

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

**FORM 10-K**

(Mark One)

- ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934  
For the Fiscal Year Ended December 31, 2021  
OR  
 TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

**Corvus Pharmaceuticals, Inc.**  
(Exact name of registrant as specified in its charter)

Delaware  
(State or other jurisdiction  
of incorporation)

001-37719  
(Commission  
File Number)

46-4670809  
(IRS Employer  
Identification Number)

863 Mitten Road, Suite 102, Burlingame, CA 94010  
(Address of principal executive offices, including Zip Code)  
Registrant's telephone number, including area code: (650) 900-4520

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

Title of each class	Trading symbol(s)	Name of each exchange on which registered
Common Stock, Par Value \$0.0001 per share	CRVS	Nasdaq Global Market

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 Section 15(d) of the Act. Yes  No

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

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

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a 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   
Non-accelerated filer

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

As of June 30, 2021, the aggregate market value of Common Stock held by non-affiliates of the registrant was approximately \$65.0 million, computed by reference to the closing price as reported on The Nasdaq Stock Market. As of March 10, 2022, 46,553,511 shares of the registrant's common stock were outstanding.

**DOCUMENTS INCORPORATED BY REFERENCE**

Portions of the registrant's definitive proxy statement to be filed for its 2021 Annual Meeting of Stockholders are incorporated by reference into Part III hereof. Such proxy statement will be filed with the Securities and Exchange Commission within 120 days of the end of the fiscal year covered by this Annual Report on Form 10-K.

**CORVUS PHARMACEUTICALS, INC.**  
**ANNUAL REPORT ON FORM 10-K**  
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## Forward-Looking Statements

This Annual Report on Form 10-K contains forward-looking statements that involve risks and uncertainties. All statements other than statements of historical facts contained in this report are forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as “may,” “could,” “will,” “would,” “should,” “expect,” “plan,” “anticipate,” “believe,” “estimate,” “intend,” “predict,” “seek,” “contemplate,” “potential” or “continue” or the negative of these terms or other comparable terminology. These forward-looking statements include, but are not limited to, statements about:

- The extent to which the COVID-19 coronavirus (“COVID-19”) and related governmental regulations and restrictions may impact our business, including our research, clinical trials, manufacturing and financial condition;
- our expectations and beliefs regarding the potential benefits of our product candidates;
- our expectations regarding the clinical effectiveness of our product candidates and utility of our biomarker data;
- the anticipated timing, costs and conduct of our ongoing and planned clinical trials for mupadolimab (formerly CPI-006), CPI-818 and ciforadenant (formerly CPI-444), and planned preclinical studies and clinical trials for other product candidates in our development programs;
- our ability to develop, acquire and advance product candidates into, and successfully complete, clinical trials;
- the timing of the completion of our ongoing clinical trials of mupadolimab, CPI-818 and ciforadenant and the timing and availability of clinical data from such clinical trials;
- clinical and regulatory development plans with respect to mupadolimab, CPI-818 and ciforadenant and our other product candidates;
- our expectations regarding the potential market size and the size of the patient populations for mupadolimab, CPI-818 and ciforadenant and our other product candidates, if approved for commercial use;
- our ability to commercialize mupadolimab and our other product candidates, if approved;
- our commercialization, marketing and manufacturing capabilities and strategy;
- the pricing and reimbursement of our product candidates, if approved;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our product candidates, including the projected terms of patent protection;
- our or any existing or future collaborator’s ability to obtain and maintain intellectual property protection for our technologies and product candidates and our ability to operate our business without infringing the intellectual property rights of others;
- our ability to establish and maintain collaborations and retain commercial rights for our product candidates in such collaborations;
- the potential benefits of strategic collaborations, including our collaboration with Angel Pharmaceuticals, and our ability to enter into strategic arrangements;

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- developments and projections relating to our competitors and our industry, including competing therapies;
- our estimates regarding the effect of changes in the tax code as a result of recent federal tax legislation and uncertainty as to how some of those changes may be applied;
- our estimates regarding expenses, future revenue, capital requirements and needs for additional financing; and
- our financial performance.

Any forward-looking statements in this Annual Report on Form 10-K reflect our current views with respect to future events or to our future financial performance and involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by these forward-looking statements. Factors that may cause actual results to differ materially from current expectations include, among other things, those listed under Part I, Item 1A. Risk Factors and discussed elsewhere in this Annual Report on Form 10-K. Given these uncertainties, you should not place undue reliance on these forward-looking statements. Except as required by law, we assume no obligation to update or revise these forward-looking statements for any reason, even if new information becomes available in the future.

This Annual Report on Form 10-K also contains estimates, projections and other information concerning our industry, our business and the markets for certain drugs, including data regarding the estimated size of those markets, their projected growth rates and the incidence of certain medical conditions. Information that is based on estimates, forecasts, projections or similar methodologies is inherently subject to uncertainties, and actual events or circumstances may differ materially from events and circumstances reflected in this information. Unless otherwise expressly stated, we obtained this industry, business, market and other data from reports, research surveys, studies and similar data prepared by third parties, industry, medical and general publications, government data and similar sources. In some cases, we do not expressly refer to the sources from which this data is derived. In that regard, when we refer to one or more sources of this type of data in any paragraph, you should assume that other data of this type appearing in the same paragraph is derived from the same sources, unless otherwise expressly stated or the context otherwise requires.

Except where the context otherwise requires, in this Annual Report on Form 10-K, “we,” “us,” “our” and the “Company” refer to Corvus Pharmaceuticals, Inc.

### **Trademarks**

This Annual Report on Form 10-K includes trademarks, service marks and trade names owned by us or other companies. All trademarks, service marks and trade names included in this Annual Report on Form 10-K are the property of their respective owners.

## **Risk Factor Summary**

Below is a summary of the principal factors that make an investment in our common stock speculative or risky. This summary does not address all of the risks that we face. Additional discussion of the risks summarized in this risk factor summary, and other risks that we face, can be found below under the heading “Risk Factors” and should be carefully considered, together with other information in this Annual Report on Form 10-K and our other filings with the Securities and Exchange Commission (SEC) before making investment decisions regarding our common stock.

- We have a limited operating history, have incurred significant operating losses since our inception and expect to incur significant losses for the foreseeable future. We may never generate any revenue or become profitable or, if we achieve profitability, we may not be able to sustain it.
- We will require substantial additional financing to achieve our goals, and a failure to obtain this necessary capital when needed on acceptable terms, or at all, could force us to delay, limit, reduce or terminate our product development, other operations or commercialization efforts.
- The COVID-19 pandemic could adversely impact our business, including our clinical trials, and financial condition.
- Our product candidates are in various stages of development and may fail or suffer delays that materially and adversely affect their commercial viability. If we are unable to advance our product candidates through clinical development, obtain regulatory approval and ultimately commercialize such product candidates, or experience significant delays in doing so, our business will be materially harmed.
- Clinical drug development involves a lengthy and expensive process with an uncertain outcome, and the results of preclinical studies and early clinical trials are not necessarily predictive of future results. Any product candidate we or any of our existing or potential future collaborators advance into clinical trials, including mupadolimab, CPI-818 and ciforadenant, may not have favorable results in later clinical trials, if any, or receive regulatory approval.
- Any termination or suspension of, or delays in the commencement or completion of, our planned clinical trials could result in increased costs to us, delay or limit our ability to generate revenue and adversely affect our commercial prospects.
- Our product candidates are subject to extensive regulation, compliance with which is costly and time consuming, and such regulation may cause unanticipated delays or prevent the receipt of the required approvals to commercialize our product candidates.
- We are conducting clinical trials for mupadolimab, CPI-818 and ciforadenant, and we and Angel Pharmaceuticals may in the future, conduct additional clinical trials of product candidates, at sites outside the United States, and the FDA may not accept data from trials conducted in foreign locations.
- If we encounter difficulties enrolling subjects in our clinical trials, our clinical development activities could be delayed or otherwise adversely affected.

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- The occurrence of serious complications or side effects in connection with use of our product candidates, either in clinical trials or post-approval, could lead to discontinuation of our clinical development programs, refusal of regulatory authorities to approve our product candidates or, post-approval, revocation of marketing authorizations or refusal to approve new indications, which could severely harm our business, prospects, operating results and financial condition.
- We may not be successful in our efforts to identify or discover additional product candidates.
- We rely, and expect to continue to rely, on third parties to conduct our clinical trials. If these third parties do not meet our deadlines or otherwise conduct the trials as required, our clinical development programs could be delayed or unsuccessful and we may not be able to obtain regulatory approval for or commercialize our product candidates when expected, or at all.
- We rely on third parties to conduct some or all aspects of our manufacturing, research and preclinical and clinical testing, and these third parties may not perform satisfactorily.
- We, or our third-party manufacturers, may be unable to successfully scale-up manufacturing of our product candidates in sufficient quality and quantity, which would delay or prevent us from developing our product candidates and commercializing approved products, if any.
- If we are unable to commercialize our product candidates or if we experience significant delays in obtaining regulatory approval for, or commercializing, any or all of our product candidates, our business will be materially and adversely affected.
- If we do not achieve our projected development goals in the time frames we announce and expect, the commercialization of our products may be delayed and, as a result, our stock price may decline.
- We face competition from entities that have developed or may develop product candidates for cancer, including companies developing novel treatments and technology platforms. If these companies develop technologies or product candidates more rapidly than we do or their technologies are more effective, our ability to develop and successfully commercialize product candidates may be adversely affected.
- An active, liquid and orderly market for our common stock may not be sustained.
- The trading price of the shares of our common stock could be highly volatile, and investors in our common stock could incur substantial losses.

## Part I

### Item 1. Business

#### Overview

We are a clinical stage biopharmaceutical company. Our strategy is to focus our efforts on the development of immune modulator product candidates with the potential to treat solid cancers, T-cell lymphomas, autoimmune diseases and infectious diseases. We have built a pipeline of five programs, three of which are in clinical development.

Our lead product candidate is mupadolimab (formerly CPI-006), a humanized monoclonal antibody that is designed to react with a specific site on CD73. In both preclinical and in vivo studies in cancer patients and patients with COVID-19, mupadolimab has demonstrated binding to various immune cells and the enhancement of immune responses by activating B cells. We believe mupadolimab has the potential to be an important new therapeutic agent with a novel mechanism of action for the treatment of a broad range of cancers and infectious diseases.

Our next product candidate, CPI-818, is a selective, covalent inhibitor of ITK and is in a multi-center Phase 1/1b clinical trial in patients with various malignant T-cell lymphomas. CPI-818 is designed to inhibit the proliferation of certain malignant T-cells, and we believe it also has the potential to regulate the growth of abnormal T cells involved in autoimmunity and allergy.

Our third product candidate, ciforadenant (formerly CPI-444), is an oral, small molecule antagonist of the A2A receptor for adenosine with which we completed a Phase 2 expansion protocol in combination with Genentech, Inc.'s cancer immunotherapy, Tecentriq® (atezolizumab) for patients with either advanced or refractory renal cell cancer ("RCC"). Ciforadenant is designed to disable a tumor's ability to subvert attack by the immune system by blocking the binding of immunosuppressive adenosine in the tumor microenvironment to the A2A receptor.

