51	02/05/2029
	01/23/2020	01/23/2020	—	102,000	—	(1)	3.23	01/22/2030
Stanford Peng	09/06/2016	09/22/2016	161,492	—	—		0.65	09/21/2026
	09/06/2016	03/14/2017	37,267	—	—		0.65	03/13/2027
	01/02/2018	01/02/2018	47,395	17,605	—	(1)	11.31	01/01/2028
	09/28/2018	09/28/2018	125,000	125,000	—	(2)	6.33	09/27/2028
	02/06/2019	02/06/2019	34,375	40,625	—	(1)	6.51	02/05/2029
	04/22/2019	04/22/2019	50,000	—	—	(3)	7.20	04/21/2029
	01/23/2020	01/23/2020	—	108,000	—	(1)	3.23	01/22/2030
	09/15/2020	09/15/2020	—	—	80,000	(4)	8.28	09/14/2030

(1) 1/4th of the shares will vest on the one-year anniversary of the vesting commencement date, and 1/36th of the remaining shares shall vest on each monthly anniversary thereafter, such that 100% of the shares shall be vested and exercisable as of the four-year anniversary of the vesting commencement date.

(2) 1/2 of the shares subject to the option become vested and exercisable on October 1, 2020 and the balance of the shares subject to the option become vested and exercisable on October 1, 2022, subject to continued service through each such date.

(3) 100% of the shares underlying the option vested upon the achievement of specified performance goals that were achieved prior to April 16, 2023, as determined by the board of directors or the compensation committee of the board of directors.

(4) The shares underlying the option will vest in two equal tranches upon the achievement of specified performance goals that are achieved on or prior to the expiration of the options, as determined by the board of directors or the compensation committee of the board of directors.

401(k) Plan

We have adopted the WTIA 401(k) Multiple Employer Plan, maintained by Washington Technology Industry Association, which is a defined contribution retirement plan, in which all Alpine employees providing at least 20 hours of service a week are eligible to participate. This plan provides our eligible employees with an opportunity to save for retirement on a tax advantaged basis, and participants are able to defer a portion of their eligible compensation. All participants' interests in their deferrals are 100% vested when contributed. The 401(k) plan permits us to make matching contributions and profit-sharing contributions to eligible participants. We have not provided a discretionary company match to employee contributions during the periods presented. Pre-tax contributions are allocated to each participant's individual account and are then invested in selected investment alternatives according to the participants' directions. The 401(k) plan is intended to qualify under Sections 401(a) and 501(a) of the Internal Revenue Code. As a tax-qualified retirement plan, contributions to the 401(k) plan and earnings on those contributions are not taxable to the employees until distributed from the 401(k) plan and all contributions are deductible by us when made. The 401(k) plan also permits contributions to be made on a post-tax basis for those employees participating in the Roth 401(k) plan component.

Director Compensation

Director Compensation Policy

In July 2015, our board of directors approved a director compensation policy for our non-employee directors that became effective following our initial public offering and which was most recently amended in March 2021. For purposes of the policy, the board of directors classified each director into one of the two following categories: (1) an "employee director," is a director who is employed by us; and (2) a "non-employee director," is a director who is not an employee director. Only non-employee directors will receive compensation under the director compensation policy. Non-employee directors will receive compensation in the form of equity and cash under the director compensation policy, as described below. We believe our non-employee director compensation program provides reasonable compensation to our non-employee directors that is appropriately aligned with our peers and is commensurate with the services and contributions of our non-employee directors.

Non-employee directors receive an initial stock option grant to purchase shares of our common stock upon appointment or election to the board of directors. Pursuant to amendments made in March 2019, the size of the initial stock option grant was set at 15,000 shares. Non-employee directors also receive on an annual basis, an additional stock option grant to purchase 7,650 shares. In March 2021, the policy was amended to increase the initial option grant to 20,000 shares and to increase the annual option grant to 10,000 shares. The annual grants occur on the first trading day in January of each year. All options have an exercise price equal to the closing price of our common stock as reported by Nasdaq on the date of grant, are subject to vesting in 36 equal monthly installments over a three-year period from the grant date for initial option grants, or in 12 equal monthly installments over a 12-month period from the grant date for annual stock option grants, subject to further evaluation by the compensation committee. On a change in control, all outstanding, unvested options held by non-employee directors are expected to vest in full.

Each non-employee director is eligible to receive the following cash annual retainer, which will be paid quarterly in arrears on a prorated basis.

Annual retainer for board membership	$ 40,000
Annual retainer for board chairperson	25,000
Annual retainer for audit committee chairperson	15,000
Annual retainer for audit committee member	7,500
Annual retainer for compensation committee chairperson	10,000
Annual retainer for compensation committee member	5,000
Annual retainer for nominating and corporate governance committee chairperson	7,500
Annual retainer for nominating and corporate governance committee member	3,750

2020 Director Compensation Table

The following table shows for the fiscal year ended December 31, 2020 certain information with respect to the compensation of our non-employee directors who served on our board of directors during any part of 2020.

Name	Fees Earned or paid in Cash ($)	Option Awards ($)(1)	Total ($)
Robert Conway(2)	$ 58,750	$ 17,179	$ 75,929
Min Cui, Ph.D.(3)(10)	44,049	17,179	61,228
Natasha Hernday(4)(10)	2,840	112,849	115,689
Christopher Peetz(5)	47,500	17,179	64,679
Paul Sekhri(6)(10)	49,504	17,179	66,683
Peter Thompson, M.D.(7)	52,500	17,179	69,679
James N. Topper, M.D., Ph.D.(8)	50,000	17,179	67,179
Jay Venkatesan, M.D.(9)	40,000	17,179	57,179

(1) Amounts shown in this column do not reflect dollar amounts actually received by our non-employee directors. Instead, these amounts reflect the aggregate grant date fair value of the stock options granted, computed in accordance with the provisions of FASB ASC Topic 718.
(2) As of December 31, 2020, Mr. Conway held outstanding options to purchase 30,085 shares of common stock.
(3) As of December 31, 2020, Dr. Cui held outstanding options to purchase 15,300 shares of common stock.
(4) As of December 31, 2020, Ms. Hernday held outstanding options to purchase 15,000 shares of common stock.
(5) As of December 31, 2020, Mr. Peetz held outstanding options to purchase 22,950 shares of common stock.
(6) As of December 31, 2020, Mr. Sekhri held outstanding options to purchase 28,255 shares of commons stock. Mr. Sekhri resigned from the board of directors effective December 10, 2020.
(7) As of December 31, 2020, Dr. Thompson held outstanding options to purchase 22,950 shares of common stock.
(8) As of December 31, 2020, Dr. Topper held outstanding options to purchase 22,950 shares of common stock.
(9) As of December 31, 2020, Dr. Venkatesan held outstanding options to purchase 130,363 shares of common stock.
(10) Mr. Sekhri submitted his resignation from the board of directors effective December 10, 2020. In connection with Mr. Sekhri's resignation, Dr. Cui was appointed to the compensation committee. Also effective December 10, 2020, Ms. Hernday joined our board of directors and replaced Mr. Sekhri as a member of the audit committee.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters.

Securities Authorized for Issuance Under Equity Compensation Plans

The following table provides information as of December 31, 2020, with respect to the shares of our common stock that may be issued under existing equity compensation plans:

	A	B	C
Plan Category	**Number of Securities to be Issued Upon Exercise of Outstanding Options and Rights**	**Weighted-Average Exercise Price of Outstanding Options and Rights**	**Number of Securities Remaining Available for Future Issuance Under Equity Compensation Plans (Excluding Securities Reflected in Column A) (1)**
Equity compensation plans approved by security holders			
Amended and Restated 2015 Stock Plan, as amended, or the 2015 Stock Plan	1,268,057	$ 2.94	—
2015 Equity Incentive Plan	339,548	$ 12.42	—
2018 Equity Incentive Plan	2,580,162	$ 5.52	887,901
Employee Stock Purchase Plan	—	N/A	45,211
Total	4,187,767	$ 5.29	933,112

(1) Represents the number of securities remaining available for future issuance under the 2015 Equity Incentive Plan, the 2015 Stock Plan, the 2018 Equity Incentive Plan and the Employee Stock Purchase Plan. The number of shares available for issuance under the 2018 Equity Incentive Plan is subject to an annual increase on the first day of each year equal to the lesser of (a) 1,500,000 shares or (b) 5% of the total number of shares of common stock outstanding on December 31 of the preceding calendar year or (c) a lesser number of shares of common stock approved by the board of directors prior to January 1 of a given year.

Principal Stockholders

The following table sets forth certain information with respect to the beneficial ownership of our common stock as of March 1, 2021 for:

- each person who we know beneficially owns more than 5% of our common stock;
- each of our directors;
- each of our named executive officers; and

- all of our directors and executive officers as a group.

The percentage of beneficial ownership shown in the table is based upon 23,882,138 shares outstanding as of March 1, 2021.

We have determined beneficial ownership in accordance with the rules of the SEC. Except as indicated by the footnotes below, we believe, based on the information furnished to us, that the persons and entities named in the table below have sole voting and investment power with respect to all shares of common stock that they beneficially own, subject to applicable community property laws.

In computing the number of shares beneficially owned by a person and the percentage ownership of that person, we take into account shares of common stock issuable pursuant to stock options, warrants and restricted stock units that may be exercised or that are scheduled to vest on or before the 60th day after March 1, 2021. These shares are deemed to be outstanding and beneficially owned by the person holding those options, warrants or restricted stock units for the purpose of computing the percentage ownership of that person, but they are not treated as outstanding for the purpose of computing the percentage ownership of any other person.

Except as otherwise noted below, the address for each person or entity listed in the table is c/o Alpine Immune Sciences, Inc., 188 East Blaine Street, Suite 200, Seattle, Washington 98102.

	Common Stock Beneficially Owned	
Name of Beneficial Owner	**Shares**	**Percentage**
5% Stockholders:		
Decheng Capital China Life Sciences USD Fund III, L.P.(1)	4,400,371	17.5 %
OrbiMed Private Investments VI, LP(2)	3,216,206	13.4 %
Alpine Immunosciences, L.P.(3)	3,075,421	12.8 %
Frazier Life Sciences VIII, L.P.(4)	2,716,701	11.3 %
Omega Fund VI, L.P(5)	1,670,370	6.9 %
Entities affiliated with Avidity Partners Management LP (6)	1,470,390	6.1 %
Directors and Executive Officers:		
Mitchell H. Gold(7)	4,195,825	16.9 %
Paul Rickey(8)	207,624	*
Stanford Peng(9)	525,317	2.2%
Jay Venkatesan(10)	3,443,037	14.3 %
Peter Thompson(11)	3,241,068	13.5 %
James N. Topper(12)	2,741,563	11.4 %
Robert Conway(13)	57,717	*
Christopher Peetz (14)	24,862	*
Min Cui(15)	4,415,670	17.6 %
Natasha Hernday (16)	3,578	*
All current directors and executive officers as a group (10 persons)(17)	15,780,840	58.0 %

(*) Less than one percent.

(1) According to a Schedule 13D/A filed on August 3, 2020 with the Securities and Exchange Commission, or SEC, Decheng Capital Management III (Cayman), LLC ("Decheng Capital Management") and Min Cui may be deemed to beneficially own 4,400,371 shares which are held by Decheng Capital China Life Sciences USD Fund III, L.P. ("Decheng"), including 1,234,636 shares issuable upon the exercise of warrants that are exercisable within 60 days of March 1, 2021. Decheng Capital Management is the general partner of Decheng. Dr. Cui is the sole manager of Decheng Capital Management and may be deemed to have voting and investment power with respect to the shares held by Decheng and as a result may be deemed to have beneficial ownership of such shares. The address for Decheng is 3000 Sand Hill Road, Building 2, Suite 110, Menlo Park, California 94025.

(2) According to a Schedule 13D filed on December 30, 2020 with the SEC, OrbiMed Advisors LLC and OrbiMed Capital GP VI LLC may be deemed to beneficially own 3,216,206 shares which are held by OrbiMed Private Investments VI, LP, including 145,251 shares issuable upon the exercise of warrants, which are exercisable within 60 days of March 1,

2021. OrbiMed Capital GP VI LLC (“GP VI”) is the general partner of OrbiMed Private Investments VI, LP. OrbiMed Advisors LLC (“OrbiMed Advisors”) is the managing member of GP VI. Carl L. Gordon, Sven H. Borho and Jonathan T. Silverstein share voting and investment power over the shares held by OrbiMed Private Investments VI, LP and as a result may be deemed to have beneficial ownership of such shares. Dr. Thompson, an employee of OrbiMed Advisors, may be deemed to have beneficial ownership of such shares. Each of GP VI, OrbiMed Advisors, Carl L. Gordon, Sven H. Borho, Jonathan T. Silverstein and Dr. Thompson disclaims beneficial ownership of the shares held by OrbiMed Private Investments VI, LP, except to the extent of its or his pecuniary interest therein, if any. The address for OrbiMed Private Investments VI, LP is 601 Lexington Avenue, 54th Floor, New York, New York 10022.

(3) According to a Schedule 13D/A filed on December 22, 2020 with the SEC, Alpine BioVentures, GP, LLC, Mitchell H. Gold and Jay Venkatesan may be deemed to beneficially own 3,075,421 shares which are held by Alpine Immunosciences, L.P., including 74,441 shares issuable upon the exercise of warrants, which are exercisable within 60 days of March 1, 2021. Alpine BioVentures GP, LLC is the general partner of Alpine Immunosciences, L.P. Dr. Gold and Dr. Venkatesan are the Managing Partners of Alpine BioVentures GP, LLC. Dr. Gold and Dr. Venkatesan are also limited partners of Alpine Immunosciences, L.P. By virtue of such relationships, Dr. Gold and Dr. Venkatesan may be deemed to have voting and investment power with respect to the shares held by Alpine Immunosciences, L.P. and as a result may be deemed to have beneficial ownership of such shares. Each of Dr. Gold and Dr. Venkatesan disclaims beneficial ownership of the shares held by Alpine Immunosciences, L.P., except to the extent of his pecuniary interest therein, if any. The address for Alpine Immunosciences, L.P. is 600 Stewart Street, Suite 1503, Seattle Washington 98101.

(4) According to a Schedule 13D/A filed on July 30, 2020 with the SEC, FHM Life Sciences VIII, L.P., FHM Life Sciences VIII, L.L.C., James Topper and Patrick J. Heron may be deemed to beneficially own 2,716,701 shares which are held by Frazier Life Sciences VIII, L.P., including 145,251 shares issuable upon the exercise of warrants that are exercisable within 60 days of March 1, 2021. FHM Life Sciences VIII, LP is the general partner of Frazier Life Sciences VIII, L.P. and FHM Life Sciences VIII, LLC is the general partner of FHM Life Sciences VIII, LP. Dr. Topper and Patrick J. Heron are the sole members of FHM Life Sciences VIII, LLC and therefore share voting and investment power over the shares held by Frazier Life Sciences VIII, L.P. Dr. Topper and Mr. Heron disclaim beneficial ownership of the shares held by Frazier Life Sciences VIII, L.P. except to the extent of their pecuniary interests in such shares, if any. The address for Frazier Life Sciences VIII, L.P. is 601 Union Street, Suite 3200, Seattle, Washington 98101.

(5) According to a Schedule 13-G filed on August 6, 2020 with the SEC, consists of 1,284,900 shares of common stock and warrants to purchase up to an aggregate of 385,470 shares of common stock held directly by Omega Fund VI, L.P. (“Omega Fund”). Omega Fund VI GP Manager, Ltd. (“Omega Ltd.”) serves as the general partner of Omega Fund VI GP, L.P. ("Omega GP"), which serves as the general partner of Omega Fund; and each of Omega Ltd and Omega GP may be deemed to own beneficially the shares held by Omega Fund. Claudio Nessi, Otello Stampacchia and Anne-Mari Paster are the directors of Omega Ltd and may be deemed to beneficially own the shares held directly by Omega Fund. The address for Omega Fund is 888 Boylston Street, Suite 1111, Boston, MA 02199.

(6) According to a Schedule 13 G filed with the SEC on February 16, 2021, Avidity Partners Management LP (“APM LP”), Avidity Partners Management (GP) LLC (“APM GP”), Avidity Capital Partners Fund (GP) LP (“ACPF”), Avidity Capital Partners (GP) LLC (“ACP”) share voting and dispositive power with respect to 1,470,390 shares, of which 1,312,916 shares are further subject to shared voting and dispositive power with Avidity Master Fund LP (“AMF” and, together with APM LP, APM GP, ACPF and ACP, the “Avidity Funds”). According to the Company’s records, these shares also include 222,390 shares issuable upon exercise of outstanding warrants. David Witzke and Michael Gregory directly or indirectly control the Avidity Funds and as a result may be deemed to have voting and dispositive power over the securities held directly by the Avidity Funds. The address of Avidity Partners Management LP is 2828 N Harwood Street, Suite 1220, Dallas, TX 75201.

(7) Consists of (i) 310,039 shares of our common stock held directly by Dr. Gold, (ii) 810,365 shares of our common stock issuable upon the exercise of options within 60 days of March 1, 2021, (iii) 3,000,980 shares of our common stock held directly by Alpine Immunosciences, L.P and (iv) 74,441 shares of our common stock issuable upon the exercise of warrants held by Alpine Immunosciences, L.P. which are exercisable within 60 days of March 1, 2021. Please see footnote 3 regarding Dr. Gold’s voting and investment power over the shares held by Alpine Immunosciences, L.P.

(8) Consists of (i) 24,027 shares of our common stock held directly by Mr. Rickey and (ii) 183,597 shares of our common stock issuable upon the exercise of options within 60 days of March 1, 2021.

(9) Consists of (i) 24,371 shares of our common stock held directly by Dr. Peng and (ii) 500,946 shares of our common stock issuable upon the exercise of options within 60 days of March 1, 2021.

(10) Consists of (i) 202,763 shares of our common stock held directly by Dr. Venkatesan, (ii) 37,266 shares of our common stock held in trust for the benefit of Dr. Venkatesan’s children, (iii) 127,587 shares of our common stock issuable upon the exercise of options within 60 days of March 1, 2021, (iv) 3,038,246 shares of our common stock held directly by Alpine Immunosciences, L.P., and (v) 74,441 shares of our common stock issuable upon the exercise of warrants held by Alpine Immunosciences, L.P. which are exercisable within 60 days of March 1, 2021. Please see footnote 3 regarding Dr. Venkatesan’s voting and investment power over the shares held by Alpine Immunosciences, L.P.

(11) Consists of (i) 24,862 shares of our common stock issuable upon the exercise of options within 60 days of March 1, 2021, (ii) 3,070,955 shares of our common stock held directly by OrbiMed Private Investments VI, LP and (iii) 145,251 shares of our common stock issuable upon the exercise of warrants held by OrbiMed Private Investments VI, LP which are exercisable within 60 days of March 1, 2021. Please see footnote 2 regarding Dr. Thompson's voting and investment power over the shares held by OrbiMed Private Investments VI, LP.

(12) Consists of (i) 24 862 shares of our common stock issuable upon the exercise of options within 60 days of March 1, 2021, (ii) 2,571,450 shares of our common stock held directly by Frazier Life Sciences VIII, L.P. and (iii) 145,251 shares of our common stock issuable upon the exercise of warrants held by Frazier Life Sciences VIII, L.P. which are exercisable within 60 days of March 1, 2021. Please see footnote 4 regarding Dr. Topper's voting and investment power over the shares held by Frazier Life Sciences VIII, L.P.

(13) Consists of (i) 15,000 shares of our common stock held directly by Mr. Conway, (ii) 10,000 shares of our common stock held indirectly through the Robert E. Conway Revocable Trust and Carolyn J. Conway Revocable Trust, and (iii) 32,717 shares of our common stock issuable upon exercise of options within 60 days of March 1, 2021.

(14) Consist of 24,862 shares of our common stock issuable upon the exercise of options within 60 days of March 1, 2021.

(15) Consists of (i) 15,299 shares of our common stock issuable upon the exercise of options within 60 days of March 1, 2021, (ii) 3,165,735 shares of our common stock held directly by Decheng Capital China Life Sciences USD Fund III, L.P. and (iii) 1,234,636 shares of our common stock issuable upon the exercise of warrants held by Decheng Capital China Life Sciences USD Fund III, L.P. which are exercisable within 60 days of March 1, 2021. Please see footnote 1 regarding Dr. Cui's voting and investment power over the shares held by Decheng Capital China Life Sciences USD Fund III, L.P.

(16) Consists of 3,578 shares of our common stock issuable upon the exercise of options within 60 days of March 1, 2021.

(17) Includes only current directors and executive officers serving in such capacity as of March 1, 2021. Includes 1,748,675 shares of our common stock issuable upon the exercise of options within 60 days of March 1, 2021 and 1,599,579 shares of our common stock issuable upon the exercise of warrants within 60 days of March 1, 2021.

Item 13. Certain Relationships and Related Transactions, and Director Independence.

Related Party Transaction Policy

Our board of directors has adopted a written policy governing the review and approval of related party transactions. The audit committee of our board of directors has the primary responsibility for reviewing and approving or disapproving related party transactions, as designated in the audit committee charter. In addition, our Code of Business Conduct and Ethics requires that each of our employees and directors inform his or her superior or the chairman of the audit committee, respectively, of any material transaction or relationship that comes to his or her attention that could reasonably be expected to create a conflict of interest. Further, at least annually, each director and executive officer will complete a detailed questionnaire that asks questions about any business relationship that may give rise to a conflict of interest and all transactions in which we are involved and in which an executive officer, a director or a related person has a direct or indirect material interest.

Affiliations with Principal Stockholders

Dr. Gold is an executive officer, and Dr. Venkatesan was an executive officer until August 2018. Each of Drs. Venkatesan and Gold is also a member of our board of directors and, in their individual capacities, a limited partner of Alpine Immunosciences, L.P., Delaware limited partnership, which is a holder of more than 5% of our outstanding capital stock. In addition, each of Drs. Venkatesan and Gold, in their individual capacities, is a Managing Partner of Alpine BioVentures, GP, LLC, a Delaware limited liability company, which is the general partner of Alpine Immunosciences, L.P.

Dr. James N. Topper is a member of our board of directors and, in his individual capacity, is a managing member of FHM Life Sciences VIII, LLC, a Delaware limited liability company. FHM Life Sciences VIII, LLC is the general partner of FHM Life Sciences VIII, LP, a Delaware limited partnership. FHM Life Sciences VIII, LP is the general partner of Frazier Life Sciences VIII, L.P., a Delaware limited partnership, which is a holder of more than 5% of our outstanding capital stock.

Mr. Peetz is a member of our board of directors and, in his individual capacity, is an Entrepreneur-in-Residence at Frazier Healthcare Partners, which is an affiliate of Frazier Life Sciences VIII, L.P.

Dr. Peter Thompson is a member of our board of directors and, in his individual capacity, is an employee of OrbiMed Advisors LLC. OrbiMed Advisors LLC is the managing member of OrbiMed Capital GP VI LLC. OrbiMed Capital GP VI LLC is the general partner of OrbiMed Private Investments VI, LP, which is a holder of more than 5% of our outstanding capital stock.

Dr. Min Cui is a member of our board of directors and, in his individual capacity, is the manager of Decheng Capital Management III (Cayman), LLC, which in turn is the general partner of Decheng Capital China Life Sciences USD Fund III, L.P. Decheng Capital China Life Sciences USD Fund III, L.P. is a holder of more than 5% of our outstanding capital stock.

Indemnification Agreements

We have entered into indemnification agreements with each of our directors and with each of our executive officers. Pursuant to the indemnification agreements, we have agreed to indemnify and hold harmless these directors and officers to the fullest extent permitted by applicable law. The agreements generally cover expenses that a director or officer incurs or amounts that a director or officer becomes obligated to pay because of any proceeding to which he or she is made or threatened to be made a party or participant by reason of his or her service as a current or former director, officer, employee or agent of Alpine Immune Sciences. The agreements also provide for the advancement of expenses to the directors and executive officers subject to specified conditions. There are certain exceptions to our obligation to indemnify the directors and officers, including any intentional misconduct or act where the director or officer did not in good faith believe he or she was acting in our best interests, with respect to "short-swing" profit claims under Section 16(b) of the 1934 Act and, with certain exceptions, with respect to proceedings that he or she initiates.

January 2019 and July 2020 Private Placements

July 2020 Private Placement

On July 24, 2020, we entered into a securities purchase agreement in connection with the sale and issuance of 5,139,610 units and 790,710 prefunded units for an aggregate purchase price of $60.0 million. Each unit was sold at a purchase price of $10.1175 per unit and consists of one share of our common stock plus a warrant to purchase 0.3 shares of common stock at an exercise price of $12.74 per share. Each prefunded unit consists of one prefunded warrant to purchase one share of common stock at an exercise price of $0.001 per share and one warrant to purchase 0.3 shares of common stock at an exercise price of $12.74 per share.

None of the purchasers in the July 2020 private placement was a greater than 5% holder of our outstanding capital stock prior to the July 2020 private placement.

We also entered into a registration rights agreement with the investors in the July 2020 private placement, including Omega Fund VI, L.P. and entities affiliated with Avidity Partners Management LP. The registration rights agreement required us to register the resale of the shares of common stock issued and issuable upon the exercise of warrants and prefunded warrants. We filed a registration statement on Form S-1 on August 11, 2020 covering the resale of such shares, which registration statement was declared effective by the Securities and Exchange Commission on August 18, 2020.

January 2019 Private Placement

On January 15, 2019, we entered into a securities purchase agreement in connection with the sale and issuance of 4,706,700 units for $5.37 per unit representing (i) 4,706,700 shares of our common stock and (ii) warrants to purchase an additional 1,835,610 shares of common stock for $12.74 per share, with each unit consisting of one share of common stock and a warrant to purchase 0.39 of a share of common stock.

The following table summarizes the purchases on January 18, 2019 of our securities by our 5% stockholders at the time of the January 2019 private placement:

Name of Purchaser	Number of Shares of Common Stock Purchased	Number of Shares of Common Stock Subject to Warrants	Aggregate Purchase Price
Alpine Immunosciences, L.P.	190,875	74,771	$ 1,024,998.75
OrbiMed Private Investments VI, LP	372,439	145,251	$ 1,999,997.43
Frazier Life Sciences VIII, L.P.	372,439	145,251	$ 1,999,997.43

We also entered into a registration rights agreement with the investors in the January 2019 private placement, including the investors set forth in the immediately preceding table and Decheng Capital China Life Sciences USD Fund III, L.P., or Decheng. Prior to the January 2019 private placement, Decheng was not a greater than 5% holder of our outstanding capital stock. The registration rights agreement required us to register the resale of the shares of common stock issued and issuable

upon the exercise of warrants. We filed a registration statement on Form S-1 on March 18, 2019 covering the resale of such shares, which registration statement was declared effective by the Securities and Exchange Commission on April 4, 2019.

Indebtedness of Directors and Officers

None of our current or former directors or executive officers is indebted to us, nor are any of these individuals indebted to another entity which indebtedness is the subject of a guarantee, support agreement, letter of credit or other similar arrangement or understanding provided by us.

Other Transactions

We have granted stock options and/or restricted stock units to our named executive officers, other executive officers and our directors.

Director Independence

Our board of directors has undertaken a review of its composition, the composition of its committees and the independence of current directors and considered whether any such director has a material relationship with us that could compromise his or her ability to exercise independent judgment in carrying out his or her responsibilities. Based upon information requested from and provided by each current director concerning his or her background, employment and affiliations, including family relationships, the board of directors has determined that (1) none of our current directors except for Drs. Gold and Venkatesan, has a relationship which would interfere with the exercise of independent judgment in carrying out the responsibilities of a director and that each of these directors is an "independent director" as defined under the rules of the Nasdaq. The board of directors also determined that Messrs. Conway (chairman) and Peetz and Ms. Hernday, who comprise our audit committee, Drs. Topper (chairman), Thompson and Cui, who comprise our compensation committee, and Drs. Thompson (chairman) and Cui and Mr. Conway, who comprise our nominating and corporate governance committee, satisfy the independence standards for those committees established by applicable SEC rules and the rules of Nasdaq.

Item 14. Principal Accounting Fees and Services.

The following table presents fees for professional audit services and other services rendered to our company by EY for the years ended December 31, 2020 and 2019.

	Year Ended December 31,	
Fee Category	**2020**	**2019**
Audit fees(1)	$ 531,725	$ 393,778
Audit-related fees(2)	30,000	—
Tax fees(3)	45,873	—
All other fees(4)	—	—
Total fees	$ 607,598	$ 393,778

(1) Audit fees consist of fees for professional services provided in connection with the audit of our annual consolidated financial statements, review of our quarterly consolidated financial statements, procedures for comfort letters, consents and assistance with and review of documents filed with the SEC.
(2) Audit-related fees consist of assurance and related services that are reasonably related to the performance of the audit or review of our financial statements and are not reported under "Audit Fees".
(3) Tax fees consist of fees associated with tax compliance, tax advice and tax planning fees.
(4) All other fees include any fees billed that are not audit fees, audit-related fees or tax fees.

All fees described above were pre-approved by the audit committee.

Audit Committee Policy on Pre-Approval of Audit and Permissible Non-Audit Services of Independent Registered Public Accounting Firm

Pursuant to its charter, the audit committee must review and approve, in advance, the scope and plans for the audits and the audit fees and approve in advance (or, where permitted under the rules and regulations of the SEC, subsequently) all non-audit services to be performed by the independent auditor that are not otherwise prohibited by law and any associated fees. All fees paid to EY for 2020 and 2019 were pre-approved by our audit committee. The audit committee may delegate to one or more members of the committee the authority to pre-approve audit and permissible non-audit services, as long as this pre-approval is presented to the full committee at scheduled meetings.

PART IV

Item 15. Exhibits, Financial Statement Schedules.

(a) The financial statements, schedules and exhibits filed as a part of this Annual Report on Form 10-K are as follows:

(a) Financial statements – The financial statements included in Item 8 are filed as part of this Annual Report on Form 10-K.

(b) Financial Statement Schedules – All schedules have been omitted because they are not applicable or required, or the information required to be set forth therein is included in the consolidated financial statements or notes thereto included in Item 8 of this Annual Report on Form 10-K.

(c) Exhibits – The exhibits required to be filed as part of this report are listed in the Exhibit List attached hereto and are incorporated herein by reference.

INDEX TO EXHIBITS

		Incorporated by Reference			
Exhibit Number	**Description**	**Form**	**File No.**	**Exhibit**	**Filing Date**
3.1	Amended and Restated Certificate of Incorporation of the Registrant, as amended	10-K	001-37449	3.1	March 28, 2018
3.2+	Amended and Restated Bylaws of the Registrant				
4.1	Form of Common Stock Certificate of the Registrant	10-K	001-37449	4.1	March 28, 2018
4.2	Second Amended and Restated Warrant to Purchase Common Stock, dated February 18, 2011, issued to Horizon Credit I LLC	S-1	333-204127	4.2	May 13, 2015
4.3	Second Amended and Restated Warrant to Purchase Common Stock, dated February 18, 2011, issued to Horizon Credit II LLC	S-1	333-204127	4.3	May 13, 2015
4.4	Warrant to Purchase Shares, dated December 16, 2016, by and between Alpine Immune Sciences, Inc. and Silicon Valley Bank	10-K	001-37449	4.5	March 28, 2018
4.5	Form of Warrant to Purchase Shares of Common Stock issued to certain service providers on April 12, 2017 pursuant to the Amended and Restated 2015 Stock Plan, as amended	10-K	001-37449	4.6	March 28, 2018
4.6	Form of Warrant to Purchase Common Stock issued pursuant to the Securities Purchase Agreement, dated January 15, 2019, by and among the Registrant and the Purchasers party thereto	8-K	001-37449	10.3	January 16, 2019
4.7	Warrant to Purchase Common Stock, dated August 26, 2019, by and between Alpine Immune Sciences, Inc. and Silicon Valley Bank	8-K	001-37449	4.1	August 28, 2019
4.8	Form of Warrant to Purchase Common Stock issued pursuant to the Securities Purchase Agreement, dated July 24, 2020, by and among Alpine Immune Sciences, Inc. and the Purchasers party thereto	8-K	001-37449	10.3	July 24, 2020
4.9	Form of Prefunded Warrant to Purchase Common Stock issued pursuant to the Securities Purchase Agreement, dated July 24, 2020, by and among Alpine Immune Sciences, Inc. and the Purchasers party thereto	8-K	001-37449	10.4	July 24, 2020
4.10+	Description of Capital Stock				
10.1*	Nivalis Therapeutics, Inc. 2015 Equity Incentive Plan	S-8	333-205220	4.4	June 25, 2015
10.2*	Form of Notice of Stock Option Grant and Stock Option Agreement for Employees under the Nivalis Therapeutics, Inc. 2015 Equity Incentive Plan	S-8	333-205220	4.5	June 25, 2015

Exhibit Number	Description	Incorporated by Reference			
		Form	File No.	Exhibit	Filing Date
10.3*	Form of Notice of Stock Option Grant and Stock Option Agreement for Non-Employee Directors under the Nivalis Therapeutics, Inc. 2015 Equity Incentive Plan	S-8	333-205220	4.6	June 25, 2015
10.4*	Nivalis Therapeutics, Inc. Employee Stock Purchase Plan	S-8	333-205220	4.7	June 25, 2015
10.5*	Form of Indemnification Agreement entered into by and between the Registrant and its directors and officers	S-1	333-204127	10.18	May 13, 2015
10.6*+	Non-Employee Director Compensation Guidelines				
10.7*	Change of Control and Severance Policy	8-K	001-37449	10.1	December 11, 2017
10.8*	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	March 28, 2018
10.9*	Employment Agreement, dated as of January 1, 2018, by and between the Registrant and Paul Rickey	10-K	001-37449	10.35	March 28, 2018
10.10*	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	March 28, 2018
10.11*	Alpine Immune Sciences, Inc. (now known as AIS Operating Co., Inc.) Amended and Restated 2015 Stock Plan, as amended	S-8 POS	333-218134	4.1	September 11, 2017
10.12*	Form of Option Agreement under the Alpine Immune Sciences, Inc. (now known as AIS Operating Co., Inc.) Amended and Restated 2015 Stock Plan, as amended	S-8 POS	333-218134	4.2	September 11, 2017
10.13*	Alpine Immune Sciences, Inc. 2018 Equity Incentive Plan, as amended	8-K	001-37449	10.1	June 17, 2020
10.14*	Form of Stock Option Agreement under the 2018 Equity Incentive Plan	8-K	001-37449	10.2	June 14, 2018
10.15*	Form of Restricted Stock Unit Agreement under the 2018 Equity Incentive Plan	8-K	001-37449	10.1	January 27, 2020
10.16	Securities Purchase Agreement, dated January 15, 2019, by and among the Company and the Purchasers	8-K	001-37449	10.1	January 16, 2019
10.17	Registration Rights Agreement, dated January 15, 2019, by and among the Company and the Purchasers	8-K	001-37449	10.2	January 16, 2019
10.18*	Alpine Immune Sciences, Inc. Executive Incentive Compensation Plan	8-K	001-37449	10.1	April 1, 2019
10.19	Lease Agreement, dated March 14, 2019, by and between the Company and ARE Seattle No. 28, LLC	10-Q	001-37449	10.6	May 9, 2019
10.20	Amended and Restated Loan and Security Agreement, dated August 26, 2019, by and among Alpine Immune Sciences, Inc., AIS Operating Co., Inc. and Silicon Valley Bank	8-K	001-37449	10.1	August 28, 2019
10.21**	Option and License Agreement, dated June 17, 2020, by and between Alpine Immune Sciences, Inc. and AbbVie Ireland Unlimited Company	10-Q	001-37449	10.2	August 11, 2020
10.22	Securities Purchase Agreement, dated July 24, 2020, by and among Alpine Immune Sciences, Inc. and the Purchasers named therein	8-K	001-37449	10.1	July 24, 2020
10.23	Registration Rights Agreement, dated July 24, 2020, by and among Alpine Immune Sciences, Inc. and the Purchasers named therein	8-K	001-37449	10.2	July 24, 2020
21.1	List of subsidiaries of the Registrant	10-K	001-37449	21.1	March 28, 2018
23.1+	Consent of Independent Registered Public Accounting Firm				

Exhibit Number	Description	Incorporated by Reference			
		Form	File No.	Exhibit	Filing Date
24.1+	Powers of Attorney (contained on signature page)				
31.1+	Certification of Principal Executive Officer Required Under Rules 13a-14(a) and 15d-14(a) of the Securities Exchange Act of 1934, as amended				
31.2+	Certification of Principal Financial Officer Required Under Rules 13a-14(a) and 15d-14(a) of the Securities Exchange Act of 1934, as amended				
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. Section 1350				
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. Section 1350				
101.INS+	Inline XBRL Instance Document				
101.SCH+	Inline XBRL Taxonomy Extension Schema Document				
101.CAL+	Inline XBRL Taxonomy Extension Calculation Linkbase Document				
101.LAB+	Inline XBRL Taxonomy Extension Label Linkbase Document				
101.PRE+	Inline XBRL Taxonomy Extension Presentation Linkbase Document				
101.DEF+	Inline XBRL Taxonomy Extension Definition Linkbase Document				
104	Cover page formatted as Inline XBRL and contained in Exhibit 101				

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

† All schedules and exhibits to the Merger Agreement have been omitted pursuant to Item 601(b)(2) of Regulation S-K. A copy of any omitted schedule and/or exhibit will be furnished to the Securities and Exchange Commission upon request.

\+ Filed herewith.

\# Portions of this exhibit have been omitted pursuant to a request for confidential treatment and the omitted portions have been filed separately with the Securities and Exchange Commission.

** Certain portions of this exhibit have been omitted because they are not material and would likely cause competitive harm to the registrant if disclosed.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended, the Registrant has duly caused this Report to be signed on its behalf by the undersigned, thereunto duly authorized**.**

ALPINE IMMUNE SCIENCES, INC.

Date: March 18, 2021	By:	/s/ *Mitchell H. Gold, M.D.*
	Name:	Mitchell H. Gold, M.D.
	Title	Executive Chairman and Chief Executive Officer

ALPINE IMMUNE SCIENCES, INC.

Date: March 18, 2021	By:	/s/ *Paul Rickey*
	Name:	Paul Rickey
	Title:	Senior Vice President and Chief Financial Officer

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Mitchell H. Gold, M.D. and Paul Rickey, and each of them, with full power of substitution and resubstitution and full power to act without the other, as his or her true and lawful attorney-in-fact and agent to act in his or her name, place and stead and to execute in the name and on behalf of each person, individually and in each capacity stated below, and to file, any and all documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing, ratifying and confirming all that said attorneys-in-fact and agents or any of them or their and his or her substitute or substitutes, may lawfully do or cause to be done by virtue thereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, this Report has been signed below by the following persons on behalf of the Registrant in the capacities and on the dates indicated.

Name	Title	Date
/s/ *Mitchell H. Gold, M.D.* **Mitchell H. Gold, M.D.**	Chief Executive Officer and Executive Chairman of the Board of Directors (Principal Executive Officer)	March 18, 2021
/s/ *Paul Rickey* **Paul Rickey**	Senior Vice President and Chief Financial Officer (Principal Accounting and Financial Officer)	March 18, 2021
/s/ *Peter Thomson, M.D.* **Peter Thompson, M.D.**	Director	March 18, 2021
/s/ *James N. Topper, M.D., Ph.D.* **James N. Topper, M.D., Ph.D.**	Director	March 18, 2021
/s/ *Jay Venkatesan, M.D.* **Jay Venkatesan, M.D.**	Director	March 18, 2021
/s/ *Robert Conway* **Robert Conway**	Director	March 18, 2021
/s/ *Natasha Hernday* **Natasha Hernday**	Director	March 18, 2021
/s/ Christopher Peetz **Christopher Peetz**	Director	March 18, 2021
/s/ Xiangmin Cui, Ph.D. **Xiangmin Cui, Ph.D.**	Director	March 18, 2021

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Alpine Immune Sciences, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Alpine Immune Sciences, Inc. as of December 31, 2020 and 2019, the related consolidated statements of operations and comprehensive income (loss), stockholder's equity and cash flows for each of the three years in the period ended December 31, 2020, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2020 and 2019, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2020, in conformity with U.S. generally accepted accounting principles.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2015.
Seattle, WA
March 18, 2021

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

	December 31, 2020	December 31, 2019
Assets		
Current assets:		
Cash and cash equivalents	$ 34,959	$ 16,123
Short-term investments	70,622	24,397
Restricted cash, current	—	132
Prepaid expenses and other current assets	1,520	1,650
Total current assets	107,101	42,302
Restricted cash, noncurrent	254	254
Property and equipment, net	1,785	1,552
Operating lease, right-of-use asset	9,401	9,985
Long-term investments	25,549	—
Total assets	$ 144,090	$ 54,093
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 582	$ 1,543
Accrued liabilities	5,777	5,285
Deferred revenue, current	31,627	1,435
Operating lease liability, current	655	—
Current portion of long-term debt	2,526	418
Total current liabilities	41,167	8,681
Deferred revenue, noncurrent	21,348	—
Operating lease liability, noncurrent	11,815	11,429
Long-term debt	7,602	4,509
Total liabilities	81,932	24,619
Commitments and contingencies		
Preferred stock, $0.001 par value per share; 10,000,000 shares authorized at December 31, 2020 and 2019; zero shares issued and outstanding at December 31, 2020 and 2019	—	—
Stockholders' equity:		
Common stock, $0.001 par value per share; 200,000,000 shares authorized at December 31, 2020 and 2019; 23,853,650 shares issued and 23,803,183 shares outstanding at December 31, 2020; 18,638,359 shares issued and 18,587,892 shares outstanding at December 31, 2019	24	19
Treasury stock, at cost; 50,467 shares at December 31, 2020 and 2019	—	—
Additional paid-in capital	177,947	117,371
Accumulated other comprehensive gain (loss)	53	10
Accumulated deficit	(115,866)	(87,926)
Total stockholders' equity	62,158	29,474
Total liabilities and stockholders' equity	$ 144,090	$ 54,093

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

ALPINE IMMUNE SCIENCES, INC.
CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE INCOME (LOSS)
(in thousands, except share and per share amounts)

	Years Ended December 31,		
	2020	2019	2018
Collaboration revenue	$ 9,335	$ 1,740	$ 705
Operating expenses:			
Research and development	27,185	35,847	28,970
General and administrative	10,899	9,467	8,362
Loss on sale of intangible asset	—	—	1,203
Total operating expenses	38,084	45,314	38,535
Loss from operations	(28,749)	(43,574)	(37,830)
Other income (expense):			
Interest expense	(775)	(338)	(319)
Interest income	245	1,248	1,296
Other income	1,333	812	—
Loss before taxes	(27,946)	(41,852)	(36,853)
Income tax benefit	6	—	366
Net loss	$ (27,940)	$ (41,852)	$ (36,487)
Comprehensive income (loss):			
Unrealized gain (loss) on investments	(15)	29	46
Unrealized gain (loss) on foreign currency translation	58	(6)	—
Comprehensive loss	$ (27,897)	$ (41,829)	$ (36,441)
Weighted-average shares used to compute basic and diluted net loss per share	20,826,466	18,358,864	13,849,470
Basic and diluted net loss per share	$ (1.34)	$ (2.28)	$ (2.63)