Our molecularly targeted product candidates are designed to exhibit a high degree of specificity, which we believe has the potential to provide greater safety compared to other cancer therapies and may facilitate their development either as monotherapies or in combination with other cancer therapies such as immune checkpoint inhibitors or chemotherapy.

We believe the breadth and status of our pipeline demonstrates our management team's expertise in understanding and developing immunology focused assets as well as in identifying product candidates that can be in-licensed and further developed internally to treat many types of cancer. We hold worldwide rights to all of our product candidates (other than in greater China).

Our diverse and versatile product candidates have also enabled us to address markets in foreign markets. In October 2020, we announced the formation and launch of Angel Pharmaceuticals Co., Ltd. ("Angel Pharmaceuticals"), a new China based biopharmaceutical company with a mission to bring innovative quality medicines to Chinese patients for treatment of serious diseases including cancer, autoimmune diseases and infectious diseases. We formed Angel Pharmaceuticals as a wholly owned subsidiary and it launched with a post-money valuation of approximately \$106.0 million, based on an approximate \$41.0 million cash investment from a Chinese investor group that includes funds associated with Tigermed and Betta Pharmaceuticals, Hisun Pharmaceuticals and Zhejiang Puissance Capital. Such cash is not available for our use. Contemporaneously with the financing, Angel Pharmaceuticals licensed the rights to develop and commercialize our three clinical-stage candidates – mupadolimab, CPI-818 and ciforadenant – in greater China and obtained global rights to our BTK inhibitor preclinical programs. Under the collaboration, we currently have a 49.7% equity interest in Angel Pharmaceuticals, excluding 7% of Angel's equity reserved for issuance under the Employee Stock Ownership Plan ("ESOP"), and are entitled to designate three individuals on Angel's five-person Board of Directors.

**Product Pipeline**

Our product candidate pipeline includes the following:

Target	Indication	DEVELOPMENT STATUS				
		Lead Optimization	IND-Enabling	Phase 1/1b	Phase 1b/2	Phase 3
B Cell Activator & Anti-CD73	NSCLC	Mupadolimab (CPI-006)				
	HNSCC	Mupadolimab (CPI-006)				
ITK Inhibitor	T-cell lymphoma	CPI-818				
	Autoimmune lympho-proliferative disease	CPI-818				
A2AR Inhibitor	Renal cell cancer	Ciforadenant				
Anti-CXCR2	Multiple cancers	CPI-182				
	Inflammation	CPI-182				
A2BR Inhibitor	Fibrosis	CPI-935				

**Mupadolimab, B-Cell Activating anti-CD73 antibody.** CD73 is an ectonucleotidase often found on lymphocytes, tumors and other tissues and is believed to play an important role in tumor immune suppression by catalyzing the production of extracellular adenosine. CD73 also is a cellular adhesion molecule involved in lymphocyte activation and trafficking to lymphoid tissues. CD73 is expressed in lymph nodes where it plays a role in immune response to antigens. These functions of CD73 are independent of adenosine production.

Mupadolimab is an investigational, humanized, engineered anti CD73 monoclonal antibody that is designed to bind to a critical epitope involved in B cell signaling, which are the cells responsible for antibody production and presentation of antigens to T cells, which are involved in cell mediated immunity to cancers and infectious agents. In preclinical studies, mupadolimab bound to B cells and triggered signaling, that resulted in activation of B cells and expression of cell surface markers involved in lymphocyte trafficking. In clinical studies, both cancer patients and patients with COVID-19 treated with mupadolimab experienced activation of B cells into antigen specific antibody producing cells. In patients, mupadolimab activated B cells, resulting in morphological and surface marker changes consistent with B cell differentiation into antibody secreting plasma cells and memory B cells, the cells responsible for immunologic memory.

Mupadolimab is also designed to inhibit the production of adenosine by blocking the catalytic conversion of adenosine monophosphate to adenosine. In the tumor microenvironment, inhibition of the production of adenosine is believed to reduce tumor mediated immunosuppression.

- Mupadolimab has potential features that we believe could distinguish it from other reported anti-CD 73 antibodies in clinical development:
  - Designed to activate B cells;
  - Absence of a “hook effect.” This suggests that mupadolimab may exhibit consistent blocking of enzymatic activity over broad range of antibody concentrations with no loss of antibody binding or enzyme inhibition at higher antibody concentrations; and
  - Did not induce loss of CD 73 target from cell surface in preclinical studies.

Our work in both cancer and viral diseases, such as COVID-19, have provided important insights and data into how we may best utilize the potential properties of our antibody candidate in the clinic. Our studies have uncovered a novel potential mechanism of action: mupadolimab is designed to activate B cells which may then be driven into antibody producing plasma cells by the presence of tumor associated antigens within the tumor. Recent work by several groups have highlighted the importance of B cells in anti-tumor immunity. As published in Nature in 2020, investigators have shown that B cell infiltration in some tumors were strong predictors of response to immunotherapies and predictors of favorable outcomes.

Cancer cells are known to express neoantigens. These antigens are derived from mutations that occur in the genome of the cancer cells. We believe that if sufficient immune responses to these antigens can be generated, it could have a beneficial effect on tumor growth or response to therapies. Various immunotherapies are now approved to enhance immune responses to tumor antigens such as anti-PD1 antibodies. In addition to neoantigens resulting from mutations, viruses can also lead to cancers, which express viral antigens that are potential targets of immunotherapies. Human papilloma virus (HPV) for example, is associated with oropharyngeal, cervical, anal, vulvar, penile and other cancers. Recent data from others have revealed that B cells in the tumor microenvironment of oropharyngeal cancers are producing antibodies to HPV related antigens that are expressed within the tumors.

The findings that mupadolimab stimulated immune responses through B cell activation has motivated us to conduct further studies of this agent in combination with anti PD1 antibodies. The rationale is that synergies may be achieved by combining activation of B cells, or stimulation of immune response, with checkpoint inhibitors such as anti PD1 antibodies, which remove the brakes on immune system. We believe mupadolimab has the potential to improve on existing immunotherapies by simultaneously stepping on the gas (stimulating) and simultaneously releasing the brakes of the immune system.

#### *Mupadolimab Oncology Phase 1/1b Clinical Trial*

In February 2018, we initiated a Phase 1/1b clinical trial with mupadolimab administered alone and in combination with citoradenant, and in combination with pembrolizumab, and in a triplet combination of mupadolimab, citoradenant and pembrolizumab. As of March 1, 2022, we have enrolled over 110 patients on this trial at doses of up to 24 mg/kg every three weeks. Key findings from this trial as of March 1, 2022 include the observation that mupadolimab was well-tolerated and evidence of B-cell activation and lymphocyte trafficking was observed in patients that received single doses as low as 1 mg/kg. Treatment with mupadolimab was also associated with increases in memory B-cells in the blood, the emergence of new B-cell clones and, in some patients, the production of novel anti-tumor antibodies.

In our ongoing Phase 1/1b cancer clinical trial with mupadolimab, we have observed evidence of anti-tumor activity in NSCLC and in oropharyngeal head and neck cancers. Based on these findings, during the second quarter, we began enrolling an expansion cohort of up to 15 patients with advanced, HPV+ head and neck cancer that have failed treatment with anti-PD-1 therapy and chemotherapy. In this cohort, mupadolimab will be given in combination with pembrolizumab. Our objective is to evaluate response rate in this expansion cohort. In the third quarter of 2021, we began enrolling an expansion of up to 15 patients with relapsed refractory NSCLC who have failed therapies with anti-PD(L)-1 therapy and chemotherapy. In this cohort, mupadolimab will be given in combination with pembrolizumab. Our objective is to evaluate response rate in this expansion cohort.

At the 2021 Annual Meeting of the Society for Immunotherapy of Cancer (“SITC”) in November 2021, we presented interim data demonstrating anti-tumor activity in NSCLC and head and neck cancer (“HNSCC”) patients treated with 12 mg./kg. or greater of mupadolimab as a single agent, in combination with citoradenant, in combination with pembrolizumab or in combination with pembrolizumab and citoradenant. These patients had advanced refractory disease and failed a median of three prior therapies. All but one had failed therapy with prior anti PD(L)-1 antibodies. There were sixteen evaluable NSCLC and HNSCC patients. Seven patients achieved tumor regression, which did not meet the criteria for partial response by RECIST. However, for the patients that showed tumor regression, six patients had progressive disease as their best response to their last treatment prior to entering the Phase 1/1b clinical trial, which indicates that the tumors in these patients were not responsive to their last therapy. The seven patients who showed tumor regression on the trial were treated for a period of 4.5 to 12.5 months.

Based on the interim results presented at SITC, we plan to initiate a randomized Phase 2 clinical trial of

mupadolimab as a front-line therapy for the treatment of patients with advanced NSCLC. The randomized, blinded trial will compare standard chemotherapy plus pembrolizumab (anti-PDL-1) with or without mupadolimab. The trial is planned to enroll approximately 150 patients with any tumor PDL-1 expression. The primary endpoint for the study will be progression free survival (“PFS”) and secondary endpoints will include objective response rate and overall survival.

In February 2021, we initiated a Phase 3 trial evaluating a single dose of mupadolimab in a global, randomized, double-blind trial designed to evaluate the efficacy and safety of mupadolimab compared to placebo in hospitalized patients with mild-to-moderate COVID-19. On July 15, 2021, we announced that we discontinued our Phase 3 clinical trial due to positive trends exhibited by COVID-19 vaccines in lowering serious infection and hospitalizations due to COVID-19. The discontinuation was not related to any safety or efficacy issues observed in the trial patients. On September 21, 2021, we published preliminary results of our discontinued Phase 3 trial. The primary endpoint of the trial was the proportion of patients free from respiratory failure or death within 28 days after receiving either mupadolimab 2mg/kg, 1mg/kg or placebo. Forty patients were enrolled in the clinical trial. In the 2mg/kg cohort, 93.3% of patients were alive and free from respiratory failure compared to 85.7% in the 1mg/kg cohort and 81.1% in the placebo. Secondary endpoints also favored mupadolimab treatment cohorts. Due to the number of participants enrolled in the trial before it was discontinued, the foregoing results were not sufficiently powered for statistical significance.

We hold a nonexclusive, worldwide license (except for greater China) for all fields of use under Scripps’ rights in a hybridoma clone expressing an anti-CD73 antibody, and to progeny, mutants or unmodified derivatives of such hybridoma and any antibodies expressed by such hybridoma. In 2016, we filed a patent application covering the composition of matter of mupadolimab. In 2019, we filed patent applications covering the use of mupadolimab for immunomodulation and enhancement of anti-tumor immunity. In 2020, we filed a provisional U.S. patent application directed to the use of mupadolimab in the treatment of COVID-19 and other infectious diseases.

**CPI-818, ITK Inhibitor.** CPI-818 is an investigational selective, orally bioavailable, covalent inhibitor of ITK designed to have low nanomolar affinity. ITK, an enzyme that functions in T cell signaling and differentiation, is expressed predominantly in T cells, which are lymphocytes that play a vital role in immune responses. One of the key survival mechanisms of tumors is believed to be the reprogramming of T cells to create an inflammatory environment that inhibits anti-tumor immune response and favors tumor growth. We believe highly selective inhibitors of this enzyme will facilitate induction of T cell anti-tumor immunity and may be useful in the treatment of T cell lymphomas.