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

ALPINE IMMUNE SCIENCES, INC.
CONSOLIDATED STATEMENT OF STOCKHOLDERS' EQUITY
(in thousands, except share and per share amounts)

	Common Stock		Treasury		Additional Paid-in Capital	Accumulated Other Comprehensive Loss	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount	Shares	Amount				
Balance, December 31, 2017	13,831,178	$ 14	50,467	$ —	$ 88,346	$ (59)	$ (9,384)	$ 78,917
Cumulative effect of changes related to adoption of new revenue standard	—	—	—	—	—	—	(203)	(203)
Exercise of stock options	23,027	—	—	—	9	—	—	9
Stock-based compensation	—	—	—	—	2,309	—	—	2,309
Unrealized gain on investments	—	—	—	—	—	46	—	46
Net loss	—	—	—	—	—	—	(36,487)	(36,487)
Balance, December 31, 2018	13,854,205	14	50,467	—	90,664	(13)	(46,074)	44,591
Issuance of Units in Private Placement, net of offering costs	4,706,700	5	—	—	23,593	—	—	23,598
Exercise of stock options	26,987	—	—	—	13	—	—	13
Stock-based compensation	—	—	—	—	3,041	—	—	3,041
Issuance of warrants					60			60
Unrealized gain on investments	—	—	—	—	—	29	—	29
Unrealized loss on foreign currency translation	—	—	—	—	—	(6)	—	(6)
Net loss	—	—	—	—	—	—	(41,852)	(41,852)
Balance, December 31, 2019	18,587,892	19	50,467	—	117,371	10	(87,926)	29,474
Issuance of Units in private offering, net of offering costs	5,139,610	5	—	—	56,253	—	—	56,258
Issuance of warrants	—	—	—	—	60	—	—	60
Issuance of common stock under equity incentive plans	75,681	—	—	—	123	—	—	123
Stock-based compensation					4,140			4,140
Unrealized loss on investments	—	—	—	—	—	(15)	—	(15)
Unrealized gain on foreign currency translation	—	—	—	—	—	58	—	58
Net loss	—	—	—	—	—	—	(27,940)	(27,940)
Balance, December 31, 2020	23,803,183	$ 24	50,467	$ —	$ 177,947	$ 53	$ (115,866)	$ 62,158

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

ALPINE IMMUNE SCIENCES, INC.
CONSOLIDATED STATEMENTS OF CASH FLOWS
(in thousands)

	Years Ended December 31,		
	2020	2019	2018
Operating activities			
Net loss	$ (27,940)	$ (41,852)	$ (36,487)
Adjustments to reconcile net loss to net cash used in operating activities:			
Gain on sale of property and equipment	5	16	—
Loss on sale of intangible asset	—	—	1,203
Depreciation expense	578	468	388
Amortization of premium/discount on investments	103	(360)	(669)
Non-cash interest expense	261	140	169
Deferred income tax	—	—	(305)
Stock-based compensation expense	4,140	3,041	2,309
Changes in operating assets and liabilities:			
Prepaid expenses and other current assets	255	(408)	66
Right-of-use asset	592	1,553	—
Accounts payable and accrued liabilities	(491)	816	5,390
Deferred revenue	51,540	1,435	(480)
Lease liabilities	1,041	(195)	—
Net cash provided by (used in) operating activities	30,084	(35,346)	(28,416)
Investing activities			
Purchases of property and equipment	(802)	(821)	(495)
Proceeds from sale of intangible asset	—	—	250
Purchase of investments	(101,328)	(59,382)	(72,863)
Maturities of investments	29,311	75,575	105,226
Proceeds from the sale of investments	—	1,391	—
Net cash (used in) provided by investing activities	(72,819)	16,763	32,118
Financing activities			
Proceeds from sale of common stock and warrants, net of offering costs	56,258	23,598	—
Proceeds from borrowings, net of issuance costs	5,000	1,977	—
Repayment of debt	—	(1,333)	(1,000)
Proceeds from exercise of stock options	123	13	9
Net cash provided by (used in) financing activities	61,381	24,255	(991)
Effect of exchange rate on cash, cash equivalents and restricted cash	58	(6)	—
Net increase in cash and cash equivalents and restricted cash	18,704	5,666	2,711
Cash and cash equivalents and restricted cash, beginning of period	16,509	10,843	8,132
Cash and cash equivalents and restricted cash, end of period	$ 35,213	$ 16,509	$ 10,843
Supplemental Information			
Recognition of right-of-use asset	$ —	$ 11,173	$ —
Cash paid for interest	$ 490	$ 170	$ 149
Discount in connection with issuance of debt	$ 334	$ —	$ —

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

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

1. Description of Business

Alpine Immune Sciences, Inc. (the "Company", "Alpine", "we", "us", or "our"), together with its consolidated subsidiaries, is a clinical-stage biopharmaceutical company dedicated to discovering and developing innovative, protein-based immunotherapies to treat cancer and autoimmune and inflammatory diseases. Our approach includes a proprietary scientific platform that converts native immune system proteins into differentiated, multi-targeted therapeutics. We believe our strategies are capable of meaningfully modulating the human immune system and significantly improving outcomes in patients with serious diseases. We were incorporated under the laws of the State of Delaware and are headquartered in Seattle, Washington.

A novel strain of coronavirus, SARS-CoV-2 ("COVID-19"), was first reported in December 2019, and subsequently declared a global pandemic by the World Health Organization in March 2020. As a result of the COVID-19 outbreak, many companies have experienced disruptions in their operations and in markets served. We have implemented some and may take additional temporary precautionary measures intended to help ensure the well-being of our employees and minimize business disruption. We considered the impact of COVID-19 on the assumptions and estimates used and determined that there were no material adverse impacts to our results of operations and financial position at December 31, 2020. The full extent of the future impacts of the continuing COVID-19 outbreak on our operations is uncertain, and may adversely impact our business, including our clinical trials.

2. Summary of Significant Accounting Policies

Basis of Presentation and Use of Estimates

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

Principles of Consolidation

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

Segments

We operate as one operating segment and use cash flow as the primary measure to manage our business.

Cash and Cash Equivalents and Restricted Cash

We consider all highly liquid investments with an original maturity of 90 days or less at the time of purchase to be cash equivalents. Cash and cash equivalents consist of deposits with commercial banks in checking and interest-bearing accounts, and highly liquid money market funds.

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

Periodically, we maintain deposits in financial institutions in excess of government insured limits. We believe we are not exposed to significant credit risk as our deposits, which are held at financial institutions, are high credit quality securities such as money market funds, U.S. Treasury securities, and commercial paper. To date, we have not realized any losses on these deposits.

Investments

Our 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 two years. These investments are classified as available-for-sale debt securities, which are recorded at fair value based on quoted prices in active markets. We classify our investments maturing within one year of the reporting date as short-term investments.

If the estimated fair value of a debt security is below its amortized cost basis, we evaluate whether it is more likely than not that we will sell the security before its anticipated recovery in market value. If an impairment exists, the security is written down to its estimated fair value and we consider whether credit losses exist for the related securities. A credit loss exists if the present value of expected cash flows is less than the amortized cost basis of the security. Credit-related losses are recognized as an allowance for credit losses on the balance sheet with a corresponding adjustment to earnings. Unrealized gains and losses that are unrelated to credit deterioration are 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 Consolidated Statements of Operations and Comprehensive Income (Loss) using the specific-identification method.

Property and Equipment

Property and equipment are stated at cost, net of accumulated depreciation. Depreciation is recorded using the straight-line method over the estimated useful lives of the assets, generally three to 5 years, while leasehold improvements are amortized over the shorter of their estimated useful lives or the related lease term. Upon retirement or sale, the cost of assets disposed of and the related accumulated depreciation are removed from the accounts and any resulting gain or loss is credited or charged to operations. Maintenance and repairs are expensed as incurred. Major improvements are capitalized as additions to property and equipment.

Impairment of Long-lived Assets

We evaluate our long-lived tangible assets for impairment whenever events or changes in circumstances indicate that the carrying amount of such assets may not be recoverable. If the carrying value exceeds the undiscounted future cash flows estimated to result from the use and eventual disposition of the asset, we write down the asset to its estimated fair value. Impairment is assessed by comparing the undiscounted cash flows expected to be generated by the asset to its carrying value. We did not record any impairments in the years ended December 31, 2020, 2019 or 2018.

Accrued Liabilities

As part of the process of preparing our consolidated financial statements, we are required to estimate accruals for professional services and research and development expenses. This process involves reviewing contracts and vendor agreements and communicating with applicable personnel to identify services that have been performed on our behalf. We estimate the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of the actual cost. We estimate accrued liabilities as of each balance sheet date based on known facts and circumstances.

Although we do not expect our estimates to be materially different from amounts actually incurred, if our estimates of the status and timing of services performed differ from the actual status and timing of services performed, we may report amounts that are too high or too low in any particular period. To date, we have not experienced any significant adjustments to our estimates.

Leases (effective January 1, 2019)

We account for our leases under Accounting Standards Codification (“ASC”) 842, Leases. Under this guidance, arrangements meeting the definition of a lease are classified as operating or financing leases, and are recorded on the consolidated balance sheet as both a right-of-use asset and lease liability, calculated by discounting fixed lease payments over the lease term at the rate implicit in the lease or our incremental borrowing rate. As we do not know the lessor’s implicit rate, we use our incremental borrowing rate at the commencement date of the lease in determining the present value of lease payments. Lease liabilities are increased by interest and reduced by payments each period, and the right-of-use asset is amortized over the lease term. For operating leases, interest on the lease liability and the amortization of the right-of-use asset result in straight-line rent expense over the lease term. For finance leases, interest on the lease liability and the amortization of the right-of-use asset results is front-loaded expense over the lease term. Variable lease expenses are recorded when incurred.

In calculating the right-of-use asset and lease liability, we elected to combine lease and non-lease components. We exclude short-term leases having initial terms of 12 months or less from the new guidance as an accounting policy election, and

recognize rent expense on a straight-line basis over the lease term. We continue to account for leases in the prior period financial statements under ASC Topic 840.

Derivative Financial Instruments

We evaluate all of our financial instruments, including prefunded warrants and warrants to purchase common stock, to determine if such instruments are derivatives or contain features qualifying as embedded derivatives. For derivative financial instruments accounted for as liabilities, the derivative instrument is initially recorded at its fair value and is then re-valued at each reporting date, with changes in the fair value reported in the Consolidated Statements of Operations and Comprehensive Income (Loss). We use the Black-Scholes option-pricing model to value the derivative instruments at inception and subsequent valuation dates. The classification of derivative instruments, including whether such instruments should be recorded as liabilities or as equity, is re-assessed at the end of each reporting period. We do not use derivative instruments to hedge exposures to cash flow, market, or foreign currency risks.

Revenue Recognition

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

Our collaboration agreements principally contain multiple performance obligations, which may include (1) grants of, or options to obtain, intellectual property licenses; (2) research and development services; and/or (3) manufacturing or supply services. Payments typically received under these arrangements include one or more of the following: non-refundable upfront license fees, option exercise fees, payment for research and/or development efforts, amounts due upon the achievement of specified objectives, and/or royalties on future product sales. Our revenue is primarily derived from our collaboration agreements with Adaptimmune Therapeutics plc (“Adaptimmune”), AbbVie Ireland Unlimited Company (“AbbVie”), as well as previously with Kite. See further discussion of our collaboration agreements in Note 11.

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

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

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

Research and Development

Research and development costs are expensed as incurred. Research and development costs include personnel costs, clinical trials, external contract research and development expenses, raw materials, drug product manufacturing costs and

allocated overhead – including depreciation, rent and utilities. Research and development costs that are paid in advance of performance are capitalized as a prepaid expense and amortized over the service period as the services are provided.

Stock-based Compensation

Stock-based compensation is recognized for all share-based payments based on the estimated fair value as of the date of grant. The fair value of our stock options is calculated using the Black-Scholes option pricing model, which requires judgmental assumptions including volatility, risk-free interest rate and expected term. Stock-based compensation is recognized over the requisite service period of the awards, usually the vesting period, on a straight-line basis. For performance-based awards where the vesting of the options may be accelerated upon the achievement of certain milestones, vesting and the related stock-based compensation is recognized as an expense when it is probable the milestone will be met. We recognize forfeiture of awards as they occur rather than estimating the expected forfeiture rate.

Income Taxes

Income taxes are accounted for using an asset and liability approach that requires the recognition of deferred tax assets and liabilities for the expected future tax consequences of temporary differences between the consolidated financial statement and tax bases of assets and liabilities at the applicable enacted tax rates. We will establish a valuation allowance for deferred tax assets if it is more likely than not that these items will expire before we are able to realize their benefits or that future deductibility is uncertain.

We recognize the tax benefit from uncertain tax positions only if it is more likely than not that the tax position will be sustained on examination by the tax authorities, based on the technical merits of the position. The tax position is measured based on the largest benefit that has a greater than 50% likelihood of being realized upon ultimate settlement. We recognize interest and penalties related to income tax matters in income tax expense if incurred.

Comprehensive Income (Loss)

Comprehensive income (loss) is comprised of net loss and certain changes in equity excluded from net loss. For the years ended December 31, 2020, 2019, and 2018, other comprehensive loss consisted of unrealized losses on our investments and unrealized losses on foreign currency translation.

Foreign Currency Translation

Our wholly-owned Australian subsidiary uses the Australian dollar as its functional currency. All assets and liabilities related to this subsidiary are translated using period-end exchange rates and revenues and expenses are translated at average exchange rates for the year. Translation adjustments are included as components of comprehensive gain (loss) in the Consolidated Statements of Operations and Comprehensive Income (Loss).

Recently Issued Accounting Pronouncements

In December 2019, the Financial Accounting Standards Board (“FASB”) issued Accounting Standards Update (“ASU”) No. 2019-12, Simplifying the Accounting for Income Taxes. The objective of the standard is to improve areas of GAAP by removing certain exceptions permitted by ASC Topic 740, Income Taxes, and clarifying existing guidance to facilitate consistent application. The standard became effective for us on January 1, 2021. We are currently evaluating the new standard, but do not expect it to have a material impact on our financial condition, results of operations, cash flows, and financial statement disclosures.

Recently Adopted Accounting Pronouncements

In November 2018, the FASB issued ASU No. 2018-18, Collaborative Arrangements: Clarifying the Interaction between Topic 808 and Topic 606. This ASU clarifies that certain transactions between collaborative arrangement participants should be accounted for as revenue when the collaborative arrangement participant is a customer in the context of a unit of account and precludes recognizing as revenue consideration received from a collaborative arrangement participant if the participant is not a customer. We adopted this ASU effective January 1, 2020 and it did not have a material impact on our financial statements and related disclosures.

In August 2018, the FASB issued ASU No. 2018-13, Fair Value Measurement. ASU 2018-13 modifies the disclosure requirements for fair value measurements by removing, modifying, or adding certain disclosures. We adopted this ASU effective January 1, 2020 and it did not have a material impact on our financial statements or related disclosures.

In June 2016, the FASB issued ASU 2016-13, Financial Instruments: Credit Losses, as clarified in ASU 2019-04 and ASU 2019-05. The objective of the standard is to provide information about expected credit losses on financial instruments at each reporting date and to change how other-than-temporary impairments on investment securities are recorded. We adopted this ASU effective January 1, 2020 and it did not have a material impact on our financial statements and related disclosures.We will continue to monitor the impact of the COVID-19 outbreak on any potential credit losses.

3. Net Loss Per Share

Basic net loss per share is computed by dividing net loss by the weighted-average number of common shares outstanding during the period.

The net loss per share for the year ended December 31, 2020 reflects 5,139,610 shares of our common stock issued pursuant to the securities offering completed in July 2020. The net loss per share for the year ended December 31, 2019 reflects 4,706,700 shares of our common stock issued pursuant to a private placement financing completed in January 2019. The increased number of shares issued in these periods has affected the year-over-year comparability of our net loss per share calculations.

The common stock issuable upon the conversion or exercise of the following dilutive securities has been excluded from the diluted net loss per share calculation because their effect would have been anti-dilutive. Diluted net loss per share, therefore, does not differ from basic net loss per share for the periods presented.

	December 31,		
	2020	2019	2018
Warrants and prefunded warrants to purchase common stock	4,464,261	1,877,094	24,123
Options to purchase common stock	4,175,345	3,252,144	2,509,850
Total	8,639,606	5,129,238	2,533,973

4. Cash Equivalents and Investments

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

	December 31, 2020			
	Amortized Cost	Gross unrealized gains	Gross unrealized losses	Fair market value
Money market funds	$ 28,424	$ —	$ —	$ 28,424
U.S. treasury bills	18,122	8	—	18,130
Corporate debt securities and commercial paper	82,047	2	(9)	82,040
Total	$ 128,593	$ 10	$ (9)	$ 128,594
Classified as:				
Cash equivalents				$ 32,423
Short-term investments				70,622
Long-term investments				25,549
Total				$ 128,594

	December 31, 2019			
	Amortized Cost	Gross unrealized gains	Gross unrealized losses	Fair market value
Money market funds	$ 9,995	$ —	$ —	$ 9,995
U.S. treasury bills	5,019	2	—	5,021
Corporate debt securities and commercial paper	21,862	14	—	21,876
Total	$ 36,876	$ 16	$ —	$ 36,892
Classified as:				
Cash equivalents				$ 12,495
Short-term investments				24,397
Total				$ 36,892

All investments held as of December 31, 2020 and 2019 were classified as available-for-sale debt securities and had contractual maturities of less than two years. There were no realized gains and losses on these securities for the periods presented.

5. Fair Value Measurements

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

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

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

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

As of December 31, 2020 and 2019, cash of $2.5 million and $3.6 million, respectively, is excluded from the fair value table below. The following tables summarize our financial assets and liabilities measured at fair value on a recurring basis (in thousands):

Assets:	December 31, 2020			
	Level 1	Level 2	Level 3	Total
Money market funds	$ 28,424	$ —	$ —	$ 28,424
U.S. treasury bills	18,130	—	—	18,130
Corporate debt securities and commercial paper	—	82,040	—	82,040
Total	$ 46,554	$ 82,040	$ —	$ 128,594

Assets:	December 31, 2019			
	Level 1	Level 2	Level 3	Total
Money market funds	$ 9,995	$ —	$ —	$ 9,995
U.S. treasury bills	5,021	—	—	5,021
Corporate debt securities and commercial paper	—	21,876	—	21,876
Total	$ 15,016	$ 21,876	$ —	$ 36,892

Our Level 2 assets consist of commercial paper and corporate debt securities. We review trading activity and pricing for our available-for-sale securities as of the measurement date. When sufficient quoted pricing for identical securities is not available, we use market pricing and other observable market inputs for similar securities obtained from various third-party data

providers. These inputs either represent quoted prices for similar assets in active markets or have been derived from observable market data.

6. Property and Equipment

Property and equipment, net consist of the following (in thousands):

	December 31,	
	2020	2019
Laboratory equipment	$ 2,604	$ 1,838
General equipment and furniture	479	486
Computer equipment and software	211	169
Leasehold improvements	85	85
Property and equipment, at cost	3,379	2,578
Less accumulated depreciation and amortization	(1,594)	(1,026)
Property and equipment, net	$ 1,785	$ 1,552

Depreciation expense was $578,000, $468,000 and $388,000 for the years ended December 31, 2020, 2019 and 2018, respectively.

7. Loss on Sale of Intangible Asset

In February 2018, we entered into an Option License Agreement ("Option Agreement") with Laurel Venture Capital Ltd. ("Laurel"), which granted Laurel a limited license to evaluate the indefinite-life GSNOR inhibitor IPR&D asset acquired as part of the merger with Nivalis in 2017. The IPR&D represents the processes, expertise, and technology employed in the development of GSNOR inhibitors and Nivalis' lead product candidate, cavosonstat. Under the Option Agreement, we received an upfront non-refundable payment of $75,000, which was recognized as revenue in our accompanying Consolidated Statements of Operations and Comprehensive Income (Loss).

In June 2018, we entered into an Asset Purchase Agreement ("Purchase Agreement") with Laurel and completed the sale of global rights to the GSNOR asset. As consideration under the Purchase Agreement, we received a non-refundable closing payment of $250,000, which was accounted for as a purchase of our intangible asset. In June 2019, we recognized as revenue an additional payment of $425,000, related to the asset purchase. In addition, we are eligible to receive milestone payments of up to $20.0 million, in the aggregate upon satisfaction by Laurel of certain regulatory approval milestones. We will also be eligible to receive royalty payments equal to a low single-digit percentage rate of worldwide net sales of any approved products.

Upon the sale of the GSNOR assets, we derecognized the full carrying value of the intangible asset of $1.5 million on our accompanying Consolidated Balance Sheets and recognized a loss on the sale of the intangible asset of $1.2 million on the accompanying Consolidated Statements of Operations and Comprehensive Income (Loss).

8. Additional Balance Sheet Information

Prepaid expenses and other current assets consist of the following (in thousands):

	December 31,	
	2020	2019
Prepaid research and development	$ 517	$ 574
Prepaid insurance	447	301
Tenant improvement allowance receivable	84	586
Prepaid other	168	89
Other receivables	304	100
Prepaid expenses and other current assets	$ 1,520	$ 1,650

Accrued liabilities consist of the following (in thousands):

	December 31,	
	2020	2019
Research and development services	$ 2,571	$ 2,543
Employee compensation	2,619	1,761
Legal and professional fees	482	515
Accrued other	105	466
Total	$ 5,777	$ 5,285

9. Long-term Debt

In December 2016, we entered into a Loan and Security Agreement (the "Original Agreement"), with Silicon Valley Bank ("SVB"), under which we borrowed $5.0 million. The Original Agreement accrued interest at a floating per annum rate equal to the lender's prime rate minus 1.75%. The Original Agreement had an interest-only period through July 2018.

In August 2019 (the "Effective Date"), we entered into an Amended and Restated Loan and Security Agreement (the "Loan Agreement") with SVB, pursuant to which SVB agreed to extend term loans to us with an aggregate principal amount of up to $15.0 million (the "Term Loans"). Borrowings under the Loan Agreement consisted of up to three separate tranches. The initial tranche of $5.0 million was funded in August 2019, $3.0 million of which was used to repay amounts owing under our Original Agreement. In March 2020, the second tranche of $5.0 million was funded to us. We did not draw down the final tranche of $5.0 million, which expired on July 31, 2020. We intend to use the debt proceeds for working capital and other general corporate purposes, including the advancement of our development programs.

The Term Loans accrue interest at a floating per annum rate of 0.25% above the prime rate, subject to a floor of 5.75%, which interest is payable monthly commencing in September 2019. Upon the occurrence and during the continuance of an event of default, a default interest rate will apply that is 4.0% above the otherwise applicable interest rate. The Term Loans were interest only until September 30, 2020, however, under the Loan Agreement our interest only period automatically extends to June 30, 2021 if we were to receive aggregate new capital of at least $40.0 million no later than June 30, 2020. We met this milestone in June 2020 in conjunction with the execution of the AbbVie agreement, discussed in detail in Note 11. As a result of the interest only extension, the Term Loans will be payable in 25 equal monthly installments of principal plus interest, with the final installment due and payable on July 1, 2023.

We may prepay all of the Term Loans subject to a prepayment fee equal to $75,000, which represents the deferred portion of the final payment due under the Original Agreement, plus the outstanding principal balance under the Term Loans at the time of such prepayment multiplied by a prepayment fee of 2.0% in the first year, 1.0% in the second year, and 0% in the third year and thereafter. Additionally, a final payment in the amount of 5.5% of the funded Term Loans is payable to SVB on the date on which the Term Loans are prepaid, paid or become due and payable in full. The final payment fees are recorded in long-term debt with an offsetting reduction to debt discount on our accompanying Consolidated Balance Sheets.

The Loan Agreement contains customary representations and warranties, events of default and affirmative and negative covenants, including, among others, covenants that limit or restrict our ability to, among other things, incur additional indebtedness, grant liens, merge or consolidate, make acquisitions, pay dividends or other distributions or repurchase equity, make investments, dispose of assets, engage in any new lines of business, and enter into certain transactions with affiliates, in each case subject to certain exceptions. 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. We were in compliance with our covenants as of December 31, 2020. As such, as of December 31, 2020, the classification of the loan is split between current and noncurrent based on the timing of payment obligations. As security for its obligations under the Loan Agreement, we granted SVB a first priority security interest on substantially all of our assets, except intellectual property, and subject to certain other exceptions.

In connection with the Loan Agreement, we issued a warrant to SVB to purchase up to 52,083 shares of our common stock at a price of $4.32 per share, 17,361 shares of which became exercisable in August 2019 after we drew down the initial tranche. In March 2020, after we drew down the second tranche of our Term Loan, an additional 17,361 shares became exercisable. The remaining warrants did not vest and expired on July 31, 2020, upon the expiration of the third tranche of our Term Loan. The fair value of the warrants on the date of issuance for the initial tranche and second tranche was $60,000 and $60,000, respectively, determined using the Black-Scholes option-pricing model, and was recorded as a component of equity and as a debt discount on our accompanying Consolidated Balance Sheets. In connection with Original Agreement, SVB also holds 7,069 fully vested common stock warrants at an exercise price of $12.38 per share.

The Term Loan was accounted for as a debt modification in a non-troubled debt restructuring, rather than a debt extinguishment, based on a comparison of the present value of the cash flows under the terms of the debt immediately before and after the Effective Date of the Term Loan, which resulted in a change of less than 10%. As a result, the remaining unamortized debt discount recorded in connection with the Original Agreement will be amortized to interest expense over the repayment term of Loan Agreement. In connection with the initial and second tranches of the Loan Agreement, we recorded a total debt discount of $812,000, which is being amortized to interest expense using the effective interest method over the repayment term of the loan. Non-cash interest expense associated with the amortization of the discount was $261,000, $140,000, and $169,000, for years ended December 31, 2020, 2019, and 2018, respectively. The unamortized discount was $497,000 as of December 31, 2020.

Scheduled principal payments on our outstanding debt as of December 31, 2020 under our Loan Agreement, excluding final fee amounts, are as follows (in thousands):

Year Ending December 31,	Total
2021	$ 2,400
2022	4,800
2023	2,800
Total future principal payments	$ 10,000

10. Commitments and Contingencies

Operating Leases

We leased office and laboratory space located at 201 Elliott Avenue West, in Seattle, Washington, under an agreement classified as an operating lease that expired on December 31, 2019. In May 2017, as required by the terms of the lease, we entered into a line of credit to establish collateral to support the security deposit in an amount of $132,000, which was recorded as current restricted cash in the accompanying Consolidated Balance Sheets for the year ended December 31, 2019.

In March 2019, we entered into a lease for office and laboratory space located at 188 East Blaine Street, Seattle, Washington. The term of the lease is 10.8 years with one option to extend the term by 5.0 years. Our option to extend the rental term of our lease was not considered reasonably certain as of December 31, 2020. The lease term commenced in June 2019. The “Rent Commencement Date” began in March 2020, nine months after the commencement date. The annual base rent under the lease is $1.7 million for the first year and will increase by 3.0% each year thereafter. We were not required to pay base rent from the Rent Commencement Date through November 2020, the last day of the ninth month following the Rent Commencement Date. We received a tenant improvement allowance of $5.4 million, which is included in our base rent, and a maximum additional tenant improvement allowance of $1.8 million, which will result in additional rent amortized over the term of the lease at an annual rate of 8.0%. The lease also requires us to pay additional amounts for operating and maintenance expenses. In March 2019, in connection with the lease, we provided a $254,000 letter of credit as a security deposit, which is recorded as noncurrent restricted cash in our accompanying Consolidated Balance Sheets.

As of December 31, 2020, our operating lease right-of-use assets and operating lease liability associated with our leases were $9.4 million and $12.5 million, respectively. Supplemental operating lease information for the year ended December 31, 2020 was as follows (in thousands):

	For the Year Ended December 31,	
	2020	2019
Operating lease cost	$ 1,872	$ 1,905
Variable lease cost	475	370
Total lease cost	$ 2,347	$ 2,275
Other information:		
Cash paid for amounts included in the measurement of lease liabilities	$ 213	$ 837
Right-of-use assets exchanged for new operating lease liabilities	$ —	$ 11,173
Weighted-average remaining lease term (years)	9.2	10.2
Weighted-average discount rate	10.7 %	10.7 %

Variable lease costs represent our share of the landlord's operating expenses. We do not act as a lessor or have any leases classified as financing leases. Maturities of our operating lease liabilities as of December 31, 2020 are as follows (in thousands):

	Minimum Lease Payments
2021	$ 1,958
2022	2,009
2023	2,062
2024	2,116
2025	2,172
Thereafter	9,681
Total future minimum lease payments	19,998
Less: imputed interest	(7,528)
Operating lease liabilities	$ 12,470

Rent expense, which is recorded on a straight-line basis, was $811,000 for the year ended December 31, 2018.

Contingencies

Certain credits received related to our research and development expenditures and recorded within other income in our accompanying Consolidated Statements of Operations and Comprehensive Income (Loss) are subject to review by foreign taxing authorities. It is reasonably possible we may incur losses upon the completion of these reviews ranging from $0 to $1.8 million, which we could be required to repay to certain tax authorities.

11. Collaboration and License Agreement

AbbVie

In June 2020, we entered into an option and license agreement with AbbVie (the "AbbVie Agreement") for the development of ALPN-101. The AbbVie Agreement grants AbbVie the exclusive option to purchase an exclusive worldwide license to ALPN-101 (the "License Option"). The License Option is exercisable by AbbVie at any time and will expire 90 days from the achievement of certain development milestones. If AbbVie exercises the License Option, AbbVie will take over the future development and commercialization. Prior to the exercise of the License Option, we will perform research and development services, including conducting a Phase 2 study in systemic lupus erythematosus, based on an agreed-upon development plan (the "Development Plan"). We will be fully responsible for all costs incurred to conduct the activities under the Development Plan, provided that, AbbVie may be responsible for increased costs under the Development Plan in connection with certain material amendments proposed by AbbVie. We will also be solely responsible, at our sole cost and expense, for manufacturing and regulatory filings for ALPN-101 necessary to complete activities under the Development Plan.

In June 2020, in connection with the execution of the AbbVie Agreement, AbbVie paid us a nonrefundable upfront payment of $60.0 million. Prior to the exercise of the License Option, AbbVie has agreed to make cash payments upon our achievement of certain predefined pre-option development milestones (the "Alpine Development Milestones") up to an aggregate amount of $75.0 million. If AbbVie exercises the License Option, they will pay a one-time cash payment of $75.0 million. Following the exercise of the License Option, AbbVie has also agreed to make aggregate cash payments of up to $205.0 million upon AbbVie's achievement of certain development and commercial milestones and additional aggregate cash

payments of up to $450.0 million upon AbbVie's achievement of certain sales-based cash milestones, collectively referred to as (the "AbbVie Milestones"). Subsequent to commercialization, we are also eligible to receive high single-digit to low double-digit percentage royalties on worldwide net sales of licensed products.

For revenue recognition purposes, we determined that our contractual promises in the AbbVie Agreement are not distinct and are interdependent with our performance obligation to provide research and development services under the Development Plan. Thus, all contractual promises related to the upfront payment and Alpine's Development Milestones were combined into a single performance obligation. We determined the Alpine Development Milestone payments are probable of significant revenue reversal as the achievement is highly dependent on factors outside our control. Therefore, these milestone payments are fully constrained and were not included in the transaction price. We will re-evaluate the transaction price each reporting period and update as uncertain events are resolved or other changes in circumstances occur.

The License Option and the AbbVie Milestones were not determined to be performance obligations at the inception of the contract as they did not represent material rights. If exercised, the License Option and AbbVie Milestones will be accounted for as a separate contract and will be recognized as revenue if and when triggered. Any consideration related to sales-based royalties and profit-sharing payments will be recognized when the related sales occur.

We use a cost-based input method to measure progress toward completion of the performance obligation and to calculate the corresponding revenue to recognize each period. In applying the cost-based input, we use actual costs incurred relative to budgeted costs for the combined performance obligation. These costs consist primarily of internal personnel efforts and third-party contract costs relative to the level of patient enrollment in the study. Revenue will be recognized based on the level of costs incurred relative to the total budgeted costs for the performance obligation. A cost-based input method of revenue recognition requires management to make estimates of costs to complete our performance obligation. In making such estimates, significant judgment is required to evaluate assumptions related to cost estimates. The cumulative effect of revisions to estimated costs to complete our performance obligation will be recorded in the period in which changes are identified and amounts can be reasonably estimated. A significant change in these assumptions and estimates could have a material impact on the timing and amount of revenue recognized in future periods.

We recognized revenue from the AbbVie Agreement of $7.0 million for the year ended December 31, 2020. As of December 31, 2020 the remaining balance of the transaction price is $53.0 million and is recorded as current and noncurrent deferred revenue on our accompanying Consolidated Balance Sheets. We expect to recognize the remaining deferred revenue over the remainder of our Development Plan, which began in June 2020 and ends upon the later of the exercise or expiration of the option.

Adaptimmune

In May 2019, we entered into a collaboration and licensing agreement with Adaptimmune (the "Adaptimmune Agreement ") to develop next-generation SPEAR T cell products. Under the Adaptimmune Agreement, we are to perform certain research services and grant Adaptimmune an exclusive license to programs from our secreted immunomodulatory protein ("SIP") and transmembrane immunomodulatory protein ("TIP") technologies. In June 2019, under the terms of the Adaptimmune Agreement, we received an upfront license payment of $2.0 million, and through December 31, 2020 we have received an additional $1.6 million in research support payments to fund ongoing programs. These payments were recorded as deferred revenue upon receipt and were recognized to revenue based on employee hours contributed to each performance obligation. In the fourth quarter of 2020, based on the completion of our initial research and development efforts in connection with our performance obligations, we recognized the remaining balance in deferred revenue associated with Adaptimmune on our accompanying Consolidated Balance Sheets. Under the Adaptimmune Agreement, we have recognized revenue of $2.3 million and $1.3 million for the years ended December 31, 2020 and 2019, respectively. In addition, we are eligible for additional research support payments, one-time payments and downstream development and commercialization milestones of up to $288.0 million, if all pre-specified milestones for each program are achieved. We are also eligible to receive low-single digit royalties on worldwide net sales of the applicable products.

Kite

In October 2015, we entered into a collaboration and licensing agreement (the "Kite Collaboration Agreement") with Kite, providing Kite with access to two TIP programs for use in Kite's engineered cellular therapy program. In May 2019, Kite provided us notice of termination of the Kite Collaboration Agreement following the expiration of the research term. Upon termination, the confidentiality and indemnity obligations of the parties survived and the licenses granted to Kite under the Kite Collaboration Agreement terminated. Pursuant to the terms of the Kite Collaboration Agreement, the termination was effective in June 2019, thirty days after the effectiveness of Kite's notice.

Per the terms of the Kite Collaboration Agreement, we recorded no revenue for the years ended December 31, 2020 and 2019, and $630,000 for the year ended December 31, 2018. On January 1, 2018, we adopted the new revenue standard using the modified retrospective method. Our Kite Collaboration Agreement was the only contract that was impacted by the adoption of the new revenue standard. The cumulative effect adjustment recorded upon the adoption of the new revenue standard resulted in a $203,000 decrease to the opening balance of retained earnings and a $203,000 increase to deferred revenue as of January 1, 2018. As a result, we recognized $203,000 in higher revenue for the year ended December 31, 2018, as compared to what would have been recorded under previous accounting guidance.

12. Stockholders' Equity

Common Stock

Shares of common stock reserved for future issuance were as follows:

	December 31,	
	2020	2019
Shares to be issued upon exercise of outstanding stock options	4,175,345	3,252,144
Shares to be issued upon conversion of common stock warrants and prefunded warrants	4,464,261	1,877,094
Shares available for future stock grants	887,901	269,959
Shares to be issued under employee stock purchase plan	45,211	45,211
Shares of common stock reserved for future issuance	9,572,718	5,444,408

Securities Offerings

In July 2020, we entered into a securities purchase agreement (the "Securities Purchase Agreement") for a private placement with a select group of institutional investors, pursuant to which we sold 5,139,610 units (the "Common Units") and 790,710 units (the "Prefunded Warrant Units"), for an aggregate purchase price of $60.0 million. Each Common Unit consists of one share of our common stock plus a warrant to purchase 0.3 shares of common stock (the "Common Stock Warrants"), and each Prefunded Warrant Unit consists of one prefunded warrant to purchase one share of common stock (the "Prefunded Warrants") plus 0.3 Common Stock Warrants. The Prefunded Warrant Units and the Common Units are collectively referred to as the "Units" and each Unit has a purchase price of $10.1175. Pursuant to the terms of the Securities Purchase Agreement, we issued warrants to purchase 1,779,096 shares of common stock with an exercise price of $12.74 and a term of 3.5 years. Additionally, we issued 790,710 Prefunded Warrants, which became fully exercisable upon the closing date and have an exercise price of $0.001 per share. We incurred $3.7 million in financing costs associated with the Securities Purchase Agreement, which was netted against the proceeds within additional-paid-in-capital on our accompanying Consolidated Balance Sheets.

In January 2019, we entered into a securities purchase agreement (the "Purchase Agreement") with a limited number of accredited investors, pursuant to which we sold 4,706,700 units (the "2019 Units") for an aggregate purchase price of $25.3 million in a private placement (the "Private Placement"). Each 2019 Unit has a purchase price of $5.37 and consists of one share of our common stock and a warrant to purchase 0.39 shares of common stock. Pursuant to the terms of the Purchase Agreement, we issued 4,706,700 shares of common stock and warrants to purchase an aggregate of 1,835,610 shares of common stock. The warrants have an exercise price of $12.74 and have a term of five years. We incurred $1.7 million in financing costs associated with the Purchase Agreement, which was netted against the proceeds within additional-paid-in-capital on our accompanying Consolidated Balance Sheets.

The issuance of the securities sold under the Securities Purchase Agreement and the Purchase Agreement have not been registered under the Securities Act of 1933, as amended, or state securities laws and may not be offered or sold in the United States absent registration with the SEC or an applicable exemption from such registration requirements. We filed registration statements for the Securities Purchase Agreement and the Purchase Agreement with the SEC, which were declared effective by

the SEC in August 2018 and April 2019, respectively, which cover the resale of the shares of common stock issuable in connection with the private placements and upon exercise of the warrants.

In June 2018, we entered into an equity distribution agreement, ("Equity Distribution Agreement"), with Piper Jaffray & Co., ("Piper Jaffray"), pursuant to which we may sell shares of our common stock through an "at the market" equity offering program for up to $50.0 million, in gross cash proceeds. The Equity Distribution Agreement was terminated by us upon written notice to Piper Jaffray in March 2021. As of December 31, 2020, no sales under our Equity Distribution Agreement have occurred.

Common Stock Warrants

We have issued warrants in connection with our SVB loans, to certain non-employee professional advisers, and in connection with our Private Placement. We also assumed warrants in connection with the merger. No warrants were exercised or forfeited during the year ended December 31, 2020. Excluding the prefunded warrants issued in connection with the Securities Purchase Agreement discussed above, the table below summarizes our warrant activity:

	Warrants Outstanding	Weighted-average Exercise Price	Weighted-average Remaining Contract Term (in years)
Outstanding at December 31, 2019	1,877,094	$ 12.82	4.11
Granted	1,796,457	$ 12.66	3.13
Outstanding at December 31, 2020	3,673,551	$ 12.74	3.12
Exercisable at December 31, 2020	3,672,776	$ 12.74	3.12

Equity Incentive Plans

In June 2018 our stockholders approved, the 2018 Equity Incentive Plan ("2018 Plan"). Upon adoption, we ceased granting stock awards under the Nivalis Therapeutics, Inc. 2015 Equity Incentive Plan (the "2015 EIP") and the Amended and Restated 2015 Stock Plan (the "2015 Plan"), collectively, the "Legacy Plans". All shares of common stock subject to awards under the Legacy Plans that expire or terminate without having been exercised in full, or are forfeited to or repurchased by the company, will be added to the 2018 Plan, up to a maximum of 1,972,784 shares. In June 2020, in conjunction with our annual meeting of stockholders, our stockholders approved an additional increase of 743,515 shares authorized under our 2018 Plan.

Under our 2018 Plan we may issue stock options, stock appreciation rights, restricted stock, restricted stock units ("RSUs") or performance shares. As of December 31, 2020 we have only issued stock options and RSUs. Our 2018 Plan provides for an annual increase in the number of shares reserved for insurance equal to the lesser of (1) 5% of the number of shares of common stock outstanding as of the last day of the preceding calendar year or (2) 1,500,000. However, our board of directors may act prior to January 1 of a given year to provide that there will be no January 1 increase for such year or that the increase for such year will be a lesser number of shares. On January 1, 2021, a total of 1,190,159 additional shares were automatically added to the shares authorized under the 2018 Plan.

In July 2017, in connection with the merger, we assumed Nivalis' Employee Stock Purchase Plan (the "ESPP") and the 2015 EIP. Upon assumption of the ESPP, there were 45,211 shares available for issuance under the ESPP. As of December 31, 2020, we have not activated the ESPP.

Stock options granted under our equity plans generally vest within four years and vested options are exercisable from the grant date until ten years after the date of grant. Vesting of certain employee options may be accelerated in the event of a change in control of the Company. We grant stock options to employees with exercise prices equal to the fair value of our common stock on the date of grant. The term of incentive stock options may not exceed ten years from the date of grant. We utilize newly issued shares to satisfy option exercises.

As of December 31, 2020, a total of 5,426,703 shares of common stock were authorized for issuance under our 2018 Plan, 2015 Plan and 2015 EIP. A summary of stock option activity under our plans is presented below:

	Options Outstanding	Weighted-average Exercise Price	Weighted-average Remaining Contract Term (in years)	Aggregate Intrinsic Value (in thousands)
Outstanding at December 31, 2019	3,252,144	$ 5.91		
Granted	1,312,950	$ 4.55		
Exercised	(26,641)	$ 4.65		
Forfeited	(208,108)	$ 7.57		
Expired	(155,000)	$ 8.84		
Outstanding at December 31, 2020	4,175,345	$ 5.30	7.69	$ 30,883
Vested and expected to vest after December 31, 2020	4,035,345	$ 5.19	7.62	$ 30,278
Exercisable at December 31, 2020	2,208,114	$ 5.07	6.79	$ 17,011

As of December 31, 2020, there was $5.7 million of unrecognized stock-based compensation expense related to approximately 2.0 million nonvested awards that are expected to be recognized over a weighted-average period of 2.4 years. The aggregate intrinsic value of stock options exercised during the years ended December 31, 2020, 2019 and 2018 was $104,000, $155,000 and $214,000, respectively. We utilize newly issued shares to satisfy option exercises. The total fair value of options vested during the years ended December 31, 2020, 2019 and 2018 was $4.2 million, $3.0 million and $1.8 million, respectively.

In January 2020, we issued 156,326 RSUs at a grant date fair value of $3.23 per share to certain employees in lieu of cash incentive compensation. Half of the outstanding shares underlying each RSU vested on June 30, 2020, and the remaining half vested on December 31, 2020. For the year ended December 31, 2020, the fair value of RSUs vesting and the aggregate intrinsic value of RSUs released were $461,000 and $1.6 million, respectively.