T cell signaling involving ITK is required in the development of T cells within the thymus, where ITK regulates the production of various T cell subsets and functions. The ITK cell signaling pathway is similar to the signaling that occurs in B cells, which is mediated by a homologous enzyme known as BTK, the target of ibrutinib, an approved treatment for patients with B cell lymphomas and leukemias. We believe that inhibiting ITK in malignant T cells may be of therapeutic benefit in patients with T cell leukemias and lymphomas, analogous to the effects of ibrutinib on B cell lymphomas and leukemias. In malignant T cells, ITK was found to be over expressed specifically in certain T cell lymphomas, including peripheral T cell lymphoma (“PTCL”), angioimmunoblastic T cell lymphoma (“AITL”) and in a subgroup of T lymphoblastic leukemia and lymphoma (“T ALL”).

In ITK genetic knockout mice, which completely lack expression of ITK, T cells exhibit defects in T helper cell differentiation and cytokine secretion but retain the ability to differentiate into cytotoxic T cells that secrete IL 2 and IFN $\gamma$ , which are the cells responsible for tumor rejection. We believe that skewing T helper cell differentiation to favor cytotoxic T cells may be beneficial in treating many types of cancer.

We have developed CPI-818 by targeting the cysteine amino acid residue at position 442 in the ITK protein. We believe covalent targeting of ITK has the potential to provide a selective and prolonged duration of activity without the need for high systemic exposures and thereby improve the therapeutic window. This approach was previously used by our cofounders to generate ibrutinib. We believe that the potential selectivity of CPI-818 could mimic the immune properties seen in ITK knockout mice and skew the immune response toward a more favorable anti-tumor immune response. In addition, ITK plays a role in the proliferation of some T-cell lymphomas and we believe its inhibition could lead to growth arrest and/or tumor cell cytotoxicity. In our preclinical studies of CPI-818, objective tumor responses were observed in dogs with spontaneous T-cell lymphomas.

CPI-818 is orally bioavailable and has achieved cellular occupancy of the target *in vivo* in various animal

models. Pre-clinical studies have demonstrated that CPI-818 was well-tolerated *in vivo* and resulted in inhibition of T-cell activation. In March of 2019, we initiated a phase 1/1b study of CPI-818 in patients with advanced refractory T-cell lymphomas.

CPI-818 is currently being studied in a Phase 1/1b clinical trial that was designed to select the recommended dose of CPI-818 and evaluate its safety, pharmacokinetics (“PK”), target occupancy, biomarkers and efficacy. The study employed an adaptive, expansion cohort design, with an initial phase that evaluated escalating doses (100, 200, 400, 600 mg taken twice a day) in successive cohorts of patients, followed by a second phase that is designed to evaluate safety and tumor response to the recommended dose of CPI-818 in disease-specific patient cohorts. By protocol design, treatment is discontinued after one year or upon disease progression. The study enrolled 25 patients from the United States, Australia and South Korea with several types of advanced, refractory T cell lymphomas, including nine patients with peripheral T-cell lymphoma (“PTCL”), 12 patients with cutaneous T-cell lymphoma (“CTCL”), and four patients with other T-cell lymphomas. All patients had failed multiple prior therapies.

In December 2020 at the American Society of Hematology Annual Meeting, we presented preliminary Phase 1/1b clinical data with CPI-818 in refractory T cell lymphomas in patients receiving adequate doses of the drug. The data presented was as follows:

- Of the seven evaluable patients with PTCL, there were two objective tumor responses as of the cut-off date of October 5, 2020:
  - One patient, who previously failed chemotherapy and high dose chemotherapy with autologous bone marrow transplantation, achieved a complete response (“CR”) with CPI-818 at month 8 that remained ongoing after 12 months on study. The patient received CPI-818 for 12 months and the CR persisted beyond discontinuation of therapy (per the study protocol, the patient stopped receiving therapy after 12 months on study).
  - One patient who failed multiple prior therapies achieved a partial response at four months on therapy. This patient then went on to receive a bone marrow transplant.
- Of the 11 evaluable patients with CTCL:
  - One patient achieved a complete response in lymph node disease and continued to have stable cutaneous disease at more than 12 months on therapy as of November 2, 2020.
  - Three patients achieved stable disease on therapy for between 3 and 5 months.
- There was a dose dependent increase in receptor occupancy, with trough occupancy >75% observed at the 200, 400 and 600 mg doses.
- No dose limiting toxicities and no grade 3 or 4 treatment related adverse events have been observed to date.

Based on the interim results from our Phase 1/1b clinical trial, Angel Pharmaceuticals, has joined this clinical trial with a goal of enrolling patients with PTCL. PTCL is more common in China than the United States representing approximately 26% of non-Hodgkins lymphomas in China. In January 2022, Angel Pharmaceuticals announced the enrollment of the first patient in the clinical trial.

We have filed patent applications covering composition of matter and uses of our ITK inhibitors and hold exclusive worldwide rights (except for greater China) for all indications.

**Ciforadenant Adenosine A2A Receptor Antagonist.** Ciforadenant is an oral, small molecule antagonist of the A2A receptor for adenosine that we in-licensed from Vernalis (R&D) Limited (“Vernalis”) in February 2015. Since licensing ciforadenant, we have conducted extensive laboratory studies *in vitro* and *in vivo* in animal models to evaluate ciforadenant’s immune enhancing and anti-tumor properties. In these studies, orally administered ciforadenant inhibited tumor growth in multiple mouse models of cancer as a single agent, in combination with anti-PD-1, in combination with anti-PD-L1, in combination with other immuno oncology agents and in combination with certain chemotherapy drugs.

We also have shown *in vitro* that ciforadenant blocked adenosine mediated immunosuppression by restoring T cell function. In addition, we have shown anti-tumor activity in mice for a significant time following oral administration, which appeared to be mediated through a long lasting memory immune response.

Adenosine activates an immune checkpoint, the adenosine A2A receptor, that is used by the body to limit inflammation and immune responses. It is produced during acute, inflammatory processes in two steps. Increased levels of adenosine seen in tumors interact with the A2A and A2B receptors expressed on several cells of the immune system, including T cells, NK cells, macrophages, dendritic cells and myeloid derived suppressor cells, as well as other cells, which has the effect of dampening the immune response to the tumor.

A significant body of data indicates that targeting the adenosine cancer axis through the A2A receptor can promote anti-tumor immune responses leading to tumor regression. Consistent with studies of the inhibition of the A2A receptor, A2A receptor gene knockout mice, which completely lack expression of the A2A receptor, exhibit improved anti-tumor immunity. In addition, several preclinical tumor model studies have shown that treatment with A2A receptor inhibitors leads to tumor regression that is enhanced when administered in combination with various other checkpoint inhibitors, such as anti-PD-1 therapies and anti-CTLA 4 therapies. Preclinical studies in animal tumor models have examined use of ciforadenant in combination with anti PD1, in combination with anti CTLA4 and as a triplet of ciforadenant, anti PD1 and anti CTLA-4 antibodies. In our published studies in Cancer Immunology Research, combinations of ciforadenant with anti CTLA-4 have resulted in a high portion of cured animals, even when administered to animals with established tumors. These results provided the rationale for the use of ciforadenant in combination with nivolumab and ipilimumab in renal cell cancer patients.

In January 2016, we began enrolling patients in a large expansion cohort trial for ciforadenant. This Phase 1/1b clinical trial is designed to examine safety, tolerability, biomarkers and preliminary efficacy of ciforadenant in several solid tumor types, both as a single agent and in combination with Genentech, Inc.'s cancer immunotherapy, Tecentriq, a fully humanized monoclonal antibody targeting PD-(L)1. In 2018, we amended our Phase 1/1b protocol to enroll patients in a Phase 1b/2 clinical trial with RCC who have failed therapies with both anti-PD-(L)1 antibodies and TKIs.

#### *Interim Results Published in the Journal Cancer Discovery*

Results in 68 patients with treatment-refractory RCC were published in January 2020 in the journal Cancer Discovery.

Key findings from the published results include:

- Disease control for more than 6 months was observed in 39% and 17% of patients receiving combination therapy and monotherapy, respectively.
- For patients receiving combination therapy, 11% experienced a confirmed partial response (“PR”) (as determined by RECIST criteria). Several additional patients experienced tumor regression not meeting the criteria for a PR. For patients receiving monotherapy, one patient experienced a confirmed PR, one experienced an unconfirmed PR, and several patients experienced tumor regression not meeting the PR criteria.
- Responses were seen in both the combination therapy and monotherapy arms, and in patients who failed prior anti-PD-(L)1 therapy.
- Progression-free survival (as assessed by RECIST criteria) was 5.8 months with combination therapy and 4.1 months with monotherapy.
- Overall survival (OS) was 90% at 25 months follow-up with combination therapy and 69% at 16 months follow-up with monotherapy.
- Combination therapy was superior to monotherapy with respect to OS, response rate, disease control rate and progression-free survival.

- The recently described adenosine gene signature (AdenoSig) showed a statistically significant correlation with tumor response and disease control rates ( $p < 0.008$ ). We evaluated adenosine gene signatures in pretreatment biopsies from 30 patients. Of the patients showing a low adenosine gene signature, none exhibited signs of tumor regression. In contrast, patients with a high adenosine gene signature had a 17% (N=18) overall response rate by RECIST criteria.
- Ciforadenant was well tolerated with grade 3 adverse events that were infrequent (less than 5%) and reversible.

This study supports the tumor immune enhancing potential of adenosine pathway blockade. The unique mechanism of action and safety results suggest that this treatment, if successfully developed and approved, may be valuable, particularly in patients who have failed anti-PD-(L)1 therapy or as a combination to prevent the development of resistance. The studies also demonstrate that RCC exhibited high levels of adenosine pathway related genes.

#### *Updated Data at the ASCO20 Virtual Scientific Program*

Updated data on 51 RCC patients that were treated with ciforadenant monotherapy or in combination with Genentech's Tecentriq® (atezolizumab), an anti-PD-L1 antibody, and whose tumors were biopsied to test with the adenosine gene signature was reported at ASCO 2020. The key updates from the presentation include:

- 31 patients (30 evaluable) were positive for the adenosine signature and 20 patients were negative. Patients had a median of three prior therapies, including 86% that failed a prior anti-PD-(L)1 therapy.
- In the AdenoSig positive group, there were five PRs, (as assessed by RECIST criteria) for an ORR of 17% and six additional patients that had tumor regression not meeting the criteria for a PR.
- In the AdenoSig negative group, there were no PRs and no patients with tumor regression.
- In the AdenoSig positive group, the progression free survival curve plateaued at 23% at 40 weeks, compared to declining to 0% in the AdenoSig negative group.

We are now planning a Phase 1b/2 clinical trial of ciforadenant in a triplet combination with ipilimumab, and nivolumab. We plan to conduct this clinical trial with the Kidney Cancer Consortium. The trial is planned to enroll approximately 60 patients. The endpoint of the trial is deep response rate defined as greater than 50% reduction of tumor volume. Deep response rates in renal cell cancer have been found to correlate with long term progression free survival. The adenosine signature biomarker will also be evaluated in tumor biopsy specimens.