Stock-Based Compensation Expense

The fair value of RSUs is equal to the closing stock price on the date of grant. We use the Black-Scholes option pricing model to estimate the fair value of stock options at the grant date. The Black-Scholes option pricing model requires us to make certain estimates and assumptions, including assumptions related to the expected price volatility of our stock, the period during which the options will be outstanding, the rate of return on risk-free investments, and the expected dividend yield of our stock. The fair values of stock options granted to employees were calculated using the following assumptions:

	Years Ended December 31,		
	2020	2019	2018
Weighted-average estimated fair value at grant	$3.03	$4.14	$5.43
Risk-free interest rate (1)	38% - 1.68%	1.42% - 2.63%	2.27% - 3.07%
Expected term of options (in years) (2)	5.27 - 6.90	5.27 – 6.08	5.50 – 7.00
Expected stock price volatility (3)	73% - 82%	70% - 77%	70% - 77%
Expected dividend yield (4)	—%	—%	—%

(1) The risk-free interest rate assumption was based on zero-coupon U.S. Treasury instruments that had terms consistent with the expected term of our stock option grants.

(2) We used the “simplified method” for options to determine the expected term of stock options granted, since we do not have sufficient historical exercise data to provide a reasonable basis upon which to estimate expected term due to the limited time our shares have been publicly traded. Under this approach, the weighted-average expected life is presumed to be the average of the vesting term and the contractual term of the option.

(3) Volatility is a measure of the amount by which a financial variable, such as share price, has fluctuated or is expected to fluctuate during a period. We analyzed the stock price volatility of companies at a similar stage of development to estimate expected volatility of our stock price.

(4) We have never declared or paid any cash dividends and do not presently plan to pay cash dividends in the foreseeable future.

Stock-based compensation expense is classified in the Consolidated Statements of Operations and Comprehensive Income (Loss) as follows (in thousands):

	Years Ended December 31,		
	2020	2019	2018
Employee:			
Research and development	$ 2,145	$ 1,608	$ 890
General and administrative	1,955	1,359	1,385
Non-Employee:			
Research and development	34	68	16
General and administrative	6	6	18
Total stock-based compensation expense	$ 4,140	$ 3,041	$ 2,309

13. Income Taxes

On December 22, 2017, H.R.1, commonly referred to as the Tax Cuts and Jobs Act (TCJA) (“Tax Act”) was enacted into law in the United States of America. We continue to consider the impact of the Base Erosion and Anti-Abuse Tax ("BEAT"), Global Intangible Low-Taxed Income (“GILTI”), the deduction for foreign derived intangible income and other provisions of the Tax Act on an on-going basis. We have elected to treat taxes due on future U.S. inclusions in taxable income under the GILTI provision as a current-period expense when incurred. As such, expected future GILTI inclusions have not been factored into the measurement of our deferred taxes.

Our income (loss) before taxes is derived from domestic (United States) and foreign (Australian) sources as follows (in thousands):

	Years Ended December 31,	
	2020	2019
Domestic	$ (28,356)	$ (38,234)
Foreign	410	(3,618)
Total	$ (27,946)	$ (41,852)

The provision for income taxes is composed of the following (in thousands):

	Years Ended December 31,	
	2020	2019
Current:		
U.S. - Federal	$ —	$ —
U.S. - State	(6)	—
Foreign	—	—
Total current	(6)	—
Deferred:		
U.S. - Federal	—	—
U.S. - State	—	—
Foreign	—	—
Total deferred	—	—
Total income tax benefit	$ (6)	$ —

The effective tax rate of the provision for income taxes differs from the federal statutory rate as follows:

	Years Ended December 31,	
	2020	2019
U.S. Statutory rate	21.0 %	21.0 %
Effect of:		
Permanent differences	0.1 %	(0.1)%
Federal research and development credit	2.6 %	1.1 %
Change in valuation allowance	(20.7)%	(19.8)%
Stock-based compensation	(2.8)%	(0.5)%
Foreign rate differential	(0.1)%	0.6 %
Other	(0.1)%	(2.3)%
Effective income tax rate	— %	— %

We recorded a tax benefit of $6,000 for the year ended December 31, 2020 and no tax expense for the year ended December 31, 2019, representing an effective tax rates of 0.0% for the years ended December 31, 2020 and 2019. The difference between the U.S. federal statutory tax rates of 21% and our effective tax rate in all periods is primarily due to a full valuation allowance related to our deferred tax assets and the generation and consumption of federal R&D tax credits.

Deferred income taxes reflect the net tax effects of temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. The following table represents the significant components of our deferred tax assets and liabilities for the periods presented (in thousands):

	December 31,	
	2020	2019
Deferred tax assets:		
Net operating loss	$ 21,992	$ 17,193
Research and development credits	4,044	3,182
Intangible asset basis	24	35
Lease liability	2,619	2,400
Stock based compensation	1,337	1,586
Other	72	1
Gross deferred tax assets	30,088	24,397
Valuation allowance	(27,851)	(22,040)
Total deferred tax assets, net of valuation allowance	2,237	2,357
Deferred tax liabilities:		
Prepaid expenses	(125)	(75)
Fixed asset basis	(137)	(185)
Right-of-use asset basis	(1,975)	(2,097)
Total deferred tax liability	(2,237)	(2,357)
Net deferred tax assets and liabilities	$ —	$ —

A valuation allowance is provided for deferred tax assets where the recoverability of the assets is uncertain. The determination to provide a valuation allowance is dependent upon the assessment of whether it is more likely than not that sufficient taxable income will be generated to utilize the deferred tax assets. Based on the weight of the available evidence, which includes our historical operating losses, uncertainty of future taxable income, and the accumulated deficit, we provided a full valuation allowance against our deferred tax assets. The valuation allowance increased by $5.8 million and $8.3 million during the year ended December 31, 2020 and 2019, respectively.

We have net operating loss (“NOL”) carryforwards as follows (in thousands):

	December 31,	
	2020	2019
Federal (before January 1, 2018)	$ 11,094	$ 11,094
Federal (after January 1, 2018)	$ 91,868	$ 67,500
State	$ 6,433	$ 6,433
Foreign	$ —	$ 787

Federal NOL carryforwards created before January 1, 2018 begin to expire in 2037. Federal NOL carryforwards created after January 1, 2018 carryforward indefinitely. State NOL carryforwards begin to expire in 2038. Foreign NOLs carryforward indefinitely.

We have net research and development tax credit carryforwards as follows (in thousands):

	December 31,	
	2020	2019
Federal	$ 5,063	$ 3,986

Federal research and development tax credit carryforwards begin to expire in 2035.

Current tax laws impose substantial restrictions on the utilization of R&D credit and NOL 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 NOLs and R&D tax credit carryforwards. Under Internal Revenue Code Section 382 and 383, the 2017 merger with Nivalis is likely considered an ownership change with respect to the potential limitation of the Nivalis federal tax credits and NOLs. As such, it is likely that any future utilization of Nivalis federal tax credits and NOLs is substantially limited. Therefore, as of December 31, 2018, all Nivalis tax credit and NOL carryforwards have been reduced to zero.

We account for uncertainty in income taxes in accordance with ASC 740. Tax positions are evaluated in a two-step process, whereby we first determine whether it is more likely than not that a tax position will be sustained upon examination by the tax authority, including resolutions of any related appeals or litigation processes, based on technical merit. If a tax position meets the more-likely-than-not recognition threshold it is then measured to determine the amount of benefit to recognize in the financial statements. The tax position is measured as the largest amount of benefit that is greater than 50% likely of being realized upon ultimate settlement.

The following table summarized the activity related to unrecognized tax benefits (in thousands):

	December 31,	
	2020	2019
Unrecognized benefits – beginning of year	$ 775	$ 469
Gross increases (decreases) – prior year tax positions	(7)	—
Gross increases – current year tax positions	222	306
Unrecognized benefit – end of year	$ 990	$ 775

All of the unrecognized tax benefits as of December 31, 2020 are accounted for as a reduction in our deferred tax assets. Due to our valuation allowance, none of the $990,000 of unrecognized tax benefits would affect our effective tax rate, if recognized. We do not believe it is reasonably possible that our unrecognized tax benefits will significantly change in the next twelve months.

We recognize interest and penalties related to unrecognized tax benefits as income tax expense. There were no accrued interest or penalties related to unrecognized tax benefits for 2020 and 2019.

We do not expect any significant change in our unrecognized tax benefits during the next twelve months.

Our material income tax jurisdictions are the United States (federal), California (state), and Australia (foreign). We are subject to audit for tax years 2012 and forward for federal purposes, 2015 and forward for California purposes, and 2019 and forward for foreign purposes.

14. Related Party Transactions

In January 2019, in connection with our Purchase Agreement we sold an aggregate of 935,753 shares of common stock and issued warrants to purchase an aggregate of 364,943 shares of common stock for gross proceeds of approximately $5.0 million to certain of our 5% stockholders. See Part III, Item 13 of this Form 10-K for additional information.

None of the purchasers in the July 2020 private placement was a greater than 5% holder of our outstanding capital stock prior to the July 2020 private placement.

15. 401(k) Retirement Plan

We have adopted a 401(k) plan. All employees are eligible to participate, provided they meet the requirements of the plan. To date, we have not matched employee contributions to the plan.

AMENDED AND RESTATED BYLAWS OF ALPINE IMMUNE SCIENCES, INC.

ARTICLE I - CORPORATE OFFICES

1.1 REGISTERED OFFICE.

The registered office of Alpine Immune Sciences, Inc. (the "Corporation") shall be fixed in the Corporation's certificate of incorporation, as the same may be amended from time to time (the "certificate of incorporation").

1.2 OTHER OFFICES.

The Corporation's board of directors (the "Board") may at any time establish other offices at any place or places where the Corporation is qualified to do business.

ARTICLE II - MEETINGS OF STOCKHOLDERS

2.1 PLACE OF MEETINGS.

Meetings of stockholders shall be held at any place, within or outside the State of Delaware, designated by the Board. The Board may, in its sole discretion, determine that a meeting of stockholders shall not be held at any place, but may instead be held solely by means of remote communication as authorized by Section 211(a)(2) of the General Corporation Law of the State of Delaware (the "DGCL"). In the absence of any such designation or determination, stockholders' meetings shall be held at the Corporation's principal executive office.

2.2 ANNUAL MEETING.

The Board shall designate the date and time of the annual meeting. At the annual meeting, directors shall be elected and other proper business properly brought before the meeting in accordance with Section 2.4 may be transacted.

2.3 SPECIAL MEETING.

A special meeting of the stockholders may be called at any time by the Secretary of the Corporation at the direction of the Board, pursuant to a resolution adopted by a majority of the entire Board, but such special meetings may not be called by any other person or persons.

No business may be transacted at such special meeting other than the business specified in such notice to stockholders. Nothing contained in this paragraph of this Section 2.3 shall be construed as limiting, fixing, or affecting the time when a meeting of stockholders called by action of the Board may be held.

2.4 ADVANCE NOTICE PROCEDURES FOR BUSINESS BROUGHT BEFORE A MEETING.

(i) At an annual meeting of the stockholders, only such business shall be conducted as shall have been properly brought before the meeting. To be properly brought before an annual meeting, business must be (a) specified in a notice of meeting given by or at the direction of the Board, (b) if not specified in a notice of meeting, otherwise brought before the meeting by or at the direction of the Board or the chairperson of the Board, or (c) otherwise properly brought before the meeting by a stockholder present in person who (A)(1) was a beneficial owner of shares of the Corporation both at the time of giving the notice provided for in this Section 2.4 and at the time of the meeting, (2) is entitled to vote at the meeting and (3) has complied with this Section 2.4 in all applicable respects, or (B) properly made such proposal in accordance with Rule 14a-8 under the Securities Exchange Act of

1934, as amended, and the rules and regulations promulgated thereunder (as so amended and inclusive of such rules and regulations, the "Exchange Act"). The foregoing clause (c) shall be the exclusive means for a stockholder to propose business to be brought before an annual meeting of the stockholders. The only matters that may be brought before a special meeting are the matters specified in the notice of meeting given by or at the direction of the person calling the meeting pursuant to Section 2.3 of these bylaws, and stockholders shall not be permitted to propose business to be brought before a special meeting of the stockholders. For purposes of this Section 2.4, "present in person" shall mean that the stockholder proposing that the business be brought before the annual meeting of the Corporation, or, if the proposing stockholder is not an individual, a qualified representative of such proposing stockholder, appear at such annual meeting. A "qualified representative" of such proposing stockholder shall be, if such proposing stockholder is (x) a general or limited partnership, any general partner or person who functions as a general partner of the general or limited partnership or who controls the general or limited partnership, (y) a corporation or a limited liability company, any officer or person who functions as an officer of the corporation or limited liability company or any officer, director, general partner or person who functions as an officer, director or general partner of any entity ultimately in control of the corporation or limited liability company or (z) a trust, any trustee of such trust. Stockholders seeking to nominate persons for election to the Board must comply with Section 2.5 of these bylaws, and this Section 2.4 shall not be applicable to nominations except as expressly provided in Section 2.5 of these bylaws.

(ii) Without qualification, for business to be properly brought before an annual meeting by a stockholder, the stockholder must (a) provide Timely Notice (as defined below) thereof in writing and in proper form to the Secretary of the Corporation and (b) provide any updates or supplements to such notice at the times and in the forms required by this Section 2.4. To be timely, a stockholder's notice must be delivered to, or mailed and received at, the principal executive offices of the Corporation not less than ninety (90) days nor more than one hundred twenty (120) days prior to the one-year anniversary of the preceding year's annual meeting; *provided, however*, that if the date of the annual meeting is more than thirty (30) days before or more than sixty (60) days after such anniversary date, notice by the stockholder to be timely must be so delivered, or mailed and received, not later than the ninetieth (90th) day prior to such annual meeting or, if later, the tenth (10th) day following the day on which public disclosure of the date of such annual meeting was first made (such notice within such time periods, "Timely Notice"). In no event shall any adjournment or postponement of an annual meeting or the announcement thereof commence a new time period for the giving of Timely Notice as described above.

(iii) To be in proper form for purposes of this Section 2.4, a stockholder's notice to the Secretary shall set forth:

(a) As to each Proposing Person (as defined below), (A) the name and address of such Proposing Person (including, if applicable, the name and address that appear on the Corporation's books and records); and (B) the class or series and number of shares of the Corporation that are, directly or indirectly, owned of record or beneficially owned (within the meaning of Rule 13d-3 under the Exchange Act) by such Proposing Person, except that such Proposing Person shall in all events be deemed to beneficially own any shares of any class or series of the Corporation as to which such Proposing Person has a right to acquire beneficial ownership at any time in the future (the disclosures to be made pursuant to the foregoing clauses (A) and (B) are referred to as "Stockholder Information");

(b) As to each Proposing Person, (A) the full notional amount of any securities that, directly or indirectly, underlie any "derivative security" (as such term is defined in Rule 16a-1(c) under the Exchange Act) that constitutes a "call equivalent position" (as such term is defined in Rule 16a-1(b) under the Exchange Act) ("Synthetic Equity Position") and that is, directly or indirectly, held or maintained by such Proposing Person with respect to any shares of any class or series of shares of the Corporation; *provided* that, for the purposes of the definition of "Synthetic Equity Position," the term "derivative security" shall also include any security or instrument that would not otherwise constitute a "derivative security" as a result of any feature that would make any conversion, exercise or similar right or privilege of such security or instrument becoming determinable only at some future date or upon the happening of a future occurrence, in which case the determination of the amount of securities into which such security or instrument would be convertible or exercisable shall be made assuming that such security or instrument is immediately convertible or exercisable at the time of such determination; and, *provided*,

further, that any Proposing Person satisfying the requirements of Rule 13d-1(b)(1) under the Exchange Act (other than a Proposing Person that so satisfies Rule 13d-1(b)(1) under the Exchange Act solely by reason of Rule 13d-1(b)(1)(ii)(E)) shall not be deemed to hold or maintain the notional amount of any securities that underlie a Synthetic Equity Position held by such Proposing Person as a hedge with respect to a bona fide derivatives trade or position of such Proposing Person arising in the ordinary course of such Proposing Person's business as a derivatives dealer, (B) any rights to dividends on the shares of any class or series of shares of the Corporation owned beneficially by such Proposing Person that are separated or separable from the underlying shares of the Corporation, (C)(x) if such Proposing Person is (i) a general or limited partnership, syndicate or other group, the identity of each general partner and each person who functions as a general partner of the general or limited partnership, each member of the syndicate or group and each person controlling the general partner or member, (ii) a corporation or a limited liability company, the identity of each officer and each person who functions as an officer of the corporation or limited liability company, each person controlling the corporation or limited liability company and each officer, director, general partner and person who functions as an officer, director or general partner of any entity ultimately in control of the corporation or limited liability company or (iii) a trust, any trustee of such trust (each such person or persons set forth in the preceding clauses (i), (ii) and (iii), a "Responsible Person"), any fiduciary duties owed by such Responsible Person to the equity holders or other beneficiaries of such Proposing Person and any material interests or relationships of such Responsible Person that are not shared generally by other record or beneficial holders of the shares of any class or series of the Corporation and that reasonably could have influenced the decision of such Proposing Person to propose such business to be brought before the meeting, and (y) if such Proposing Person is a natural person, any material interests or relationships of such natural person that are not shared generally by other record or beneficial holders of the shares of any class or series of the Corporation and that reasonably could have influenced the decision of such Proposing Person to propose such business to be brought before the meeting, (D) any material shares or any Synthetic Equity Position in any principal competitor of the Corporation in any principal industry of the Corporation held by such Proposing Persons, (E) a summary of any material discussions regarding the business proposed to be brought before the meeting (x) between or among any of the Proposing Persons or (y) between or among any Proposing Person and any other record or beneficial holder of the shares of any class or series of the Corporation (including their names), (F) any material pending or threatened legal proceeding in which such Proposing Person is a party or material participant involving the Corporation or any of its officers or directors, or any affiliate of the Corporation, (G) any other material relationship between such Proposing Person, on the one hand, and the Corporation, any affiliate of the Corporation or any principal competitor of the Corporation, on the other hand, (H) any direct or indirect material interest in any material contract or agreement of such Proposing Person with the Corporation, any affiliate of the Corporation or any principal competitor of the Corporation (including, in any such case, any employment agreement, collective bargaining agreement or consulting agreement) and (I) any other information relating to such Proposing Person that would be required to be disclosed in a proxy statement or other filing required to be made in connection with solicitations of proxies or consents by such Proposing Person in support of the business proposed to be brought before the meeting pursuant to Section 14(a) of the Exchange Act (the disclosures to be made pursuant to the foregoing clauses (A) through (I) are referred to as "Disclosable Interests"); *provided*, *however*, that Disclosable Interests shall not include any such disclosures with respect to the ordinary course business activities of any broker, dealer, commercial bank, trust company or other nominee who is a Proposing Person solely as a result of being the stockholder directed to prepare and submit the notice required by these bylaws on behalf of a beneficial owner; and

(c) As to each item of business that the stockholder proposes to bring before the annual meeting, (A) a brief description of the business desired to be brought before the annual meeting, the reasons for conducting such business at the annual meeting and any material interest in such business of each Proposing Person, (B) the text of the proposal or business (including the text of any resolutions proposed for consideration and in the event that such business includes a proposal to amend the bylaws of the Corporation, the language of the proposed amendment), (C) a reasonably detailed description of all agreements, arrangements and understandings between or among any of the Proposing Persons or between or among any Proposing Person and any other person or entity (including their names) in connection with the proposal of such business by such stockholder and (D) any other information relating to such item of business that would be required to be disclosed in a proxy statement or other filing required to be made in connection with solicitations of proxies in support of the business proposed to be brought before the meeting pursuant to Section 14(a) of the Exchange Act; *provided*, *however*, that the disclosures required by this Section 2.4(iii) shall not include any disclosures with respect to any broker, dealer, commercial

bank, trust company or other nominee who is a Proposing Person solely as a result of being the stockholder directed to prepare and submit the notice required by these bylaws on behalf of a beneficial owner.

(iv) For purposes of this Section 2.4, the term "Proposing Person" shall mean (a) the stockholder providing the notice of business proposed to be brought before an annual meeting, (b) the beneficial owner or beneficial owners, if different, on whose behalf the notice of the business proposed to be brought before the annual meeting is made and (c) any participant (as defined in paragraphs (a)(ii)-(vi) of Instruction 3 to Item 4 of Schedule 14A) with such stockholder in such solicitation or associate (within the meaning of Rule 12b-2 under the Exchange Act for the purposes of these bylaws) of such stockholder or beneficial owner.

(v) A Proposing Person shall update and supplement its notice to the Corporation of its intent to propose business at an annual meeting, if necessary, so that the information provided or required to be provided in such notice pursuant to this Section 2.4 shall be true and correct as of the record date for notice of the meeting and as of the date that is ten (10) business days prior to the meeting or any adjournment or postponement thereof, and such update and supplement shall be delivered to, or mailed and received by, the Secretary at the principal executive offices of the Corporation not later than five (5) business days after the record date for notice of the meeting (in the case of the update and supplement required to be made as of such record date), and not later than eight (8) business days prior to the date for the meeting or, if practicable, any adjournment or postponement thereof (and, if not practicable, on the first practicable date prior to the date to which the meeting has been adjourned or postponed) (in the case of the update and supplement required to be made as of ten (10) business days prior to the meeting or any adjournment or postponement thereof).

(vi) Notwithstanding anything in these bylaws to the contrary, no business shall be conducted at an annual meeting that is not properly brought before the meeting in accordance with this Section 2.4. The presiding officer of the meeting shall, if the facts warrant, determine that the business was not properly brought before the meeting in accordance with this Section 2.4, and if he or she should so determine, he or she shall so declare to the meeting and any such business not properly brought before the meeting shall not be transacted.

(vii) This Section 2.4 is expressly intended to apply to any business proposed to be brought before an annual meeting of stockholders, other than any proposal made in accordance with Rule 14a-8 under the Exchange Act and included in the Corporation's proxy statement. In addition to the requirements of this Section 2.4 with respect to any business proposed to be brought before an annual meeting, each Proposing Person shall comply with all applicable requirements of the Exchange Act with respect to any such business. Nothing in this Section 2.4 shall be deemed to affect the rights of stockholders to request inclusion of proposals in the Corporation's proxy statement pursuant to Rule 14a-8 under the Exchange Act.

(viii) For purposes of these bylaws, "public disclosure" shall mean disclosure in a press release reported by a national news service or in a document publicly filed by the Corporation with the Securities and Exchange Commission pursuant to Sections 13, 14 or 15(d) of the Exchange Act.

2.5 ADVANCE NOTICE PROCEDURES FOR NOMINATIONS OF DIRECTORS.

(i) Nominations of any person for election to the Board at an annual meeting or at a special meeting (but only if the election of directors is a matter specified in the notice of meeting given by or at the direction of the person calling such special meeting) may be made at such meeting only (a) by or at the direction of the Board, including by any committee or persons authorized to do so by the Board or these bylaws, or (b) by a stockholder present in person (A) who was a beneficial owner of shares of the Corporation both at the time of giving the notice provided for in this Section 2.5 and at the time of the meeting, (B) is entitled to vote at the meeting and (C) has complied with this Section 2.5 as to such notice and nomination. The foregoing clause (b) shall be the exclusive means for a stockholder to make any nomination of a person or persons for election to the Board at an annual meeting or special meeting. For purposes of this Section 2.5, "present in person" shall mean that the stockholder proposing that the business be brought before the meeting of the Corporation, or, if the proposing stockholder is not an individual, a qualified representative of such stockholder, appear at such meeting. A "qualified representative" of such proposing stockholder shall be, if such proposing stockholder is (x) a general or limited partnership, any

general partner or person who functions as a general partner of the general or limited partnership or who controls the general or limited partnership, (y) a corporation or a limited liability company, any officer or person who functions as an officer of the corporation or limited liability company or any officer, director, general partner or person who functions as an officer, director or general partner of any entity ultimately in control of the corporation or limited liability company or (z) a trust, any trustee of such trust.

(ii) Without qualification, for a stockholder to make any nomination of a person or persons for election to the Board at an annual meeting, the stockholder must (a) provide Timely Notice (as defined in Section 2.4(ii) of these bylaws) thereof in writing and in proper form to the Secretary of the Corporation, (b) provide the information with respect to such stockholder and its proposed nominee as required by this Section 2.5, and (c) provide any updates or supplements to such notice at the times and in the forms required by this Section 2.5. Without qualification, if the election of directors is a matter specified in the notice of meeting given by or at the direction of the person calling such special meeting, then for a stockholder to make any nomination of a person or persons for election to the Board at a special meeting, the stockholder must (a) provide timely notice thereof in writing and in proper form to the Secretary of the Corporation at the principal executive offices of the Corporation, (b) provide the information with respect to such stockholder and its proposed nominee as required by this Section 2.5, and (c) provide any updates or supplements to such notice at the times and in the forms required by this Section 2.5. To be timely, a stockholder's notice for nominations to be made at a special meeting must be delivered to, or mailed and received at, the principal executive offices of the Corporation not earlier than the one hundred twentieth (120th) day prior to such special meeting and not later than the ninetieth (90th) day prior to such special meeting or, if later, the tenth (10th) day following the day on which public disclosure (as defined in Section 2.4(ix) of these bylaws) of the date of such special meeting was first made. In no event shall any adjournment or postponement of an annual meeting or special meeting or the announcement thereof commence a new time period for the giving of a stockholder's notice as described above.

(iii) To be in proper form for purposes of this Section 2.5, a stockholder's notice to the Secretary shall set forth:

(a) As to each Nominating Person (as defined below), the Stockholder Information (as defined in Section 2.4(iii)(a) of these bylaws) except that for purposes of this Section 2.5, the term "Nominating Person" shall be substituted for the term "Proposing Person" in all places it appears in Section 2.4(iii)(a);

(b) As to each Nominating Person, any Disclosable Interests (as defined in Section 2.4(iii)(b), except that for purposes of this Section 2.5 the term "Nominating Person" shall be substituted for the term "Proposing Person" in all places it appears in Section 2.4(iii)(b) and the disclosure with respect to the business to be brought before the meeting in Section 2.4(iii)(b) shall be made with respect to the election of directors at the meeting);

(c) As to each person whom a Nominating Person proposes to nominate for election as a director, (A) all information with respect to such proposed nominee that would be required to be set forth in a stockholder's notice pursuant to this Section 2.5 if such proposed nominee were a Nominating Person, (B) all information relating to such proposed nominee that is required to be disclosed in a proxy statement or other filings required to be made in connection with solicitations of proxies for election of directors in a contested election pursuant to Section 14(a) under the Exchange Act (including such proposed nominee's written consent to being named in the proxy statement as a nominee and to serving as a director if elected), (C) a description of any direct or indirect material interest in any material contract or agreement between or among any Nominating Person, on the one hand, and each proposed nominee or his or her respective associates or any other participants in such solicitation, on the other hand, including, without limitation, all information that would be required to be disclosed pursuant to Item 404 under Regulation S-K if such Nominating Person were the "registrant" for purposes of such rule and the proposed nominee were a director or executive officer of such registrant (the disclosures to be made pursuant to the foregoing clauses (A) through (C) are referred to as "Nominee Information"), and (D) a completed and signed questionnaire, representation and agreement as provided in Section 2.5(vi); and

(d) The Corporation may require any proposed nominee to furnish such other information (A) as may reasonably be required by the Corporation to determine the eligibility of such proposed nominee to serve as an independent director of the Corporation in accordance with the Corporation's Corporate Governance Guidelines or (B) that could be material to a reasonable stockholder's understanding of the independence or lack of independence of such proposed nominee.

(iv) For purposes of this Section 2.5, the term "Nominating Person" shall mean (a) the stockholder providing the notice of the nomination proposed to be made at the meeting, (b) the beneficial owner or beneficial owners, if different, on whose behalf the notice of the nomination proposed to be made at the meeting is made and (c) any associate of such stockholder or beneficial owner or any other participant in such solicitation.

(v) A stockholder providing notice of any nomination proposed to be made at a meeting shall further update and supplement such notice, if necessary, so that the information provided or required to be provided in such notice pursuant to this Section 2.5 shall be true and correct as of the record date for notice of the meeting and as of the date that is ten (10) business days prior to the meeting or any adjournment or postponement thereof, and such update and supplement shall be delivered to, or mailed and received by, the Secretary at the principal executive offices of the Corporation not later than five (5) business days after the record date for notice of the meeting (in the case of the update and supplement required to be made as of such record date), and not later than eight (8) business days prior to the date for the meeting or, if practicable, any adjournment or postponement thereof (and, if not practicable, on the first practicable date prior to the date to which the meeting has been adjourned or postponed) (in the case of the update and supplement required to be made as of ten (10) business days prior to the meeting or any adjournment or postponement thereof).

(vi) To be eligible to be a nominee for election as a director of the Corporation at an annual or special meeting, the proposed nominee must be nominated in the manner prescribed in Section 2.5 and must deliver (in accordance with the time period prescribed for delivery in a notice to such proposed nominee given by or on behalf of the Board), to the Secretary at the principal executive offices of the Corporation, (a) a completed written questionnaire (in a form provided by the Corporation) with respect to the background, qualifications, stock ownership and independence of such proposed nominee and (b) a written representation and agreement (in form provided by the Corporation) that such proposed nominee (A) is not and, if elected as a director during his or her term of office, will not become a party to (1) any agreement, arrangement or understanding with, and has not given and will not give any commitment or assurance to, any person or entity as to how such proposed nominee, if elected as a director of the Corporation, will act or vote on any issue or question (a "Voting Commitment") or (2) any Voting Commitment that could limit or interfere with such proposed nominee's ability to comply, if elected as a director of the Corporation, with such proposed nominee's fiduciary duties under applicable law, (B) is not, and will not become a party to, any agreement, arrangement or understanding with any person or entity other than the Corporation with respect to any direct or indirect compensation or reimbursement for service as a director and (C) if elected as a director of the Corporation, will comply with all applicable corporate governance, conflict of interest, confidentiality, stock ownership and trading and other policies and guidelines of the Corporation applicable to directors and in effect during such person's term in office as a director (and, if requested by any proposed nominee, the Secretary of the Corporation shall provide to such proposed nominee all such policies and guidelines then in effect).

(vii) In addition to the requirements of this Section 2.5 with respect to any nomination proposed to be made at a meeting, each Proposing Person shall comply with all applicable requirements of the Exchange Act with respect to any such nominations.

(viii) No proposed nominee shall be eligible for nomination as a director of the Corporation unless such proposed nominee and the Nominating Person seeking to place such proposed nominee's name in nomination have complied with this Section 2.5, as applicable. The presiding officer at the meeting shall, if the facts warrant, determine that a nomination was not properly made in accordance with this Section 2.5, and if he or she should so determine, he or she shall so declare such determination to the meeting, the defective nomination shall be disregarded and any ballots cast for the proposed nominee in question (but in the case of any form of ballot listing other qualified nominees, only the ballots case for the nominee in question) shall be void and of no force or effect.

2.6 NOTICE OF STOCKHOLDERS' MEETINGS.

Unless otherwise provided by law, the certificate of incorporation or these bylaws, the notice of any meeting of stockholders shall be sent or otherwise given in accordance with either Section 2.7 or Section 8.1 of these bylaws not less than ten (10) nor more than sixty (60) days before the date of the meeting to each stockholder entitled to vote at such meeting. The notice shall specify the place, if any, date and hour of the meeting, the means of remote communication, if any, by which stockholders and proxy holders may be deemed to be present in person and vote at such meeting, and, in the case of a special meeting, the purpose or purposes for which the meeting is called.

2.7 MANNER OF GIVING NOTICE; AFFIDAVIT OF NOTICE.

Notice of any meeting of stockholders shall be deemed given:

(i) if mailed, when deposited in the U.S. mail, postage prepaid, directed to the stockholder at his or her address as it appears on the Corporation's records; or

(ii) if electronically transmitted as provided in Section 8.1 of these bylaws.

An affidavit of the secretary or an assistant secretary of the Corporation or of the transfer agent or any other agent of the Corporation that the notice has been given by mail or by a form of electronic transmission, as applicable, shall, in the absence of fraud, be prima facie evidence of the facts stated therein.

2.8 QUORUM.

Unless otherwise provided by law, the certificate of incorporation or these bylaws, the holders of a majority in voting power of the stock issued and outstanding and entitled to vote, present in person, or by remote communication, if applicable, or represented by proxy, shall constitute a quorum for the transaction of business at all meetings of the stockholders. If, however, a quorum is not present or represented at any meeting of the stockholders, then either (i) the chairperson of the meeting or (ii) a majority in voting power of the stockholders entitled to vote at the meeting, present in person, or by remote communication, if applicable, or represented by proxy, shall have power to adjourn the meeting from time to time in the manner provided in Section 2.9 of these bylaws until a quorum is present or represented. At such adjourned meeting at which a quorum is present or represented, any business may be transacted that might have been transacted at the meeting as originally noticed.

2.9 ADJOURNED MEETING; NOTICE.

When a meeting is adjourned to another time or place, unless these bylaws otherwise require, notice need not be given of the adjourned meeting if the time, place, if any, thereof, and the means of remote communications, if any, by which stockholders and proxy holders may be deemed to be present in person and vote at such adjourned meeting are announced at the meeting at which the adjournment is taken. At the adjourned meeting, the Corporation may transact any business which might have been transacted at the original meeting. If the adjournment is for more than thirty (30) days, or if after the adjournment a new record date is fixed for the adjourned meeting, a notice of the adjourned meeting shall be given to each stockholder of record entitled to vote at the meeting.

2.10 CONDUCT OF BUSINESS.

The chairperson of any meeting of stockholders shall determine the order of business and the procedure at the meeting, including such regulation of the manner of voting and the conduct of business.

2.11 VOTING.

The stockholders entitled to vote at any meeting of stockholders shall be determined in accordance with the provisions of Section 2.13 of these bylaws, subject to Section 217 (relating to voting rights of fiduciaries, pledgors and joint owners of stock) and Section 218 (relating to voting trusts and other voting agreements) of the DGCL.

Except as may be otherwise provided in the certificate of incorporation or these bylaws, each stockholder shall be entitled to one (1) vote for each share of capital stock held by such stockholder.

At all duly called or convened meetings of stockholders, at which a quorum is present, for the election of directors, a plurality of the votes cast shall be sufficient to elect a director. Except as otherwise provided by the certificate of incorporation, these bylaws, the rules or regulations of any stock exchange applicable to the Corporation, or applicable law or pursuant to any regulation applicable to the Corporation or its securities, all other elections and questions presented to the stockholders at a duly called or convened meeting, at which a quorum is present, shall be decided by the majority of the votes cast affirmatively or negatively (excluding abstentions and broker non-votes) and shall be valid and binding upon the Corporation.

2.12 STOCKHOLDER ACTION BY WRITTEN CONSENT WITHOUT A MEETING.

Subject to the rights of the holders of the shares of any series of Preferred Stock or any other class of stock or series thereof having a preference over the Common Stock as to dividends or upon liquidation, any action required or permitted to be taken by the stockholders of the Corporation must be effected at a duly called annual or special meeting of stockholders of the Corporation and may not be effected by any consent in writing by such stockholders.

2.13 RECORD DATE FOR STOCKHOLDER NOTICE; VOTING; GIVING CONSENTS.

In order that the Corporation may determine the stockholders entitled to notice of or to vote at any meeting of stockholders or any adjournment thereof, or entitled to receive payment of any dividend or other distribution or allotment of any rights, or entitled to exercise any rights in respect of any change, conversion or exchange of stock or for the purpose of any other lawful action, the Board may fix, in advance, a record date, which record date shall not precede the date on which the resolution fixing the record date is adopted and which shall not be more than sixty (60) nor less than ten (10) days before the date of such meeting, nor more than sixty (60) days prior to any other such action.

If the Board does not so fix a record date:

(i) The record date for determining stockholders entitled to notice of or to vote at a meeting of stockholders shall be at the close of business on the day next preceding the day on which notice is given, or, if notice is waived, at the close of business on the day next preceding the day on which the meeting is held.

(ii) The record date for determining stockholders for any other purpose shall be at the close of business on the day on which the Board adopts the resolution relating thereto.

A determination of stockholders of record entitled to notice of or to vote at a meeting of stockholders shall apply to any adjournment of the meeting; *provided, however*, that the Board may fix a new record date for the adjourned meeting.

2.14 PROXIES.

Each stockholder entitled to vote at a meeting of stockholders may authorize another person or persons to act for such stockholder by proxy authorized by an instrument in writing or by a transmission permitted by law filed in accordance with the procedure established for the meeting, but no such proxy shall be voted or acted upon after three (3) years from its date, unless the proxy provides for a longer period. The revocability of a proxy that states on its face that it is irrevocable shall be governed by the provisions of Section 212 of the DGCL. A proxy may be in the form of a telegram, cablegram or other means of electronic transmission which sets forth or is submitted with information from which it can be determined that the telegram, cablegram or other means of electronic transmission was authorized by the stockholder.

2.15 LIST OF STOCKHOLDERS ENTITLED TO VOTE.

The officer who has charge of the stock ledger of the Corporation shall prepare and make, at least ten (10) days before every meeting of stockholders, a complete list of the stockholders entitled to vote at the meeting, arranged in alphabetical order, and showing the address of each stockholder and the number of shares registered in the name of each stockholder. The Corporation shall not be required to include electronic mail addresses or other electronic contact information on such list. Such list shall be open to the examination of any stockholder, for any purpose germane to the meeting for a period of at least ten (10) days prior to the meeting: (i) on a reasonably accessible electronic network, provided that the information required to gain access to such list is provided with the notice of the meeting, or (ii) during ordinary business hours, at the Corporation's principal executive office. In the event that the Corporation determines to make the list available on an electronic network, the Corporation may take reasonable steps to ensure that such information is available only to stockholders of the Corporation. If the meeting is to be held at a place, then the list shall be produced and kept at the time and place of the meeting during the whole time thereof, and may be inspected by any stockholder who is present. If the meeting is to be held solely by means of remote communication, then the list shall also be open to the examination of any stockholder during the whole time of the meeting on a reasonably accessible electronic network, and the information required to access such list shall be provided with the notice of the meeting. Such list shall presumptively determine the identity of the stockholders entitled to vote at the meeting and the number of shares held by each of them.

2.16 INSPECTORS OF ELECTION.

Before any meeting of stockholders, the Board shall appoint an inspector or inspectors of election to act at the meeting or its adjournment and make a written report thereof. The number of inspectors shall be either one (1) or three (3). If any person appointed as inspector fails to appear or fails or refuses to act, then the chairperson of the meeting may, and upon the request of any stockholder or a stockholder's proxy shall, appoint a person to fill that vacancy.

Such inspectors shall:

(i) determine the number of shares outstanding and the voting power of each, the number of shares represented at the meeting, the existence of a quorum, and the authenticity, validity, and effect of proxies;

(ii) receive votes or ballots;

(iii) hear and determine all challenges and questions in any way arising in connection with the right to vote;

(iv) count and tabulate all votes;

(v) determine when the polls shall close;

(vi) determine the result; and

(vii) do any other acts that may be proper to conduct the election or vote with fairness to all stockholders.

The inspectors of election shall perform their duties impartially, in good faith, to the best of their ability and as expeditiously as is practical. If there are three (3) inspectors of election, the decision, act or certificate of a majority is effective in all respects as the decision, act or certificate of all. Any report or certificate made by the inspectors of election is prima facie evidence of the facts stated therein.

ARTICLE III - DIRECTORS

3.1 POWERS.

Subject to the provisions of the DGCL and any limitations in the certificate of incorporation or these bylaws relating to action required to be approved by the stockholders or by the outstanding shares, the business and affairs of the Corporation shall be managed and all corporate powers shall be exercised by or under the direction of the Board.

3.2 NUMBER OF DIRECTORS.

The authorized number of directors shall be determined from time to time by resolution of the Board, provided the Board shall consist of at least one (1) member. No reduction of the authorized number of directors shall have the effect of removing any director before that director's term of office expires.

3.3 ELECTION, QUALIFICATION AND TERM OF OFFICE OF DIRECTORS.

Except as provided in Section 3.4 of these bylaws, each director, including a director elected to fill a vacancy, shall hold office until the expiration of the term for which elected and until such director's successor is elected and qualified or until such director's earlier death, resignation or removal. Directors need not be stockholders unless so required by the certificate of incorporation or these bylaws. The certificate of incorporation or these bylaws may prescribe other qualifications for directors.

If so provided in the certificate of incorporation, the directors of the Corporation shall be divided into three (3) classes.

3.4 RESIGNATION AND VACANCIES.

Any director may resign at any time upon notice given in writing or by electronic transmission to the Corporation. When one or more directors so resigns and the resignation is effective at a future date, a majority of the directors then in office, including those who have so resigned, shall have power to fill such vacancy or vacancies, the vote thereon to take effect when such resignation or resignations shall become effective, and each director so chosen shall hold office as provided in this section in the filling of other vacancies.

Unless otherwise provided in the certificate of incorporation or these bylaws, vacancies and newly created directorships resulting from any increase in the authorized number of directors shall, unless the Board determines by resolution that any such vacancies or newly created directorships shall be filled by stockholders, be filled only by a majority of the directors then in office, although less than a quorum, or by a sole remaining director. Any director elected in accordance with the preceding sentence shall hold office for the remainder of the full term of the director for which the vacancy was created or occurred and until such director's successor shall have been elected and qualified. A vacancy in the Board shall be deemed to exist under these bylaws in the case of the death, removal or resignation of any director.

3.5 PLACE OF MEETINGS; MEETINGS BY TELEPHONE.

The Board may hold meetings, both regular and special, either within or outside the State of Delaware.

Unless otherwise restricted by the certificate of incorporation or these bylaws, members of the Board, or any committee designated by the Board, may participate in a meeting of the Board, or any committee, by means of conference telephone or other communications equipment by means of which all persons participating in the meeting can hear each other, and such participation in a meeting pursuant to this bylaw shall constitute presence in person at the meeting.

3.6 REGULAR MEETINGS.

Regular meetings of the Board may be held without notice at such time and at such place as shall from time to time be determined by the Board.

3.7 SPECIAL MEETINGS; NOTICE.

Special meetings of the Board for any purpose or purposes may be called at any time by the Board, the chief executive officer, the president, the secretary or a majority of the authorized number of directors. Notice of the time and place of special meetings shall be:

(i) delivered personally by hand, by courier or by telephone;

(ii) sent by United States first-class mail, postage prepaid;

(iii) sent by facsimile; or

(iv) sent by electronic mail, directed to each director at that director's address, telephone number, facsimile number or electronic mail address, as the case may be, as shown on the Corporation's records.

If the notice is (i) delivered personally by hand, by courier or by telephone, (ii) sent by facsimile or (iii) sent by electronic mail, it shall be delivered or sent at least twenty-four (24) hours before the time of the holding of the meeting. If the notice is sent by U.S. mail, it shall be deposited in the U.S. mail at least four (4) days before the time of the holding of the meeting. Any oral notice may be communicated to the director. The notice need not specify the place of the meeting (if the meeting is to be held at the Corporation's principal executive office) nor the purpose of the meeting.

3.8 QUORUM.

At all meetings of the Board, a majority of the authorized number of directors shall constitute a quorum for the transaction of business. The vote of a majority of the directors present at any meeting at which a quorum is present shall be the act of the Board, except as may be otherwise specifically provided by statute, the certificate of incorporation or these bylaws. If a quorum is not present at any meeting of the Board, then the directors present thereat may adjourn the meeting from time to time, without notice other than announcement at the meeting, until a quorum is present.