The issued U.S. patents that we in licensed from Vernalis for ciforadenant are directed to the composition of matter of ciforadenant and its method-of-use for treating disorders treatable by purine receptor blocking. The composition of matter patent covering ciforadenant is expected to expire in the United States in July 2029, excluding any patent term extension that may be available. We hold an exclusive, worldwide license (except for greater China) under these patent rights and related know how, including a limited right to grant sublicenses, for all fields of use, to develop, manufacture and commercialize products containing certain adenosine receptor antagonists, including ciforadenant. We have also filed patent applications covering the use of ciforadenant in combination with other checkpoint inhibitors, and the use of various biomarkers to select and monitor patients receiving therapy.

***CPI-182, Anti-CXCR2 Antibody designed to block inflammation and Myeloid Suppression.*** In 2017, we in-licensed this monoclonal antibody designed to block CXCR2, a novel target expressed on neutrophils and various inflammatory cells including myeloid derived suppressor cells ("MDSC"). Preclinical studies have demonstrated that this antibody blocked neutrophil function and migration, and MDSCs. MDSCs are involved in tumor immunosuppression and blockade of these cells may improve anti-tumor immunity. A publication describing this antibody was published in the journal MABS in January 2021. Preclinical data in vivo in mice demonstrated that CPI-182 was active in models of rheumatoid arthritis and in models of atopic dermatitis. We believe these data support the role of CXCR in inflammatory diseases and demonstrate that CPI-182 may have the potential to treat these conditions. This product candidate is now in Investigational New Drug application ("IND")-enabling studies and scale-up

manufacturing.

**CPI-935, Adenosine A2B Receptor Antagonist.** Adenosine A2B receptors have been found to play an important role in the immune response to tumors as well as in inflammation and fibrosis. Similar to adenosine A2A receptors, adenosine binds to adenosine A2B receptors, which leads to immunosuppression. Preclinical models have shown that inhibition of A2B receptors prevented fibrosis. In 2018, we selected a development candidate for this program, a small molecule antagonist of the A2B receptor.

### **Manufacturing**

We do not own or operate, and currently have no plans to establish any manufacturing facilities. We currently rely, and expect to continue to rely, on third parties for the manufacture of our product candidates for clinical testing, as well as for manufacture of any products that we may commercialize. We are able to internally produce small quantities of our product candidates required for relatively short preclinical animal studies. We believe that this allows us to accelerate the drug development process by not having to rely on third parties for all of our research and development needs. However, we currently rely, and expect to continue to rely, on a number of contract manufacturers to produce sufficient quantities of our product candidates for use in more lengthy preclinical development and clinical trials and in relation to any future commercialization of our product candidates. Additional contract manufacturers are used to fill, label, package and distribute investigational drug products. This strategy allows us to maintain a more efficient infrastructure, avoid depending on our own manufacturing facility and equipment while simultaneously enabling us to focus our expertise on developing our products. Although we believe we have multiple potential sources for the manufacturing of our product candidates, we currently rely on several different manufacturers who supply different components of the ciforadenant and CPI-818 molecules, on one manufacturer for mupadolimab drug substance and other third-party manufacturers to produce our other product candidates.

### **Competition**

The pharmaceutical and biotechnology industries are characterized by intense competition and rely heavily on the ability to move quickly, adapt to changing medical and market needs, and develop and maintain strong intellectual property positions. We believe that the development experience of our scientific and management teams, as well as the strength and promise of our product candidates, provides us with a competitive advantage; nevertheless, we face potential competition from myriad sources, including pharmaceutical and biotechnology companies, academic institutions, governmental agencies and public and private research institutions.

Kyowa Hakko Kirin has approval in Japan and the United States for istradefylline, an A2A antagonist, in Parkinson's disease. Within oncology, Novartis has announced an exclusive licensing agreement with Palobiofarma SL and is conducting a Phase 1 trial with an A2A antagonist. AstraZeneca plc is conducting clinical trials with an A2A antagonist for use in cancer therapy. Merck KGaA has entered into a pre-clinical collaboration with Domain Therapeutics Inc. to develop programs targeting the adenosine pathway. In addition, Redoxtherapies, which was acquired by Juno Therapeutics and subsequently by Celgene, and Arcus Biosciences are developing A2A receptor antagonists for cancer. AstraZeneca, Bristol-Myers Squibb, and Novartis, in partnership with Surface Oncology, have initiated clinical trials with anti-CD73 antibodies in cancer patients. Recently, AstraZeneca reported positive results in a Phase 2 clinical trial in Stage 3 NSCLC with the combination of durvalumab and their anti CD73 antibody, oleclumab. More generally, in the field of immunoncology, there are large pharmaceutical companies with approved products or products in late-stage development that target other immune checkpoints, including PD-1, PD-L1 or CTLA-4. These companies include Bristol-Myers Squibb (nivolumab, ipilimumab), Merck (pembrolizumab), Genentech (atezolizumab) and AstraZeneca (durvalumab, tremelimumab). Janssen Pharmaceuticals and AbbVie are co-marketing Imbruvica (ibrutinib), which is a small molecule inhibitor of the kinase BTK that has also been reported to inhibit ITK.

### **Intellectual Property**

We strive to protect and enhance the proprietary technology, inventions, and improvements that are commercially important to our business, including seeking, maintaining and defending patent rights, whether developed internally or licensed from our collaborators or other third parties. Our policy is to seek to protect our proprietary

position by, among other methods, filing patent applications in the United States and in jurisdictions outside of the United States covering our proprietary technology, inventions, improvements and product candidates that are important to the development and implementation of our business. We also rely on trade secrets and know-how relating to our proprietary technology and product candidates, continuing innovation, and in-licensing opportunities to develop, strengthen and maintain our proprietary position in the field of immuno-oncology. We also plan to rely on data exclusivity, market exclusivity, and patent term extensions when available. Our commercial success will depend in part on our ability to obtain and maintain patent and other proprietary protection for our technology, inventions, and improvements; to preserve the confidentiality of our trade secrets; to obtain and maintain licenses to use intellectual property owned by third parties; to defend and enforce our proprietary rights, including any patents that we may own in the future; and to operate without infringing on the valid and enforceable patents and other proprietary rights of third parties.

We have in-licensed patents and patent applications directed to certain of our product candidates and related uses thereof. We also possess and in-license substantial know-how and trade secrets relating to the development and commercialization of our product candidates, including related manufacturing processes and technology. As of January 20, 2022, our owned and licensed patent portfolio consisted of fourteen licensed U.S. issued patents, one licensed U.S. pending patent applications, six owned U.S. issued patents, twelve owned U.S. pending patent applications, and one owned U.S. provisional patent applications directed to mupadolimab, CPI-818 and ciforadenant, and certain of our other proprietary technology, inventions, improvements or other potential product candidates. In addition, our owned and licensed patent portfolio included thirty-eight licensed patents, eight licensed patent applications, three owned patents, and seventy-one owned patent applications pending in jurisdictions outside of the United States that are foreign counterparts to one or more of the foregoing U.S. patents and patent applications. The patents and patent applications outside of the United States in our portfolio are held primarily in Europe, Canada, Japan, Australia and China.

With respect to the immuno-oncology product candidates and processes we intend to develop and commercialize in the normal course of business, we intend to pursue patent protection covering, when possible, compositions, methods of use, dosing and formulations. We may also pursue patent protection with respect to manufacturing and drug development processes and technologies.

Issued patents can provide protection for varying periods of time, depending upon the date of filing of the patent application, the date of patent issuance, and the legal term of patents in the countries in which they are obtained. In general, patents issued for applications filed in the United States can provide exclusionary rights for 20 years from the earliest effective filing date. In addition, in certain instances, the term of an issued United States patent that covers or claims an FDA approved product can be extended to recapture a portion of the term effectively lost as a result of the FDA regulatory review period, which is called patent term extension. The restoration period cannot be longer than five years and the total patent term, including the restoration period, must not exceed 14 years following FDA approval. The term of patents outside of the United States varies in accordance with the laws of the foreign jurisdiction, but typically is also 20 years from the earliest effective filing date. The issued United States patents we license from Vernalis directed to the composition of matter of ciforadenant and its method of use for treating disorders treatable by purine receptor blocking are expected to expire between May 2022 and July 2029, excluding any patent term extension that may be available. The granted U.S. and foreign patents and pending U.S. and foreign patent application and PCT International patent applications, if granted as patents, that we own directed to the composition of matter and methods of treatment for mupadolimab are expected to expire between December 2036 and June 2037, excluding any patent term extension that may be available. The granted U.S. and foreign patents and pending U.S. and foreign patent applications, if granted as patents, that we own directed to the composition of matter and methods of treatment for CPI 818 are expected to expire November 2037, excluding any patent term extension that may be available. However, the actual protection afforded by a patent varies on a product-by-product basis, from country-to-country, and depends upon many factors, including the type of patent, the scope of its coverage, the availability of regulatory-related extensions, the availability of legal remedies in a particular country, and the validity and enforceability of the patent.

The patent positions of companies like ours are generally uncertain and involve complex legal and factual questions. No consistent policy regarding the scope of claims allowable in patents in the field of immuno-oncology has emerged in the United States. The relevant patent laws and their interpretation outside of the United States is also uncertain. Changes in either the patent laws or their interpretation in the United States and other countries may diminish

our ability to protect our technology or product candidates and enforce the patent rights that we license, and could affect the value of such intellectual property. In particular, our ability to stop third parties from making, using, selling, offering to sell, or importing products that infringe our intellectual property will depend in part on our success in obtaining and enforcing patent claims that cover our technology, inventions, and improvements. With respect to both licensed and company-owned intellectual property, we cannot guarantee that patents will be granted with respect to any of our pending patent applications or with respect to any patent applications we may file in the future, nor can we be sure that any patents that may be granted to us in the future will be commercially useful in protecting our products, the methods of use or manufacture of those products. Moreover, even the issued patents that we license do not guarantee us the right to practice our technology in relation to the commercialization of our products. Patent and other intellectual property rights in the pharmaceutical and biotechnology space are evolving and involve many risks and uncertainties. For example, third parties may have blocking patents that could be used to prevent us from commercializing our product candidates and practicing our proprietary technology, and the issued patents that we in-license and those that may issue in the future may be challenged, invalidated, or circumvented, which could limit our ability to stop competitors from marketing related products or could limit the term of patent protection that otherwise may exist for our product candidates. In addition, the scope of the rights granted under any issued patents may not provide us with protection or competitive advantages against competitors with similar technology. Furthermore, our competitors may independently develop similar technologies that are outside the scope of the rights granted under any issued patents that we own or exclusively in-license. For these reasons, we may face competition with respect to our product candidates. Moreover, because of the extensive time required for development, testing and regulatory review of a potential product, it is possible that, before any particular product candidate can be commercialized, any patent protection for such product may expire or remain in force for only a short period following commercialization, thereby reducing the commercial advantage the patent provides.