A meeting at which a quorum is initially present may continue to transact business notwithstanding the withdrawal of directors, if any action taken is approved by at least a majority of the required quorum for that meeting.

3.9 BOARD ACTION BY WRITTEN CONSENT WITHOUT A MEETING.

Unless otherwise restricted by the certificate of incorporation or these bylaws, any action required or permitted to be taken at any meeting of the Board, or of any committee thereof, may be taken without a meeting if all members of the Board or committee, as the case may be, consent thereto in writing or by electronic transmission and the writing or writings or electronic transmission or transmissions are filed with the minutes of proceedings of the Board or committee. Such filing shall be in paper form if the minutes are maintained in paper form and shall be in electronic form if the minutes are maintained in electronic form.

3.10 FEES AND COMPENSATION OF DIRECTORS.

Unless otherwise restricted by the certificate of incorporation or these bylaws, the Board shall have the authority to fix the compensation of directors.

3.11 REMOVAL OF DIRECTORS.

Except as otherwise provided by the DGCL, the Board of Directors or any individual director may be removed from office only for cause at a meeting of stockholders called for that purpose, by the affirmative vote of the holders of at least sixty six and two thirds percent (66-2/3%) of the voting power of all the then outstanding shares of voting stock of the Corporation entitled to vote at an election of directors, voting together as a single class.

No reduction of the authorized number of directors shall have the effect of removing any director prior to the expiration of such director's term of office.

ARTICLE IV - COMMITTEES

4.1 COMMITTEES OF DIRECTORS.

The Board may designate one (1) or more committees, each committee to consist of one (1) or more of the directors of the Corporation. The Board may designate one (1) or more directors as alternate members of any committee, who may replace any absent or disqualified member at any meeting of the committee. In the absence or disqualification of a member of a committee, the member or members thereof present at any meeting and not disqualified from voting, whether or not such member or members constitute a quorum, may unanimously appoint another member of the Board to act at the meeting in the place of any such absent or disqualified member. Any such committee, to the extent provided in the resolution of the Board or in these bylaws, shall have and may exercise all the powers and authority of the Board in the management of the business and affairs of the Corporation, and may authorize the seal of the Corporation to be affixed to all papers that may require it; but no such committee shall have the power or authority to (i) approve or adopt, or recommend to the stockholders, any action or matter expressly required by the DGCL to be submitted to stockholders for approval, or (ii) adopt, amend or repeal any bylaw of the Corporation.

4.2 COMMITTEE MINUTES.

Each committee shall keep regular minutes of its meetings and report the same to the Board when required.

4.3 MEETINGS AND ACTION OF COMMITTEES.

Meetings and actions of committees shall be governed by, and held and taken in accordance with, the provisions of:

(i) Section 3.5 (place of meetings and meetings by telephone);

(ii) Section 3.6 (regular meetings);

(iii) Section 3.7 (special meetings and notice);

(iv) Section 3.8 (quorum);

(v) Section 7.12 (waiver of notice); and

(vi) Section 3.9 (action without a meeting),

with such changes in the context of those bylaws as are necessary to substitute the committee and its members for the Board and its members. *However*:

(i) the time of regular meetings of committees may be determined either by resolution of the Board or by resolution of the committee;

(ii) special meetings of committees may also be called by resolution of the Board; and

(iii) notice of special meetings of committees shall also be given to all alternate members, who shall have the right to attend all meetings of the committee. The Board may adopt rules for the government of any committee not inconsistent with the provisions of these bylaws.

ARTICLE V - OFFICERS

5.1 OFFICERS.

The officers of the Corporation shall be a president and a secretary. The Corporation may also have, at the discretion of the Board, a chairperson of the Board, a vice chairperson of the Board, a chief executive officer, a chief financial officer or treasurer, one (1) or more vice presidents, one (1) or more assistant vice presidents, one (1) or more assistant treasurers, one (1) or more assistant secretaries, and any such other officers as may be appointed in accordance with the provisions of these bylaws. Any number of offices may be held by the same person.

5.2 APPOINTMENT OF OFFICERS.

The Board shall appoint the officers of the Corporation, except such officers as may be appointed in accordance with the provisions of Section 5.3 of these bylaws, subject to the rights, if any, of an officer under any contract of employment.

5.3 SUBORDINATE OFFICERS.

The Board may appoint, or empower the chief executive officer or, in the absence of a chief executive officer, the president, to appoint, such other officers and agents as the business of the Corporation may require. Each of such officers and agents shall hold office for such period, have such authority, and perform such duties as are provided in these bylaws or as the Board may from time to time determine.

5.4 REMOVAL AND RESIGNATION OF OFFICERS.

Subject to the rights, if any, of an officer under any contract of employment, any officer may be removed, either with or without cause, by an affirmative vote of the majority of the Board at any regular or special meeting of the Board or, except in the case of an officer chosen by the Board, by any officer upon whom such power of removal may be conferred by the Board.

Any officer may resign at any time by giving written notice to the Corporation. Any resignation shall take effect at the date of the receipt of that notice or at any later time specified in that notice. Unless otherwise specified in the notice of resignation, the acceptance of the resignation shall not be necessary to make it effective. Any resignation is without prejudice to the rights, if any, of the Corporation under any contract to which the officer is a party.

5.5 VACANCIES IN OFFICES.

Any vacancy occurring in any office of the Corporation shall be filled by the Board or as provided in Section 5.2.

5.6 REPRESENTATION OF SHARES OF OTHER CORPORATIONS.

The chairperson of the Board, the president, any vice president, the treasurer, the secretary or assistant secretary of the Corporation, or any other person authorized by the Board or the president or a vice president, is authorized to vote, represent and exercise on behalf of the Corporation all rights incident to any and all shares of any other corporation or corporations standing in the name of the Corporation. The authority granted herein may be

exercised either by such person directly or by any other person authorized to do so by proxy or power of attorney duly executed by such person having the authority.

5.7 AUTHORITY AND DUTIES OF OFFICERS.

All officers of the Corporation shall respectively have such authority and perform such duties in the management of the business of the Corporation as may be designated from time to time by the Board or the stockholders and, to the extent not so provided, as generally pertain to their respective offices, subject to the control of the Board.

ARTICLE VI - RECORDS AND REPORTS

6.1 MAINTENANCE AND INSPECTION OF RECORDS.

The Corporation shall, either at its principal executive office or at such place or places as designated by the Board, keep a record of its stockholders listing their names and addresses and the number and class of shares held by each stockholder, a copy of these bylaws as amended to date, accounting books and other records.

Any stockholder of record, in person or by attorney or other agent, shall, upon written demand under oath stating the purpose thereof, have the right during the usual hours for business to inspect for any proper purpose the Corporation's stock ledger, a list of its stockholders, and its other books and records and to make copies or extracts therefrom. A proper purpose shall mean a purpose reasonably related to such person's interest as a stockholder. In every instance where an attorney or other agent is the person who seeks the right to inspection, the demand under oath shall be accompanied by a power of attorney or such other writing that authorizes the attorney or other agent so to act on behalf of the stockholder. The demand under oath shall be directed to the Corporation at its registered office in Delaware or at its principal executive office.

6.2 INSPECTION BY DIRECTORS.

Any director shall have the right to examine the Corporation's stock ledger, a list of its stockholders, and its other books and records for a purpose reasonably related to his or her position as a director. The Court of Chancery is hereby vested with the exclusive jurisdiction to determine whether a director is entitled to the inspection sought. The Court may summarily order the Corporation to permit the director to inspect any and all books and records, the stock ledger, and the stock list and to make copies or extracts therefrom. The Court may, in its discretion, prescribe any limitations or conditions with reference to the inspection, or award such other and further relief as the Court may deem just and proper.

ARTICLE VII - GENERAL MATTERS

7.1 EXECUTION OF CORPORATE CONTRACTS AND INSTRUMENTS.

The Board, except as otherwise provided in these bylaws, may authorize any officer or officers, or agent or agents, to enter into any contract or execute any instrument in the name of and on behalf of the Corporation; such authority may be general or confined to specific instances. Unless so authorized or ratified by the Board or within the agency power of an officer, no officer, agent or employee shall have any power or authority to bind the Corporation by any contract or engagement or to pledge its credit or to render it liable for any purpose or for any amount.

7.2 STOCK CERTIFICATES; PARTLY PAID SHARES.

The shares of the Corporation shall be represented by certificates or shall be uncertificated. Certificates for the shares of stock, if any, shall be in such form as is consistent with the certificate of incorporation and applicable law. Every holder of stock represented by a certificate shall be entitled to have a certificate signed by, or in the name of the Corporation by the chairperson or vice-chairperson of the Board, or the president or vice-president, and by the

treasurer or an assistant treasurer, or the secretary or an assistant secretary of the Corporation representing the number of shares registered in certificate form. Any or all of the signatures on the certificate may be a facsimile. In case any officer, transfer agent or registrar who has signed or whose facsimile signature has been placed upon a certificate has ceased to be such officer, transfer agent or registrar before such certificate is issued, it may be issued by the Corporation with the same effect as if he or she were such officer, transfer agent or registrar at the date of issue.

The Corporation may issue the whole or any part of its shares as partly paid and subject to call for the remainder of the consideration to be paid therefor. Upon the face or back of each stock certificate issued to represent any such partly paid shares, upon the books and records of the Corporation in the case of uncertificated partly paid shares, the total amount of the consideration to be paid therefor and the amount paid thereon shall be stated. Upon the declaration of any dividend on fully paid shares, the Corporation shall declare a dividend upon partly paid shares of the same class, but only upon the basis of the percentage of the consideration actually paid thereon.

7.3 SPECIAL DESIGNATION ON CERTIFICATES.

If the Corporation is authorized to issue more than one class of stock or more than one series of any class, then the powers, the designations, the preferences and the relative, participating, optional or other special rights of each class of stock or series thereof and the qualifications, limitations or restrictions of such preferences and/or rights shall be set forth in full or summarized on the face or back of the certificate that the Corporation shall issue to represent such class or series of stock; *provided*, *however*, that, except as otherwise provided in Section 202 of the DGCL, in lieu of the foregoing requirements, there may be set forth on the face or back of the certificate that the Corporation shall issue to represent such class or series of stock a statement that the Corporation will furnish without charge to each stockholder who so requests the powers, the designations, the preferences and the relative, participating, optional or other special rights of each class of stock or series thereof and the qualifications, limitations or restrictions of such preferences and/or rights.

7.4 LOST CERTIFICATES.

Except as provided in this Section 7.4, no new certificates for shares shall be issued to replace a previously issued certificate unless the latter is surrendered to the Corporation and cancelled at the same time. The Corporation may issue a new certificate of stock or uncertificated shares in the place of any certificate theretofore issued by it, alleged to have been lost, stolen or destroyed, and the Corporation may require the owner of the lost, stolen or destroyed certificate, or such owner's legal representative, to give the Corporation a bond sufficient to indemnify it against any claim that may be made against it on account of the alleged loss, theft or destruction of any such certificate or the issuance of such new certificate or uncertificated shares.

7.5 CONSTRUCTION; DEFINITIONS.

Unless the context requires otherwise, the general provisions, rules of construction and definitions in the DGCL shall govern the construction of these bylaws. Without limiting the generality of this provision, the singular number includes the plural, the plural number includes the singular, and the term "person" includes both a corporation and a natural person.

7.6 DIVIDENDS.

The Board, subject to any restrictions contained in either (i) the DGCL or (ii) the certificate of incorporation, may declare and pay dividends upon the shares of its capital stock. Dividends may be paid in cash, in property or in shares of the Corporation's capital stock.

The Board may set apart out of any of the funds of the Corporation available for dividends a reserve or reserves for any proper purpose and may abolish any such reserve. Such purposes shall include but not be limited to equalizing dividends, repairing or maintaining any property of the Corporation, and meeting contingencies.

7.7 FISCAL YEAR.

The fiscal year of the Corporation shall be fixed by resolution of the Board and may be changed by the Board.

7.8 SEAL.

The Corporation may adopt a corporate seal, which shall be adopted and which may be altered by the Board. The Corporation may use the corporate seal by causing it or a facsimile thereof to be impressed or affixed or in any other manner reproduced.

7.9 TRANSFER OF STOCK.

Shares of the Corporation shall be transferable in the manner prescribed by law and in these bylaws. Shares of stock of the Corporation shall be transferred on the books of the Corporation only by the holder of record thereof or by such holder's attorney duly authorized in writing, upon surrender to the Corporation of the certificate or certificates representing such shares endorsed by the appropriate person or persons (or by delivery of duly executed instructions with respect to uncertificated shares), with such evidence of the authenticity of such endorsement or execution, transfer, authorization and other matters as the Corporation may reasonably require, and accompanied by all necessary stock transfer stamps. No transfer of stock shall be valid as against the Corporation for any purpose until it shall have been entered in the stock records of the Corporation by an entry showing the names of the persons from and to whom it was transferred.

7.10 STOCK TRANSFER AGREEMENTS.

The Corporation shall have power to enter into and perform any agreement with any number of stockholders of any one or more classes of stock of the Corporation to restrict the transfer of shares of stock of the Corporation of any one or more classes owned by such stockholders in any manner not prohibited by the DGCL.

7.11 REGISTERED STOCKHOLDERS.

The Corporation:

(i) shall be entitled to recognize the exclusive right of a person registered on its books as the owner of shares to receive dividends and to vote as such owner;

(ii) shall be entitled to hold liable for calls and assessments the person registered on its books as the owner of shares; and

(iii) shall not be bound to recognize any equitable or other claim to or interest in such share or shares on the part of another person, whether or not it shall have express or other notice thereof, except as otherwise provided by the laws of Delaware.

7.12 WAIVER OF NOTICE.

Whenever notice is required to be given under any provision of the DGCL, the certificate of incorporation or these bylaws, a written waiver, signed by the person entitled to notice, or a waiver by electronic transmission by the person entitled to notice, whether before or after the time of the event for which notice is to be given, shall be deemed equivalent to notice. Attendance of a person at a meeting shall constitute a waiver of notice of such meeting, except when the person attends a meeting for the express purpose of objecting at the beginning of the meeting, to the transaction of any business because the meeting is not lawfully called or convened. Neither the business to be transacted at, nor the purpose of, any regular or special meeting of the stockholders need be specified in any written waiver of notice or any waiver by electronic transmission unless so required by the certificate of incorporation or these bylaws.

ARTICLE VIII - NOTICE BY ELECTRONIC TRANSMISSION

8.1 NOTICE BY ELECTRONIC TRANSMISSION.

Without limiting the manner by which notice otherwise may be given effectively to stockholders pursuant to the DGCL, the certificate of incorporation or these bylaws, any notice to stockholders given by the Corporation under any provision of the DGCL, the certificate of incorporation or these bylaws shall be effective if given by a form of electronic transmission consented to by the stockholder to whom the notice is given. Any such consent shall be revocable by the stockholder by written notice to the Corporation. Any such consent shall be deemed revoked if:

(i) the Corporation is unable to deliver by electronic transmission two (2) consecutive notices given by the Corporation in accordance with such consent; and

(ii) such inability becomes known to the secretary or an assistant secretary of the Corporation or to the transfer agent, or other person responsible for the giving of notice.

However, the inadvertent failure to treat such inability as a revocation shall not invalidate any meeting or other action.

Any notice given pursuant to the preceding paragraph shall be deemed given:

(i) if by facsimile telecommunication, when directed to a number at which the stockholder has consented to receive notice;

(ii) if by electronic mail, when directed to an electronic mail address at which the stockholder has consented to receive notice;

(iii) if by a posting on an electronic network together with separate notice to the stockholder of such specific posting, upon the later of (A) such posting and (B) the giving of such separate notice; and

(iv) if by any other form of electronic transmission, when directed to the stockholder.

An affidavit of the secretary or an assistant secretary or of the transfer agent or other agent of the Corporation that the notice has been given by a form of electronic transmission shall, in the absence of fraud, be prima facie evidence of the facts stated therein.

8.2 DEFINITION OF ELECTRONIC TRANSMISSION.

An “electronic transmission” means any form of communication, not directly involving the physical transmission of paper, that creates a record that may be retained, retrieved and reviewed by a recipient thereof, and that may be directly reproduced in paper form by such a recipient through an automated process.

ARTICLE IX - INDEMNIFICATION

9.1 INDEMNIFICATION OF DIRECTORS AND OFFICERS.

The Corporation shall indemnify and hold harmless, to the fullest extent permitted by the DGCL as it presently exists or may hereafter be amended, any director or officer of the Corporation who was or is made or is threatened to be made a party or is otherwise involved in any action, suit or proceeding, whether civil, criminal, administrative or investigative (a “Proceeding”) by reason of the fact that he or she, or a person for whom he or she is the legal representative, is or was a director or officer of the Corporation or is or was serving at the request of the Corporation as a director, officer, employee or agent of another corporation or of a partnership, joint venture, trust, enterprise or non-profit entity, including service with respect to employee benefit plans, against all liability and loss suffered and expenses (including attorneys’ fees) reasonably incurred by such person in connection with any such

Proceeding. Notwithstanding the preceding sentence, except as otherwise provided in Section 9.4, the Corporation shall be required to indemnify a person in connection with a Proceeding initiated by such person only if the Proceeding was authorized in the specific case by the Board.

9.2 INDEMNIFICATION OF OTHERS.

The Corporation shall have the power to indemnify and hold harmless, to the extent permitted by applicable law as it presently exists or may hereafter be amended, any employee or agent of the Corporation who was or is made or is threatened to be made a party or is otherwise involved in any Proceeding by reason of the fact that he or she, or a person for whom he or she is the legal representative, is or was an employee or agent of the Corporation or is or was serving at the request of the Corporation as a director, officer, employee or agent of another corporation or of a partnership, joint venture, trust, enterprise or non-profit entity, including service with respect to employee benefit plans, against all liability and loss suffered and expenses reasonably incurred by such person in connection with any such Proceeding.

9.3 PREPAYMENT OF EXPENSES.

The Corporation shall to the fullest extent not prohibited by applicable law pay the expenses (including attorneys' fees) incurred by any officer or director of the Corporation, and may pay the expenses incurred by any employee or agent of the Corporation, in defending any Proceeding in advance of its final disposition; *provided, however*, that, to the extent required by law, such payment of expenses in advance of the final disposition of the Proceeding shall be made only upon receipt of an undertaking by the person to repay all amounts advanced if it should be ultimately determined that the person is not entitled to be indemnified under this Article IX or otherwise.

9.4 DETERMINATION; CLAIM.

If a claim for indemnification (following the final disposition of such Proceeding) or advancement of expenses under this Article IX is not paid in full within sixty (60) days after a written claim therefor has been received by the Corporation the claimant may file suit to recover the unpaid amount of such claim and, if successful in whole or in part, shall be entitled to be paid the expense of prosecuting such claim to the fullest extent permitted by law. In any such action the Corporation shall have the burden of proving that the claimant was not entitled to the requested indemnification or payment of expenses under applicable law.

9.5 NON-EXCLUSIVITY OF RIGHTS.

The rights conferred on any person by this Article IX shall not be exclusive of any other rights which such person may have or hereafter acquire under any statute, provision of the certificate of incorporation, these bylaws, agreement, vote of stockholders or disinterested directors or otherwise.

9.6 INSURANCE.

The Corporation may purchase and maintain insurance on behalf of any person who is or was a director, officer, employee or agent of the Corporation, or is or was serving at the request of the Corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust enterprise or non-profit entity against any liability asserted against him or her and incurred by him or her in any such capacity, or arising out of his or her status as such, whether or not the Corporation would have the power to indemnify him or her against such liability under the provisions of the DGCL.

9.7 OTHER INDEMNIFICATION.

The Corporation's obligation, if any, to indemnify or advance expenses to any person who was or is serving at its request as a director, officer, employee or agent of another corporation, partnership, joint venture, trust, enterprise or non-profit entity shall be reduced by any amount such person may collect as indemnification or

advancement of expenses from such other corporation, partnership, joint venture, trust, enterprise or non-profit enterprise.

9.8 CONTINUATION OF INDEMNIFICATION.

The rights to indemnification and to prepayment of expenses provided by, or granted pursuant to, this Article IX shall continue notwithstanding that the person has ceased to be a director or officer of the Corporation and shall inure to the benefit of the estate, heirs, executors, administrators, legatees and distributees of such person.

9.9 AMENDMENT OR REPEAL.

The provisions of this Article IX shall constitute a contract between the Corporation, on the one hand, and, on the other hand, each individual who serves or has served as a director or officer of the Corporation (whether before or after the adoption of these bylaws), in consideration of such person's performance of such services, and pursuant to this Article IX the Corporation intends to be legally bound to each such current or former director or officer of the Corporation. With respect to current and former directors and officers of the Corporation, the rights conferred under this Article IX are present contractual rights and such rights are fully vested, and shall be deemed to have vested fully, immediately upon adoption of theses bylaws. With respect to any directors or officers of the Corporation who commence service following adoption of these bylaws, the rights conferred under this provision shall be present contractual rights and such rights shall fully vest, and be deemed to have vested fully, immediately upon such director or officer commencing service as a director or officer of the Corporation. Any repeal or modification of the foregoing provisions of this Article IX shall not adversely affect any right or protection (i) hereunder of any person in respect of any act or omission occurring prior to the time of such repeal or modification or (ii) under any agreement providing for indemnification or advancement of expenses to an officer or director of the Corporation in effect prior to the time of such repeal or modification.

ARTICLE X – FEDERAL FORUM SELECTION

Unless the Corporation consents in writing to the selection of an alternative forum, the federal district courts of the United States of America shall be the sole and exclusive forum for the resolution of any complaint asserting a cause of action arising under the Securities Act of 1933, as amended, against any person in connection with any offering of the Corporation's securities, including, without limitation and for the avoidance of doubt, any auditor, underwriter, expert, control person, or other defendant.