## **Licenses and Collaborations**

### ***Vernalis Licensing Agreement***

In February 2015, we entered into a license agreement with Vernalis, pursuant to which we were granted an exclusive, worldwide license under certain patent rights and know-how, including a limited right to grant sublicenses, for all fields of use to develop, manufacture and commercialize products containing certain adenosine receptor antagonists, including ciforadenant. The issued U.S. patents that we in-licensed from Vernalis pursuant to this agreement are directed to the composition of matter of ciforadenant and its method of use for treating disorders treatable by purine receptor blocking. These patents are expected to expire in the United States between January 2022 and July 2029, excluding any patent term extension that may be available. Vernalis has the first right to prosecute and maintain the licensed patent rights worldwide, subject to our right with respect to certain of the licensed patents to continue prosecution and maintenance if Vernalis elects not to do so. We also have the right to prosecute and maintain any patent rights that we may own that cover the licensed compounds that do not fall within the licensed patent rights. Pursuant to this agreement, we are required to use commercially reasonable efforts to conduct certain activities to obtain marketing authorizations for licensed products and to conduct certain preclinical and clinical studies for ciforadenant. We also must use commercially reasonable efforts to conduct certain preclinical and clinical studies to support the use of ciforadenant as an immunotherapeutic agent for cancer studies, and to meet certain specified development, regulatory and commercial milestones within specified time periods.

Pursuant to this agreement, we made a one-time cash payment to Vernalis in the amount of \$1.0 million upon entering into the agreement. We are also required to make cash milestone payments to Vernalis upon the successful completion of clinical and regulatory milestones for licensed products depending on the indications for which such licensed products are developed and upon achievement of certain sales milestones. In February 2017, we made a milestone payment of \$3 million to Vernalis following the expansion of a cohort of patients with renal cell cancer treated with single-agent ciforadenant in our Phase 1/1b clinical trial. The aggregate potential milestone payments are approximately \$220 million for all indications.

We have also agreed to pay Vernalis tiered incremental royalties based on the annual net sales of licensed products containing ciforadenant on a product-by-product and country-by-country basis, subject to certain offsets and reductions. The tiered royalty rates for products containing ciforadenant range from the mid-single digits up to the

low-double digits on a country-by-country net sales basis. The royalties on other licensed products that do not include ciferadenant also increase with the amount of net sales on a product-by-product and country-by-country basis and range from the low-single digits up to the mid-single digits on a country-by-country net sales basis.

The agreement will expire on a product-by-product and country-by-country basis upon the expiration of our payment obligations to Vernalis in respect of a particular product and country. Both parties have the right to terminate the agreement in the event of an uncured material breach by the other party. We may also terminate the agreement at our convenience by providing 90 days written notice, provided that we have not received notice of our own default under the agreement at the time we exercise such termination right. Vernalis may also terminate the agreement if we challenge a licensed patent or undergo a bankruptcy event.

### ***Scripps Licensing Agreement***

In December 2014, we entered into a license agreement with Scripps, pursuant to which we were granted a non-exclusive, world-wide license for all fields of use under Scripps' rights in certain know-how and technology related to a mouse hybridoma clone expressing an anti-human CD73 antibody, and to progeny, mutants or unmodified derivatives of such hybridoma and any antibodies expressed by such hybridoma, from which we developed mupadolimab. Scripps also granted us the right to grant sublicenses in conjunction with other proprietary rights we hold, or to others collaborating with or performing services for us. Under this license agreement, Scripps has agreed not to grant any additional commercial licenses with respect to such materials, other than march-in rights granted to the U.S. government.

Upon execution of the agreement, we made a one-time cash payment to Scripps of \$10,000 and are also obligated to pay a minimum annual fee to Scripps of \$25,000. The first minimum annual fee payment is due on the first anniversary of the effective date of the agreement and will be due on each subsequent anniversary of the effective date for the term of the agreement. We are also required to make performance-based cash payments upon successful completion of clinical and sales milestones. The aggregate potential milestone payments are \$2.6 million. We are also required to pay royalties on net sales of licensed products (including mupadolimab) sold by us, our affiliates and our sublicensees at a rate in the low-single digits. In addition, should we sublicense the rights licensed under the agreement, we have agreed to pay a percentage of sublicense revenue received at single digit percentages based on the achievement of development milestones.

Our license agreement with Scripps will terminate upon expiration of our obligation to pay royalties to Scripps under the license agreement. The license agreement is terminable by the consent of the parties, at will by us or upon providing 90 days written notice to Scripps, or by Scripps for certain material breaches by us, or if we undergo a bankruptcy event. In addition, Scripps may terminate our license on a product-by-product basis, or the entire agreement, if we fail to meet specified diligence obligations related to the development and commercialization of licensed products. Scripps may also terminate the agreement after the third anniversary of the effective date of the agreement if it reasonably believes, based on reports we provide to Scripps, that we have not used commercially reasonable efforts as required under the agreement, subject to a specified notice and cure period.

### ***Genentech Collaboration Agreements***

In October 2015, we entered into a clinical trial collaboration agreement with Genentech to evaluate the safety, tolerability and preliminary efficacy of ciferadenant combined with Genentech's investigational cancer immunotherapy, Tecentriq, a fully humanized monoclonal antibody targeting PD-L1, in a variety of solid tumors in our Phase 1/1b clinical trial. Pursuant to this agreement, we will be responsible for the conduct and cost of the relevant studies, under the supervision of a joint development committee made up of our representatives and representatives of Genentech. Genentech will supply Tecentriq. At this time, no further patients are being enrolled in this trial. As part of the agreement, we granted Genentech certain rights of first negotiation to participate in future clinical trials that we may conduct evaluating the administration of ciferadenant in combination with an anti-PD-1 or anti-PD-L1 antibody. If we do not reach agreement on the terms of any such participation by Genentech within a specified time period, we retain the right to collaborate with third parties in such activities. We also granted Genentech certain rights of first negotiation should we decide to license development and commercialization rights to ciferadenant. Should we not reach agreement

on the terms of such a license within a specified time of period, we retain the right to enter into a license with another third party. This agreement will expire after a set period of time following the provision by us of the final clinical study report to Genentech, which has not yet been finalized.

In May 2017, we entered into a second clinical trial collaboration agreement with Genentech. Under the new agreement, ciforadenant administered in combination with Tecentriq will be evaluated in a Phase 1b/2 randomized, controlled clinical study as second-line therapy in patients with NSCLC who are resistant and/or refractory to prior therapy with an anti-PD-(L)1 antibody. This study has completed patient enrollment of 16 patients. Genentech was responsible for the conduct of the study and we will share the cost of the Phase 1b/2 trial, which began enrolling patients in the fourth quarter of 2017. We are responsible for supplying ciforadenant and retain global development and commercialization rights to ciforadenant. This agreement will expire after a set period of time following the provision by Genentech of a final study report to us.

#### ***Monash License Agreement***

In April 2017, we entered into a license agreement with Monash University (“Monash”), pursuant to which we were granted an exclusive, sublicensable worldwide license under certain know-how, patent rights and other intellectual property rights controlled by Monash to research, develop, and commercialize certain antibodies directed to CXCR2 for the treatment of human diseases.

Upon execution of the agreement, we made a one-time cash payment to Monash of \$275,000 and reimbursed Monash for certain patent prosecution costs incurred prior to execution of the agreement. We are also obligated to pay an annual license maintenance fee to Monash of \$25,000 until a certain development milestone is met with respect to the licensed product, after which no further maintenance fee will be due. We are also required to make development and sales milestone payments to Monash with respect to the licensed products in the aggregate of up to \$45.1 million. We are also required to pay to Monash tiered royalties on net sales of licensed products sold by us, our affiliates and our sublicensees at a rate ranging in the low-single digits. In addition, should we sublicense our rights under the agreement, we have agreed to pay a percentage of sublicense revenue received at specified rates that are currently at low double digit percentages and decrease to single digit percentages based on the achievement of development milestones.

The term of our agreement with Monash continues until the expiration of our obligation to pay royalties to Monash thereunder. The license agreement is terminable at will by us upon providing 30 days written notice to Monash, or by either party for material breaches by the other party. In addition, Monash may terminate the entire agreement or convert the license to a non-exclusive license if we have materially breached our obligation to use commercially reasonable efforts to develop and commercialize a licensed product, subject to a specified notice and cure mechanism.

#### **Regulation**

Government authorities in the United States, at the federal, state and local level, and other countries extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, marketing and export and import of products such as those we are developing. A new drug must be approved by the FDA through the New Drug Application (“NDA”) process and a new biologic must be approved by the FDA through the Biologics License Application (“BLA”) process before it may be legally marketed in the United States.

#### ***United States Drug Development Process***

In the United States, the FDA regulates drugs under the federal Food, Drug, and Cosmetic Act (“FDCA”), and in the case of biologics, also under the Public Health Service Act (“PHSA”), and their implementing regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval may subject an applicant to administrative or judicial sanctions. These sanctions could include the FDA’s refusal to approve pending applications, withdrawal of an approval, a clinical hold, warning letters, product recalls,

product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement or civil or criminal penalties. Any agency or judicial enforcement action could have a material adverse effect on us.

The process required by the FDA before a drug or biologic may be marketed in the United States generally involves the following:

- completion of preclinical laboratory tests, animal studies and formulation studies in accordance with Good Laboratory Practice (“GLP”) regulations and other applicable regulations;
- submission to the FDA of an IND, which must become effective before human clinical trials may begin;
- approval by an institutional review board (“IRB”) or ethics committee at each clinical site before the trial is commenced;
- performance of adequate and well-controlled human clinical trials in accordance with Good Clinical Practice (“GCP”) regulations to establish the safety and efficacy of the proposed drug, or safety, purity and potency of the proposed biologic for its intended use;
- submission to the FDA of an NDA or BLA after completion of all clinical trials;
- satisfactory completion of an FDA Advisory Committee review, if applicable;
- a determination by the FDA within 60 days of its receipt of an NDA or BLA to file the application for review;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the drug is produced to assess compliance with current Good Manufacturing Practice (“cGMP”) requirements to assure that the facilities, methods and controls are adequate to preserve the drug’s identity, strength, quality and purity, and of selected clinical investigation sites to assess compliance with GCP; and
- FDA review and approval of the NDA or BLA to permit commercial marketing of the product for particular indications for use in the United States.

Once a pharmaceutical candidate is identified for development, it enters the preclinical testing stage. Preclinical tests include laboratory evaluations of product chemistry, toxicity and formulation, as well as animal studies. An IND sponsor must submit the results of the preclinical tests, together with manufacturing information and analytical data, to the FDA as part of the IND. The sponsor will also include a protocol detailing, among other things, the objectives of the clinical trial, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated, if the clinical trial lends itself to an efficacy evaluation. Some preclinical testing may continue even after the IND is submitted. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, places the clinical trial on a clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. Clinical holds also may be imposed by the FDA at any time before or during clinical trials due to safety concerns about on-going or proposed clinical trials or non-compliance with specific FDA requirements, and the trials may not begin or continue until the FDA notifies the sponsor that the hold has been lifted. All clinical trials must be conducted under the supervision of one or more qualified investigators in accordance with GCP regulations. They must be conducted under protocols detailing the objectives of the trial, dosing procedures, subject selection and exclusion criteria and the safety and effectiveness criteria to be evaluated. Each protocol must be submitted to the FDA as part of the IND, and timely safety reports must be submitted to the FDA and the investigators for serious and unexpected adverse events. An IRB at each institution participating in the clinical trial must review and approve each protocol before a clinical trial commences at that institution and must also approve the information regarding the trial and the consent form that must be provided to each trial subject or his or her legal representative, monitor the study until completed and otherwise comply with IRB regulations.

Human clinical trials are typically conducted in three sequential phases that may overlap or be combined:

- **Phase 1:** The product candidate is initially introduced into healthy human subjects and tested for safety, dosage tolerance, absorption, metabolism, distribution and excretion. In the case of some products for severe or life-threatening diseases, such as cancer, especially when the product may be too inherently toxic to ethically administer to healthy volunteers, the initial human testing is often conducted in patients.
- **Phase 2:** The product candidate is evaluated in a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and appropriate dosage.
- **Phase 3:** The product candidate is administered to an expanded patient population to provide statistically significant evidence of clinical efficacy and further test for safety, generally at geographically dispersed clinical study sites. These clinical trials are intended to establish the overall risk-benefit ratio of the product candidate and provide an adequate basis for product labeling.

Post-approval trials, sometimes referred to as Phase 4 studies, may be conducted after initial marketing approval. These trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication. In certain instances, the FDA may mandate the performance of Phase 4 clinical trials as a condition of approval of an NDA or BLA.

The FDA or the sponsor may suspend a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients. In addition, some clinical trials are overseen by an independent group of qualified experts organized by the sponsor, known as a data safety monitoring board or committee. Depending on its charter, this group may determine whether a trial may move forward at designated check points based on access to certain data from the trial.

During the development of a new drug or biologic, sponsors are given opportunities to meet with the FDA at certain points. These points may be prior to submission of an IND, at the end of Phase 2, and before an NDA or BLA is submitted. Meetings at other times may be requested. These meetings can provide an opportunity for the sponsor to share information about the data gathered to date, for the FDA to provide advice, and for the sponsor and the FDA to reach agreement on the next phase of development. Sponsors typically use the meetings at the end of the Phase 2 trial to discuss Phase 2 clinical results and present plans for the pivotal Phase 3 clinical trial that they believe will support approval of the new drug or biologic.

Concurrent with clinical trials, companies usually complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the drug and finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, the manufacturer must develop methods for testing the identity, strength, quality and purity of the final drug. In addition, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life. While the IND is active, progress reports summarizing the results of the clinical trials and nonclinical studies performed since the last progress report, among other information, must be submitted at least annually to the FDA, and written IND safety reports must be submitted to the FDA and investigators for serious and unexpected suspected adverse events, findings from other studies suggesting a significant risk to humans exposed to the same or similar drugs, findings from animal or *in vitro* testing suggesting a significant risk to humans, and any clinically important increased incidence of a serious suspected adverse reaction compared to that listed in the protocol or investigator brochure.

There are also requirements governing the reporting of ongoing clinical trials and completed trial results to public registries. Sponsors of certain clinical trials of FDA-regulated products are required to register and disclose specified clinical trial information, which is publicly available at [www.clinicaltrials.gov](http://www.clinicaltrials.gov).

### ***United States Review and Approval Process***

Assuming successful completion of all required testing in accordance with all applicable regulatory requirements, the results of product development, preclinical and other non-clinical studies and clinical trials, along with descriptions of the manufacturing process, analytical tests conducted on the chemistry of the drug, proposed labeling and other relevant information are submitted to the FDA as part of an NDA or BLA requesting approval to market the product. The submission of an NDA or BLA is subject to the payment of user fees; a waiver of such fees may be obtained under certain limited circumstances.

Within 60 days following submission of the application, the FDA reviews all NDAs and BLAs submitted to ensure that they are sufficiently complete for substantive review before it accepts them for filing. The FDA may request additional information rather than accept an NDA or BLA for filing. In this event, the NDA or BLA must be resubmitted with the additional information. The resubmitted application also is subject to review before the FDA accepts it for filing.

Once the submission is accepted for filing, the FDA begins an in depth substantive review. The FDA reviews an NDA to determine, among other things, whether a product is safe and effective for its intended use and whether its manufacturing is cGMP compliant to assure and preserve the product's identity, strength, quality and purity. The FDA reviews a BLA to determine, among other things whether the product is safe, pure and potent and the facility in which it is manufactured, processed, packed or held meets standards designed to assure the product's continued safety, purity and potency. Before approving an NDA or BLA, the FDA will inspect the facility or facilities where the product is manufactured. The FDA may refer the NDA or BLA to an advisory committee for review, evaluation and recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendation of an advisory committee, but it generally follows such recommendations.

After the FDA evaluates an NDA or BLA, it will issue an approval letter or a Complete Response Letter. An approval letter authorizes commercial marketing of the drug with prescribing information for specific indications. A Complete Response Letter indicates that the review cycle of the application is complete and the application will not be approved in its present form. A Complete Response Letter usually describes the specific deficiencies in the NDA or BLA identified by the FDA and may require additional clinical data, such as an additional clinical trial or other significant and time-consuming requirements related to clinical trials, nonclinical studies or manufacturing. If a Complete Response Letter is issued, the sponsor must resubmit the NDA or BLA, addressing all of the deficiencies identified in the letter, or withdraw the application. Even if such data and information are submitted, the FDA may decide that the NDA or BLA does not satisfy the criteria for approval. If a product receives regulatory approval, the approval may be significantly limited to specific diseases and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the product. In addition, the FDA may require a sponsor to conduct Phase 4 testing, which involves clinical trials designed to further assess a drug's safety and effectiveness after NDA or BLA approval, and may require testing and surveillance programs to monitor the safety of approved products which have been commercialized. The FDA may also place other conditions on approval including the requirement for a risk evaluation and mitigation strategy ("REMS") to assure the safe use of the drug. If the FDA concludes a REMS is needed, the sponsor of the NDA must submit a proposed REMS. The FDA will not approve the NDA without an approved REMS, if required. A REMS could include medication guides, physician communication plans or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. Any of these limitations on approval or marketing could restrict the commercial promotion, distribution, prescription or dispensing of products. Marketing approval may be withdrawn for non-compliance with regulatory requirements or if problems occur following initial marketing.

In addition, the Pediatric Research Equity Act ("PREA"), which requires a sponsor to conduct pediatric clinical trials for most drugs 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 evaluate the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations and support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The sponsor or FDA may request a deferral of pediatric clinical trials 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 clinical trials are complete or that additional safety or effectiveness data needs to be collected before the pediatric clinical trials begin. The FDA must send a non-compliance 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.

### ***Orphan Drug Designation***

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug or biologic intended to treat a rare disease or condition, which is a disease or condition that affects fewer than 200,000 individuals in the United States or, if it affects more than 200,000 individuals in the United States, there is no reasonable expectation that the cost of developing and making a drug or biologic product available in the United States for this type of disease or condition will be recovered from sales of the product. Orphan designation must be requested before submitting an NDA or BLA. After the FDA grants orphan designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If a product that has orphan designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications to market the same drug or biological product for the same disease or condition for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan exclusivity or inability to manufacture the product in sufficient quantities. The designation of such drug or biologic also entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers. However, competitors may receive approval of different products for the indication for which the orphan product has exclusivity or obtain approval for the same product but for a different indication for which the orphan product has exclusivity. Orphan exclusivity also could block the approval of a product candidate for seven years if a competitor obtains approval of the same drug or biologic as defined by the FDA or if such product candidate is determined to be contained within the competitor's product for the same indication or disease. If an orphan designated product receives marketing approval for an indication broader than what is designated, it may not be entitled to orphan exclusivity.

### ***Expedited Development and Review Programs***

The FDA has a Fast Track program that is intended to expedite or facilitate the process for reviewing product candidates that meet certain criteria. Specifically, new drugs and biologics are eligible for Fast Track designation if they are intended to treat a serious or life-threatening disease or condition and nonclinical or clinical data demonstrate the potential to address unmet medical needs for the disease or condition. Fast Track designation applies to the combination of the product candidate and the specific indication for which it is being studied. The FDA may consider for review sections of the NDA or BLA for a Fast Track review designation on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the NDA or BLA, the FDA agrees to accept sections of the NDA or BLA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the NDA or BLA.

A product candidate intended to treat a serious or life-threatening disease or condition may also be eligible for Breakthrough Therapy designation to expedite its development and review. A product candidate can receive Breakthrough Therapy designation if preliminary clinical evidence indicates that the product candidate, alone or in combination with one or more other drugs or biologics, may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The designation includes all of the fast track program features, as well as more intensive FDA interaction and guidance beginning as early as Phase 1 and an organizational commitment to expedite the development and review of the product candidate, including involvement of senior managers.

Any product candidate submitted to the FDA for approval, including a product candidate with a Fast Track designation or Breakthrough Therapy designation, may also be eligible for other types of FDA programs intended to expedite development and review, such as priority review and accelerated approval. A BLA or NDA is eligible for

priority review if the product candidate is designed to treat a serious condition, and if approved, would provide a significant improvement in safety or effectiveness compared to marketed products. The FDA will attempt to direct additional resources to the evaluation of an application designated for priority review in an effort to facilitate the review. The FDA endeavors to review applications with priority review designations within six months of the filing date as compared to ten months for review of original BLAs and new molecular entity NDAs under its standard review goals.

In addition, a product candidate may be eligible for accelerated approval. Drug and biologic product candidates intended to treat serious or life-threatening diseases or conditions may be eligible for accelerated approval upon a determination that the product candidate has an effect on 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. As a condition of approval, the FDA may require that a sponsor of a drug or biologic receiving accelerated approval perform adequate and well-controlled post-marketing clinical trials. A product receiving accelerated approval may be subjected to expedited withdrawal procedures if the sponsor fails to conduct any required post-marketing trials in a timely manner, or if such trials fail to verify the predicted clinical benefit. In addition, the FDA currently requires as a condition for accelerated approval pre-approval of promotional materials, which could adversely impact the timing of the commercial launch of the product.

Fast Track designation, Breakthrough Therapy designation, priority review and accelerated approval do not change the standards for approval but may expedite the development or approval process.

#### ***Post-approval requirements***

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product may result in restrictions on the product or even complete withdrawal of the product from the market. After approval, some types of changes to the approved product, such as adding new indications, certain manufacturing changes and additional labeling claims, are subject to further FDA review and approval. Drug and biologics manufacturers and other entities involved in the manufacture and distribution of approved drugs and biologics 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 cGMP regulations and other laws and regulations.

Any drug products manufactured or distributed pursuant to FDA approvals will be subject to continuing regulation by the FDA, including, among other things, record-keeping requirements, reporting of adverse experiences with the drug, providing the FDA with updated safety and efficacy information, drug sampling and distribution requirements, complying with certain electronic records and signature requirements, and complying with FDA promotion and advertising requirements. The FDA strictly regulates labeling, advertising, promotion and other types of information on products that are placed on the market and imposes requirements and restrictions on drug and biologics manufacturers, such as those related to direct-to-consumer advertising, the prohibition on promoting products for uses or in patient populations that are not described in the product's approved labeling (known as "off-label use"), industry-sponsored scientific and educational activities, and promotional activities involving the internet. Discovery of previously unknown problems or the failure to comply with the applicable regulatory requirements may result in restrictions on the marketing of a product or withdrawal of the product from the market as well as possible civil or criminal sanctions. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval, may subject an applicant or manufacturer to administrative or judicial civil or criminal sanctions and adverse publicity. FDA sanctions could include refusal to approve pending applications, withdrawal of an approval, clinical hold, warning or untitled letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, mandated corrective advertising or communications with doctors, debarment, restitution, disgorgement of profits, or civil or criminal penalties.