Any person or entity purchasing or otherwise acquiring or holding any interest in any security of the Corporation shall be deemed to have notice of and consented to the provisions of this Article X. This provision shall be enforceable by any party to a complaint covered by the provisions of this Article X. For the avoidance of doubt, nothing contained in this Article X shall apply to any action brought to enforce a duty or liability created by the Exchange Act or any successor thereto.

ARTICLE XI - AMENDMENTS

Subject to the limitations set forth in Section 9.9 of these bylaws or the provisions of the certificate of incorporation, the Board is expressly empowered to adopt, amend or repeal the bylaws of the Corporation. Any adoption, amendment or repeal of the bylaws of the Corporation by the Board shall require the approval of a majority of the authorized number of directors. The stockholders also shall have power to adopt, amend or repeal the bylaws of the Corporation; *provided*, *however*, that, in addition to any vote of the holders of any class or series of stock of the Corporation required by law or by the certificate of incorporation, such action by stockholders shall require the affirmative vote of the holders of at least sixty-six and two-thirds percent (66-2/3%) of the voting power of all of the then-outstanding shares of the capital stock of the Corporation entitled to vote at an election of directors.

ALPINE IMMUNE SCIENCES, INC.
CERTIFICATE OF AMENDMENT AND RESTATEMENT OF BYLAWS

The undersigned hereby certifies that he or she is the duly elected, qualified, and acting Secretary of Alpine Immune Sciences, Inc., a Delaware corporation, and that the foregoing bylaws, comprising 19 pages, were amended and restated on March 16, 2021 by the Corporation's board of directors.

IN WITNESS WHEREOF, the undersigned has hereunto set his or her hand this day of March 18, 2021.

/s/ Paul Rickey
Paul Rickey
Secretary

DESCRIPTION OF THE REGISTRANT'S SECURITIES
REGISTERED PURSUANT TO SECTION 12 OF THE
SECURITIES EXCHANGE ACT OF 1934

Alpine Immune Sciences, Inc. has one class of securities registered under Section 12 of the Securities Exchange Act of 1934, as amended: our common stock, par value $0.001 per share.

The general terms and provisions of our common stock are summarized below. This summary does not purport to be complete and is subject to, and qualified in its entirety by express reference to, the provisions of our amended and restated certificate of incorporation and our amended and restated bylaws, each of which is included as an exhibit to our Annual Reports on Form 10-K, and each of which may be amended from time to time. We encourage you to read our amended and restated certificate of incorporation and our amended and restated bylaws and the applicable provisions of the General Corporation Law of the State of Delaware, or the DGCL, for additional information.

Our authorized capital stock consists of 210,000,000 shares, of which 200,000,000 shares are designated common stock, par value $0.001 per share, and 10,000,000 shares are designated preferred stock, par value $0.001 per share.

Common Stock

Voting rights. The holders of our common stock will be entitled to one vote for each share held of record on all matters submitted to a vote of the stockholders, including the election of directors, and will not have cumulative voting rights. Unless otherwise required by law, our amended and restated certificate of incorporation, or our amended and restated bylaws, each matter submitted to a vote of our stockholders will require the approval of a majority of votes cast by stockholders represented in person or by proxy and entitled to vote on such matter, except that directors will be elected by a plurality of votes cast. Accordingly, the holders of a majority of the shares of common stock entitled to vote in any election of directors will be able to elect all of the directors standing for election, if they so choose.

Dividend rights. Holders of common stock will be entitled to receive ratably dividends if, as and when dividends are declared from time to time by our board of directors out of funds legally available for that purpose, subject to any preferential dividend rights of any then-outstanding preferred stock.

Other matters. Upon our liquidation, dissolution or winding up, the holders of common stock will be entitled to share ratably in the net assets legally available for distribution to stockholders after the payment of all of our debts and other liabilities, subject to any other distribution rights granted to holders of any outstanding preferred stock. Holders of common stock will have no preemptive or conversion rights or other subscription rights, and no redemption or sinking fund provisions will be applicable to our common stock.

Preferred Stock

Under our amended and restated certificate of incorporation, our board of directors has the authority, without further action by the stockholders (unless such stockholder action is required by applicable law or the rules of any stock exchange or market on which our securities are then traded), to designate and issue up to 10,000,000 shares of preferred stock in one or more series, to establish from time to time the number of shares to be included in each such series, to fix the rights, preferences and privileges of the shares of each wholly unissued series and any qualifications, limitations or restrictions thereon and to increase or decrease the number of shares of any such series, but not below the number of shares of such series then outstanding.

We will fix the designations, voting powers, preferences and rights of the preferred stock of each series, as well as the qualifications, limitations or restrictions thereof, in a certificate of designation relating to that series. We will file as an exhibit to the registration statement of which this prospectus is a part, or will incorporate by reference from

reports that we file with the SEC, the form of any certificate of designation that describes the terms of the series of preferred stock we are offering before the issuance of that series of preferred stock. This description will include:

- the title and stated value;
- the number of shares we are offering;
- the liquidation preference per share;
- the purchase price;
- the dividend rate, period and payment date and method of calculation for dividends;
- whether dividends will be cumulative or non-cumulative and, if cumulative, the date from which dividends will accumulate;
- the procedures for any auction and remarketing, if any;
- the provisions for a sinking fund, if any;
- the provisions for redemption or repurchase, if applicable, and any restrictions on our ability to exercise those redemption and repurchase rights;
- any listing of the preferred stock on any securities exchange or market;
- whether the preferred stock will be convertible into our common stock, and, if applicable, the conversion price, or how it will be calculated, and the conversion period;
- whether the preferred stock will be exchangeable into debt securities, and, if applicable, the exchange price, or how it will be calculated, and the exchange period;
- voting rights, if any, of the preferred stock;
- preemptive rights, if any;
- restrictions on transfer, sale or other assignment, if any;
- whether interests in the preferred stock will be represented by depositary shares;
- a discussion of any material U.S. federal income tax considerations applicable to the preferred stock;
- the relative ranking and preferences of the preferred stock as to dividend rights and rights if we liquidate, dissolve or wind up our affairs;
- any limitations on the issuance of any class or series of preferred stock ranking senior to or on a parity with the series of preferred stock as to dividend rights and rights if we liquidate, dissolve or wind up our affairs; and
- any other specific terms, preferences, rights or limitations of, or restrictions on, the preferred stock.

Delaware law provides that the holders of preferred stock will have the right to vote separately as a class (or, in some cases, as a series) on an amendment to our certificate of incorporation if the amendment would change the par value or, unless the certificate of incorporation provided otherwise, the number of authorized shares of the class or change the powers, preferences or special rights of the class or series so as to adversely affect the class or series, as the case may be. This right is in addition to any voting rights that may be provided for in the applicable certificate of designation.

Our board of directors may authorize the issuance of preferred stock with voting or conversion rights that could adversely affect the voting power or other rights of the holders of the common stock. The issuance of preferred stock, while providing flexibility in connection with possible acquisitions and other corporate purposes, could, among other things, have the effect of delaying, deferring or preventing a change in our control that may otherwise benefit holders of our common stock and may adversely affect the market price of the common stock and the voting and other rights of the holders of common stock.

Anti-Takeover Effects of Provisions of Our Amended and Restated Certificate of Incorporation and Bylaws and Delaware and Washington Law

Our amended and restated certificate of incorporation and amended and restated bylaws contain certain provisions that are intended to enhance the likelihood of continuity and stability in the composition of the board of directors and which may have the effect of delaying, deferring or preventing a future takeover or change in control unless such takeover or change in control is approved by the board of directors. These provisions include:

Classified Board

Our amended and restated certificate of incorporation provides that our board of directors will be divided into three classes of directors, with the classes as nearly equal in number as possible. At each annual meeting of the stockholders, a class of directors will be elected for a three-year term to succeed the directors of the same class whose terms are then expiring. As a result approximately one-third of our directors will be elected each year. The classification of directors will have the effect of making it more difficult for stockholders to change the composition of our board.

Our amended and restated certificate of incorporation also provides that, subject to any rights of holders of preferred stock to elect additional directors under specified circumstances, the number of directors will be fixed exclusively pursuant to a resolution adopted by our board of directors. Any additional directorships resulting from an increase in the number of directors will be distributed among the three classes so that, as nearly as possible, each class shall consist of one third of the board of directors. Our board of directors currently has seven members.

Action by Written Consent; Special Meetings of Stockholders

Our amended and restated certificate of incorporation provides that stockholder action can be taken only at an annual or special meeting of stockholders and cannot be taken by written consent in lieu of a meeting. Our amended and restated certificate of incorporation and our amended and restated bylaws also provide that, except as otherwise required by law, special meetings of the stockholders can be called only by or at the direction of the board of directors pursuant to a resolution adopted by a majority of the total number of directors. Except as described above, stockholders are not permitted to call a special meeting or to require the board of directors to call a special meeting.

Removal of Directors

Our amended and restated certificate of incorporation provides that our directors may be removed only for cause by the affirmative vote of at least 66-2/3% of the voting power of our outstanding shares of capital stock, voting together as a single class and entitled to vote in the election of directors. This requirement of a supermajority vote to remove directors could enable a minority of our stockholders to prevent a change in the composition of our board.

Advance Notice Procedures

Our amended and restated bylaws establish an advance notice procedure for stockholder proposals to be brought before an annual meeting of our stockholders, including proposed nominations of persons for election to the board of directors. Stockholders at an annual meeting are only able to consider proposals or nominations specified in the notice of meeting or brought before the meeting by or at the direction of the board of directors or by a stockholder who was a stockholder of record on the record date for the meeting, who is entitled to vote at the meeting and who has given our Secretary timely written notice, in proper form, of the stockholder's intention to bring that business before the meeting. Although the amended and restated bylaws do not give the board of directors the power to approve or disapprove stockholder nominations of candidates or proposals regarding other business to be conducted at a special or annual meeting, the amended and restated bylaws may have the effect of precluding the conduct of certain business at a meeting if the proper procedures are not followed or may discourage or deter a potential acquirer from conducting a solicitation of proxies to elect its own slate of directors or otherwise attempting to obtain control of the company.

Super Majority Approval Requirements

The DGCL generally provides that the affirmative vote of a majority of the shares entitled to vote on any matter is required to amend a corporation's certificate of incorporation or bylaws, unless either a corporation's certificate of incorporation or bylaws requires a greater percentage. Our amended and restated certificate of incorporation and amended and restated bylaws provide that the affirmative vote of holders of at least 66-2/3% of the outstanding shares of capital stock, voting together as a single class and entitled to vote in the election of directors will be

required to amend, alter, change or repeal the amended and restated bylaws and the provisions described above in the amended and restated certificate of incorporation. This requirement of a supermajority vote could enable a minority of our stockholders to exercise veto power over any such amendments.

Authorized but Unissued Shares

Our authorized but unissued shares of common stock and preferred stock will be available for future issuance without stockholder approval. These additional shares may be utilized for a variety of corporate purposes, including future public offerings to raise additional capital, corporate acquisitions and employee benefit plans. The existence of authorized but unissued shares of common stock and preferred stock could render more difficult or discourage an attempt to obtain control of a majority of our common stock by means of a proxy contest, tender offer, merger or otherwise.

Exclusive Forum

Our 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 certificate of incorporation or our 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 capital stock shall be deemed to have notice of and to have consented to this provision of our certificate of incorporation. This choice of forum provision may have the effect of discouraging lawsuits against us and our directors, officers, employees and agents. The enforceability of similar choice of forum provisions in other companies' certificates of incorporation has been challenged in legal proceedings, and it is possible that, in connection with one or more actions or proceedings described above, a court could find the provision of our certificate of incorporation to be inapplicable or unenforceable.

In addition, our amended and restated bylaws provide that the U.S. federal district courts will be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act.

Section 203 of Delaware Law

We are subject to Section 203 of the DGCL, or Section 203. In general, Section 203 prohibits a publicly-held Delaware corporation from engaging in a "business combination" with an "interested stockholder" for a three-year period following the time that this stockholder becomes an interested stockholder, unless the business combination is approved in a prescribed manner. A "business combination" includes, among other things, a merger, asset or stock sale or other transaction resulting in a financial benefit to the interested stockholder. An "interested stockholder" is a person who, together with affiliates and associates, owns, or did own within three years prior to the determination of interested stockholder status, 15% or more of the corporation's voting stock. Under Section 203, a business combination between a corporation and an interested stockholder is prohibited unless it satisfies one of the following conditions: before the stockholder became interested, the board of directors approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder; upon consummation of the transaction which resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the voting stock outstanding, shares owned by persons who are directors and also officers, and employee stock plans, in some instances; or at or after the time the stockholder became interested, the business combination was approved by the board of directors of the corporation and authorized at an annual or special meeting of the stockholders by the affirmative vote of at least two-thirds of the outstanding voting stock which is not owned by the interested stockholder. A Delaware corporation may "opt out" of these provisions with an express provision in its original certificate of incorporation or an express provision

in its certificate of incorporation or bylaws resulting from a stockholders' amendment approved by at least a majority of the outstanding voting shares. We have not opted out of these provisions. As a result, mergers or other takeover or change in control attempts of us may be discouraged or prevented.

Washington Business Corporation Act

The laws of Washington, where our principal executive offices are located, impose restrictions on certain transactions between certain foreign corporations and significant stockholders. In particular, the Washington Business Corporation Act, or WBCA, prohibits a "target corporation," with certain exceptions, from engaging in certain "significant business transactions" with a person or group of persons which beneficially owns 10% or more of the voting securities of the target corporation, an "acquiring person," for a period of five years after such acquisition, unless the transaction or acquisition of shares is approved by a majority of the members of the target corporation's board of directors prior to the time of acquisition. Such prohibited transactions may include, among other things:

- any merger or consolidation with, disposition of assets to, or issuance or redemption of stock to or from, the acquiring person;
- any termination of 5% or more of the employees of the target corporation as a result of the acquiring person's acquisition of 10% or more of the shares; and
- allowing the acquiring person to receive any disproportionate benefit as a stockholder.

After the five-year period, a significant business transaction may take place as long as it complies with certain fair price provisions of the statute or is approved at an annual or special meeting of stockholders.

We will be considered a "target corporation" so long as our principal executive office is located in Washington, and: (1) a majority of our employees are residents of the state of Washington or we employ more than one thousand residents of the state of Washington; (2) a majority of our tangible assets, measured by market value, are located in the state of Washington or we have more than $50 million worth of tangible assets located in the state of Washington; and (3) any one of the following: (a) more than 10% of our stockholders of record are resident in the state of Washington; (b) more than 10% of our shares are owned of record by state residents; or (c) 1,000 or more of our stockholders of record are resident in the state.

If we meet the definition of a target corporation, the WBCA may have the effect of delaying, deferring or preventing a change of control.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is American Stock Transfer & Trust Company, LLC. The transfer agent and registrar's address is 6201 15th Avenue, Brooklyn, NY 11219. We are currently in the process of changing our transfer agent to Broadridge Financial Solutions, Inc., which we expect will be completed by the end of April 2021.

Nasdaq Global Market Listing

Our common stock is listed on The Nasdaq Global Market under the symbol "ALPN."

Limitation of Liability and Indemnification

Our amended and restated certificate of incorporation and amended and restated bylaws provide that we will indemnify our directors and officers, and may indemnify our employees and other agents, to the fullest extent permitted by the DGCL, which prohibits our amended and restated certificate of incorporation from limiting the liability of our directors for the following:

- any breach of the director's duty of loyalty to the corporation or its stockholders;

- any act or omission not in good faith or that involves intentional misconduct or a knowing violation of law;
- unlawful payments of dividends or unlawful stock repurchases or redemptions; or
- any transaction from which the director derived an improper personal benefit.

If Delaware law is amended to authorize corporate action further eliminating or limiting the personal liability of a director, then the liability of our directors will be eliminated or limited to the fullest extent permitted by Delaware law, as so amended. Our amended and restated certificate of incorporation does not eliminate a director's duty of care and in appropriate circumstances, equitable remedies, such as injunctive or other forms of non-monetary relief, remain available under Delaware law. This provision also does not affect a director's responsibilities under any other laws, such as the federal securities laws or other state or federal laws. Under our amended and restated bylaws, we will also be empowered to purchase insurance on behalf of any person whom we are required or permitted to indemnify.

In addition to the indemnification required in our amended and restated certificate of incorporation and amended and restated bylaws, we have entered into indemnification agreements with each of our current directors and officers. These agreements provide indemnification for certain expenses and liabilities incurred in connection with any action, suit, proceeding, or alternative dispute resolution mechanism, or hearing, inquiry, or investigation that may lead to the foregoing, to which they are a party, or are threatened to be made a party, by reason of the fact that they are or were a director, officer, employee, agent, or fiduciary of our company, or any of our subsidiaries, by reason of any action or inaction by them while serving as an officer, director, agent, or fiduciary, or by reason of the fact that they were serving at our request as a director, officer, employee, agent, or fiduciary of another entity. In the case of an action or proceeding by, or in the right of, our company or any of our subsidiaries, no indemnification will be provided for any claim where a court determines that the indemnified party is prohibited from receiving indemnification. We believe that these bylaw provisions and indemnification agreements are necessary to attract and retain qualified persons as directors and officers. We also maintain directors' and officers' liability insurance.

The limitation of liability and indemnification provisions in our amended and restated certificate of incorporation and amended and restated bylaws may discourage stockholders from bringing a lawsuit against directors for breach of their fiduciary duties. They may also reduce the likelihood of derivative litigation against directors and officers, even though an action, if successful, might benefit us and our stockholders. A stockholder's investment may be harmed to the extent we pay the costs of settlement and damage awards against directors and officers pursuant to these indemnification provisions. Insofar as we may provide indemnification for liabilities arising under the Securities Act to our directors, officers, and controlling persons pursuant to the foregoing provisions, or otherwise, we have been advised that, in the opinion of the Securities and Exchange Commission, such indemnification is against public policy as expressed in the Securities Act, and is, therefore, unenforceable. There is no pending litigation or proceeding naming any of our directors or officers as to which indemnification is being sought, nor are we aware of any pending or threatened litigation that may result in claims for indemnification by any director or officer.

Alpine Immune Sciences, Inc.

Non-Employee Director Compensation Guidelines

As of March 2021

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.	Annual Retainer for Board Membership: for general availability and participation in meetings and conference calls of our Board of Directors	$	40,000
B.	Additional Retainer for Board Chairman:	$	25,000
C.	Additional Retainers for Committee Membership:		
	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 20,000 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 10,000 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.

EXHIBIT 23.1

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the following Registration Statements:

(1) Registration Statement (Form S-8 No. 333-205220) pertaining to the 2012 Stock Incentive Plan of N30 Pharmaceuticals, Inc., 2015 Equity Incentive Plan of Nivalis Therapeutics, Inc. and Employee Stock Purchase Plan of Nivalis Therapeutics, Inc.,

(2) Registration Statement (Form S-8 No. 333-211197) pertaining to the Employment Inducement Awards of Nivalis Therapeutics, Inc.,

(3) Registration Statement (Post-Effective Amendment No. 1 on Form S-8 to Form S-4 No. 333-218134) pertaining to the Amended and Restated 2015 Stock Plan of Alpine Immune Sciences, Inc.,

(4) Registration Statement (Form S-8 No. 333-223965) pertaining to the Amended and Restated 2015 Stock Plan, as amended, and the 2015 Equity Incentive Plan of Alpine Immune Sciences, Inc.,

(5) Registration Statement (Form S-8 No. 333-225792, No. 333-230369, No. 333-237479, and No. 333-239233) pertaining to the 2018 Equity Incentive Plan of Alpine Immune Sciences, Inc.,

(6) Registration Statement (Form S-1 No. 333-230365) and related Prospectus of Alpine Immune Sciences, Inc. for the registration of 6,542,310 shares of its common stock,

(7) Registration Statement (Form S-1 No. 333-244409) and related Prospectus of Alpine Immune Sciences, Inc. for the registration 7,709,416 shares of its common stock,

(8) Registration Statement (Form S-8 No. 333-230372) pertaining to the Stand-Alone Inducement Stock Option Grant of Alpine Immune Sciences, Inc., and

(9) Registration Statement (Form S-3 No. 333-239760) of Alpine Immune Sciences, Inc. to offer or sell securities for the aggregate offering price of up to $60,000,000

of our report dated March 18, 2021, with respect to the consolidated financial statements of Alpine Immune Sciences, Inc., included in this Annual Report (Form 10-K) of Alpine Immune Sciences, Inc. for the year ended December 31, 2020.

/s/ Ernst & Young

Seattle, Washington
March 18, 2021

Exhibit 31.1

CERTIFICATION PURSUANT TO
RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Mitchell H. Gold, M.D., certify that:

1. I have reviewed this Annual Report on Form 10-K 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 supervision, 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: March 18, 2021

/s/ Mitchell H. Gold, M.D.

Mitchell H. Gold, M.D.

Executive Chairman and Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATION PURSUANT TO
RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Paul Rickey, certify that:

1. I have reviewed this Annual Report on Form 10-K 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 supervision, 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: March 18, 2021

/s/ Paul Rickey

Paul Rickey

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

Exhibit 32.1

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

In connection with the Annual Report of Alpine Immune Sciences, Inc. (the "Company") on Form 10-K for the year ended December 31, 2020, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Mitchell H. Gold, M.D., 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 H. Gold, M.D.
Mitchell H. Gold, M.D.
Executive Chairman and Chief Executive Officer
(Principal Executive Officer)

March 18, 2021

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

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

Exhibit 32.2

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

In connection with the Annual Report of Alpine Immune Sciences, Inc. (the "Company") on Form 10-K for the year ended December 31, 2020, 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)

March 18, 2021

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.