### ***Marketing Exclusivity***

Market exclusivity provisions under the FDCA can also delay the submission or the approval of certain marketing applications. The FDCA provides a five-year period of non-patent data exclusivity within the United States to the first applicant to obtain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not approve or even accept for review an abbreviated new drug application (“ANDA”) or a NDA submitted under Section 505(b)(2), or 505(b)(2) NDA, submitted by another company for another drug based on the same active moiety, regardless of whether the drug is intended for the same indication as the original innovative drug or for another indication, where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement to one of the patents listed with the FDA by the innovator NDA holder. The FDCA alternatively provides three years of marketing exclusivity for an NDA, or supplement to an existing NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example new indications, dosages or strengths of an existing drug. This three-year exclusivity covers only the modification for which the drug received approval on the basis of the new clinical investigations and does not prohibit the FDA from approving ANDAs or 505(b)(2) NDAs for drugs containing the active agent for the original indication or condition of use. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

Pediatric exclusivity is a type of marketing exclusivity available in the United States. Pediatric exclusivity under the Best Pharmaceuticals for Children Act provides for an additional six months of marketing exclusivity if a sponsor conducts clinical trials in children in response to a written request from the FDA. If such written request does not include clinical trials in neonates, the FDA is required to include its rationale for not requesting those clinical trials. The FDA may request studies on approved or unapproved indications in separate written requests. The issuance of a written request does not require the sponsor to undertake the described clinical trials. In addition, orphan drug exclusivity, as described above, may offer a seven-year period of marketing exclusivity, except in certain circumstances.

### ***Biosimilars and Exclusivity***

The Affordable Care Act includes a subtitle called the Biologics Price Competition and Innovation Act of 2009 (“BPCIA”), which created an abbreviated approval pathway for biological products that are biosimilar to or interchangeable with an FDA-licensed reference biological product. The FDA has issued several guidance documents outlining an approach to review and approval of biosimilars.

Biosimilarity, which requires that there be no clinically meaningful differences between the biological product and the reference product in terms of safety, purity, and potency, can be shown through analytical studies, animal studies, and a clinical study or studies. Interchangeability requires that a product is biosimilar to the reference product and the product must demonstrate that it can be expected to produce the same clinical results as the reference product in any given patient and, for products that are administered multiple times to an individual, the biologic and the reference biologic may be alternated or switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic.

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 twelve years from the date on which the reference product was first licensed. During this twelve-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 BPCIA also created certain exclusivity periods for biosimilars approved as interchangeable products. At this juncture, it is unclear whether products deemed “interchangeable” by the FDA will, in fact, be readily substituted by pharmacies, which are governed by state pharmacy law.

## **FDA Regulation of Companion Diagnostics**

We expect that certain of our product candidates may require an *in vitro* diagnostic to identify appropriate patient populations for our product candidates. These diagnostics, often referred to as companion diagnostics, are regulated as medical devices. In the United States, the FDCA and its implementing regulations, and other federal and state statutes and regulations govern, among other things, medical device design and development, preclinical and clinical testing, premarket clearance or approval, registration and listing, manufacturing, labeling, storage, advertising and promotion, sales and distribution, export and import, and post-market surveillance. Unless an exemption applies, diagnostic tests require marketing clearance or approval from the FDA prior to commercial distribution. The two primary types of FDA marketing authorization applicable to a medical device are premarket notification, also called 510(k) clearance, and premarket approval (“PMA”). We expect that any companion diagnostic developed for our product candidates will utilize the PMA pathway.

If use of companion diagnostic is essential to safe and effective use of a drug or biologic product, then the FDA generally will require approval or clearance of the diagnostic contemporaneously with the approval of the therapeutic product. On August 6, 2014, the FDA issued a final guidance document addressing the development and approval process for “*In Vitro* Companion Diagnostic Devices.” According to the guidance, for novel product candidates, a companion diagnostic device and its corresponding drug candidate should be approved or cleared contemporaneously by FDA for the use indicated in the therapeutic product labeling. The guidance also explains that a companion diagnostic device used to make treatment decisions in clinical trials of a drug generally will be considered an investigational device, unless it is employed for an intended use for which the device is already approved or cleared. If used to make critical treatment decisions, such as patient selection, the diagnostic device generally will be considered a significant risk device under the FDA’s Investigational Device Exemption (“IDE”) regulations. Thus, the sponsor of the diagnostic device will be required to comply with the IDE regulations. According to the guidance, if a diagnostic device and a drug are to be studied together to support their respective approvals, both products can be studied in the same investigational study, if the study meets both the requirements of the IDE regulations and the IND regulations. The guidance provides that depending on the details of the study plan and subjects, a sponsor may seek to submit an IND alone, or both an IND and an IDE.

The FDA has generally required companion diagnostics intended to select the patients who will respond to cancer treatment to obtain approval of a PMA for that diagnostic simultaneously with approval of the therapeutic. The PMA process, including the gathering of clinical and preclinical data and the submission to and review by the FDA, can take several years or longer. It involves a rigorous premarket review during which the applicant must prepare and provide the FDA with reasonable assurance of the device’s safety and effectiveness and information about the device and its components regarding, among other things, device design, manufacturing and labeling. In addition, PMAs for certain devices must generally include the results from extensive preclinical and adequate and well-controlled clinical trials to establish the safety and effectiveness of the device for each indication for which FDA approval is sought. In particular, for a diagnostic, the applicant must demonstrate that the diagnostic produces reproducible results when the same sample is tested multiple times by multiple users at multiple laboratories. As part of the PMA review, the FDA will typically inspect the manufacturer’s facilities for compliance with the Quality System Regulation (“QSR”), which imposes elaborate testing, control, documentation and other quality assurance requirements.

If the FDA evaluations of both the PMA application and the manufacturing facilities are favorable, the FDA will either issue an approval letter or an approvable letter, which usually contains a number of conditions that must be met in order to secure the final approval of the PMA, such as changes in labeling, or specific additional information, such as submission of final labeling, in order to secure final approval of the PMA. If the FDA concludes that the applicable criteria have been met, the FDA will issue a PMA for the approved indications, which can be more limited than those originally sought by the applicant. The PMA can include post-approval conditions that the FDA believes necessary to ensure the safety and effectiveness of the device, including, among other things, restrictions on labeling, promotion, sale and distribution.

If the FDA’s evaluation of the PMA or manufacturing facilities is not favorable, the FDA will deny approval of the PMA or issue a not approvable letter. A not approvable letter will outline the deficiencies in the application and, where practical, will identify what is necessary to make the PMA approvable. The FDA may also determine that

additional clinical trials are necessary, in which case the PMA approval may be delayed for several months or years while the trials are conducted and then the data submitted in an amendment to the PMA. Once granted, PMA approval may be withdrawn by the FDA if compliance with post approval requirements, conditions of approval or other regulatory standards is not maintained or problems are identified following initial marketing. PMA approval is not guaranteed, and the FDA may ultimately respond to a PMA submission with a not approvable determination based on deficiencies in the application and require additional clinical trial or other data that may be expensive and time-consuming to generate and that can substantially delay approval.

After a device is placed on the market, it remains subject to significant regulatory requirements. Medical devices may be marketed only for the uses and indications for which they are cleared or approved. Device manufacturers must also establish registration and device listings with the FDA. A medical device manufacturer's manufacturing processes and those of its suppliers are required to comply with the applicable portions of the QSR, which cover the methods and documentation of the design, testing, production, processes, controls, quality assurance, labeling, packaging and shipping of medical devices. Domestic facility records and manufacturing processes are subject to periodic unscheduled inspections by the FDA. The FDA also may inspect foreign facilities that export products to the United States.

### ***Government Regulation Outside of the United States***

In addition to regulations in the United States, we are be subject to a variety of regulations in other jurisdictions governing, among other things, clinical trials, and any commercial sales and distribution of our product once approved.

Whether or not we obtain FDA approval for a product candidate, we must obtain the requisite approvals from regulatory authorities in foreign countries prior to the commencement of clinical trials or marketing of the product candidates in those countries. The requirements and process governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. Failure to comply with applicable foreign regulatory requirements, may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

#### *Non-Clinical Studies and Clinical Trials*

Similar to the U.S., the various phases of non-clinical and clinical research in the European Union ("EU") are subject to significant regulatory controls.

Non-clinical studies are performed to demonstrate the health or environmental safety of new chemical or biological substances. Non-clinical studies must be conducted in compliance with the principles of good laboratory practice ("GLP") as set forth in EU Directive 2004/10/EC. In particular, non-clinical studies, both in vitro and in vivo, must be planned, performed, monitored, recorded, reported and archived in accordance with the GLP principles, which define a set of rules and criteria for a quality system for the organizational process and the conditions for non-clinical studies. These GLP standards reflect the Organization for Economic Co-operation and Development requirements

Certain countries outside of the United States have a similar process that requires the submission of a clinical study application much like the IND prior to the commencement of human clinical studies.

Clinical studies of medicinal products in the EU must be conducted in accordance with EU and national regulations and the International Conference on Harmonization ("ICH") guidelines on GCP as well as the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki. If the sponsor of the clinical trial is not established within the EU, it must appoint an EU entity to act as its legal representative. The sponsor must take out a clinical trial insurance policy, and in most EU countries, the sponsor is liable to provide 'no fault' compensation to any study subject injured in the clinical trial.

The regulatory landscape related to clinical trials in the EU has been subject to recent changes. The EU Clinical Trials Regulation ("CTR") which was adopted in April 2014 and repeals the EU Clinical Trials Directive, became applicable on January 31, 2022. Unlike directives, the CTR is directly applicable in all EU member states without the

need for member states to further implement it into national law. The CTR notably harmonizes the assessment and supervision processes for clinical trials throughout the EU via a Clinical Trials Information System, which contains a centralized EU portal and database.

While the Clinical Trials Directive required a separate clinical trial application (“CTA”) to be submitted in each member state, to both the competent national health authority and an independent ethics committee, much like the FDA and IRB respectively, the CTR introduces a centralized process and only requires the submission of a single application to all member states concerned. The CTR allows sponsors to make a single submission to both the competent authority and an ethics committee in each member state, leading to a single decision per member state. The CTA must include, among other things, a copy of the trial protocol and an investigational medicinal product dossier containing information about the manufacture and quality of the medicinal product under investigation. The assessment procedure of the CTA has been harmonized as well, including a joint assessment by all member states concerned, and a separate assessment by each member state with respect to specific requirements related to its own territory, including ethics rules. Each member state’s decision is communicated to the sponsor via the centralized EU portal. Once the CTA is approved, clinical study development may proceed.

The CTR foresees a three-year transition period. The extent to which ongoing and new clinical trials will be governed by the CTR varies. For clinical trials whose CTA was made under the Clinical Trials Directive before January 31, 2022, the Clinical Trials Directive will continue to apply on a transitional basis for three years. Additionally, sponsors may still choose to submit a CTA under either the Clinical Trials Directive or the CTR until January 31, 2023 and, if authorised, those will be governed by the Clinical Trials Directive until January 31, 2025. By that date, all ongoing trials will become subject to the provisions of the CTR.

Medicines used in clinical trials must be manufactured in accordance with Good Manufacturing Practices (“GMP”). Other national and EU-wide regulatory requirements may also apply.

#### *Marketing Authorization*

In the EU, medicinal products can only be placed on the market after obtaining a marketing authorization (“MA”). To obtain regulatory approval of an investigational medicinal product under EU regulatory systems, we must submit a marketing authorization application (“MAA”). The process for doing this depends, among other things, on the nature of the medicinal product.

“Centralized MAs” are issued by the European Commission through the centralized procedure, based on the opinion of the European Medicines Agency’s (“EMA”) Committee for Human Medicinal Products (“CHMP”) and are valid across the entire territory of the EU. The centralized procedure is compulsory for human types of medicines such as: (i) medicinal products derived from biotechnology processes, such as genetic engineering, (ii) medicinal products that contain a new active substance indicated for the treatment of certain diseases, such as HIV/AIDS, cancer, diabetes, neurodegenerative diseases, autoimmune and other immune dysfunctions and viral diseases, (iii) designated orphan medicines and (iv) advanced therapy medicinal products (“ATMPs”), such as gene therapy, somatic cell therapy or tissue-engineered medicines. The centralized procedure may at the request of the applicant also be used in certain other cases and in particular for any other products containing new active substances not authorized in the EU or for product candidates which constitute a significant therapeutic, scientific, or technical innovation or for which the granting of authorization would be in the interests of public health in the EU. It is likely that the centralized procedure would apply to the product candidates we are developing.

Under the centralized procedure, the maximum timeframe for the evaluation of a MAA by the EMA is 210 days. In exceptional cases, the CHMP might perform an accelerated review of a MA in no more than 150 days (not including clock stops). Innovative products that target an unmet medical need and are expected to be of major public health interest may be eligible for a number of expedited development and review programs, such as the PRIME scheme, which provides incentives similar to the breakthrough therapy designation in the U.S. PRIME is a voluntary scheme aimed at enhancing the EMA’s support for the development of medicines that target unmet medical needs. It is based on increased interaction and early dialogue with companies developing promising medicines, to optimize their product development plans and speed up their evaluation to help them reach patients earlier. Product developers that benefit from

PRIME designation can expect to be eligible for accelerated assessment but this is not guaranteed. Many benefits accrue to sponsors of product candidates with PRIME designation, including but not limited to, early and proactive regulatory dialogue with the EMA, frequent discussions on clinical trial designs and other development program elements, and accelerated MAA assessment once a dossier has been submitted. Importantly, a dedicated contact and rapporteur from the CHMP is appointed early in the PRIME scheme facilitating increased understanding of the product at EMA's committee level. An initial meeting initiates these relationships and includes a team of multidisciplinary experts at the EMA to provide guidance on the overall development and regulatory strategies.

MAAs have an initial duration of five years. After these five years, the authorization may be renewed for an unlimited period on the basis of a reevaluation of the risk-benefit balance.

#### *Data and Marketing Exclusivity*

The EU also provides opportunities for market exclusivity. Upon receiving MA, reference products generally receive eight years of data exclusivity and an additional two years of market exclusivity. If granted, data exclusivity prevents generic or biosimilar applicants from relying on the preclinical and clinical trial data contained in the dossier of the reference product when applying for a generic or biosimilar MA in the EU during a period of eight years from the date on which the reference product was first authorized in the EU. During the additional two year period of market exclusivity, a generic or biosimilar MAA can be submitted, and the innovator's data may be referenced, but no generic or biosimilar product can be marketed until 10 years have elapsed from the initial MA of the reference product in the EU. The overall ten-year market exclusivity period may be extended to a maximum of eleven years if, during the first eight years of those 10 years, the MA holder obtains an authorization for one or more new therapeutic indication with significant clinical benefit over existing therapies is approved. However, there is no guarantee that a product will be considered by the EU's regulatory authorities to be a new chemical entity, and products may not qualify for data exclusivity.

There is a special regime for biosimilars, or biological medicinal products that are similar to a reference medicinal product but that do not meet the definition of a generic medicinal product, for example, because of differences in raw materials or manufacturing processes. For such products, the results of appropriate preclinical or clinical trials must be provided, and guidelines from the EMA detail the type of quantity of supplementary data to be provided for different types of biological product. There are no such guidelines for complex biological products, such as gene or cell therapy medicinal products, and so it is unlikely that biosimilars of those products will currently be approved in the EU. However, guidance from the EMA states that they will be considered in the future in light of the scientific knowledge and regulatory experience gained at the time.

#### *Orphan Medicinal Products*

The criteria for designating an "orphan medicinal product" in the EU are similar in principle to those in the United States. A medicinal product may be designated as orphan if (1) it is intended for the diagnosis, prevention or treatment of a life threatening or chronically debilitating condition; (2) either (a) such condition affects no more than five in 10,000 persons in the European Union when the application is made, or (b) the product, without the benefits derived from orphan status, would not generate sufficient return in the EU to justify investment; and (3) there exists no satisfactory method of diagnosis, prevention or treatment of such condition authorized for marketing in the EU, or if such a method exists, the product will be of significant benefit to those affected by the condition.

The application for orphan drug designation must be submitted before the MAA. Orphan medicinal products are eligible for incentives such as reduction of fees or fee waivers, protocol assistance, and access to the centralized procedure and are, upon grant of a MA, entitled to ten years of market exclusivity for the approved therapeutic indication. During the ten-year market exclusivity period, the regulatory authorities cannot accept another MAA, or grant a MA, or accept an application to extend an existing MA for a period of ten years for the same indication, in respect of a similar medicinal product. An orphan product can also obtain an additional two years of market exclusivity in the EU for orphan medicinal products that have also complied with an agreed pediatric investigation plan ("PIP"). No extension to any supplementary protection certificate can be granted on the basis of pediatric studies for orphan indications. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review

and approval process.

The 10-year market exclusivity may be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for orphan designation, for example, if the product is sufficiently profitable not to justify maintenance of market exclusivity or where the prevalence of the condition has increased above the threshold. In addition, MA may be granted to a similar product for the same indication at any time if (1) the second applicant can establish that its product, although similar, is safer, more effective or otherwise clinically superior; (2) the applicant consents to a second orphan medicinal product application; or (3) the applicant cannot supply enough orphan medicinal product.

#### *Pediatric Development*

In the EU, MAAs for new medicinal products have to include the results of trials conducted in the pediatric population, in compliance with a PIP agreed with the EMA's Pediatric Committee ("PDCO"). The PIP sets out the timing and measures proposed to generate data to support a pediatric indication of the drug for which an MA is being sought. The PDCO can grant a deferral of the obligation to implement some or all of the measures of the PIP until there are sufficient data to demonstrate the efficacy and safety of the product in adults. Further, the obligation to provide pediatric clinical trial data can be waived by the PDCO when these data are not needed or appropriate because the product is likely to be ineffective or unsafe in children, the disease or condition for which the product is intended occurs only in adult populations, or when the product does not represent a significant therapeutic benefit over existing treatments for pediatric patients. Once the MA is obtained in all member states and study results are included in the product information, even when negative, the product is eligible for a six-months supplementary protection certificate extension (if any is in effect at the time of approval) or, in the case of orphan pharmaceutical products, a two year extension of the orphan market exclusivity is granted.

#### *Post-Approval Requirements*

Similar to the United States, both MA holders and manufacturers of medicinal products are subject to comprehensive regulatory oversight by the EMA, the European Commission and/or the competent regulatory authorities of the member states. The holder of a marketing authorization must establish and maintain a pharmacovigilance system and appoint an individual qualified person for pharmacovigilance who is responsible for oversight of that system. Key obligations include expedited reporting of suspected serious adverse reactions and submission of periodic safety update reports ("PSURs").

All new MAAs must include a risk management plan ("RMP"), describing the risk management system that the company will put in place and documenting measures to prevent or minimize the risks associated with the product. The regulatory authorities may also impose specific obligations as a condition of the MA. Such risk-minimization measures or post-authorization obligations may include additional safety monitoring, more frequent submission of PSURs, or the conduct of additional clinical trials or post-authorization safety studies.

The advertising and promotion of medicinal products is also subject to laws concerning promotion of medicinal products, interactions with physicians, misleading and comparative advertising and unfair commercial practices. All advertising and promotional activities for the product must be consistent with the approved summary of product characteristics, and therefore all off-label promotion is prohibited. Direct-to-consumer advertising of prescription medicines is also prohibited in the EU. Although general requirements for advertising and promotion of medicinal products are established under EU directives, the details are governed by regulations in each member state and can differ from one country to another.

Failure to comply with EU and member state laws that apply to the conduct of clinical trials, manufacturing approval, MA of medicinal products and marketing of such products, both before and after grant of the MA, manufacturing of pharmaceutical products, statutory health insurance, bribery and anti-corruption or with other applicable regulatory requirements may result in administrative, civil or criminal penalties. These penalties could include delays or refusal to authorize the conduct of clinical trials, or to grant marketing authorizations, product withdrawals and recalls, product seizures, suspension, withdrawal or variation of the marketing authorization, total or partial suspension

of production, distribution, manufacturing or clinical trials, operating restrictions, injunctions, suspension of licenses, fines and criminal penalties.

The aforementioned EU rules are generally applicable in the European Economic Area (“EEA”), which consists of the 27 EU member states plus Norway, Liechtenstein and Iceland.

For other countries outside of the EU, such as countries in Eastern Europe, Latin America or Asia, the requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. In all cases, again, the clinical trials are conducted in accordance with GCP and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

If we fail to comply with applicable foreign regulatory requirements, we may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

#### *Regulation of Companion Diagnostics*

In the EU, in vitro diagnostic medical devices are regulated by Directive 98/79/EC which regulates the placing on the market, the CE marking, the essential requirements, the conformity assessment procedures, the registration obligations for manufacturers and devices as well as the vigilance procedure. In vitro diagnostic medical devices must comply with the requirements provided for in the Directive, and with further requirements implemented at national level (as the case may be).

The regulation of companion diagnostics will be subject to further requirements once the in-vitro medical diagnostic devices Regulation (No 2017/746) (“IVDR”) will become applicable on 26 May 2022. However on October 14, 2021, the European Commission proposed a “progressive” roll-out of the IVDR to prevent disruption in the supply of in vitro diagnostic medical devices. The European Parliament and Council voted to adopt the proposed regulation on December 15, 2021 and the regulation entered into force on January 2022. The IVDR will fully apply on May 26, 2022 but there will be a tiered system extending the grace period for many devices (depending on their risk classification) before they have to be fully compliant with the regulation.

The IVDR introduces a new classification system for companion diagnostics which are now specifically defined as diagnostic tests that support the safe and effective use of a specific medicinal product, by identifying patients that are suitable or unsuitable for treatment. Companion diagnostics will have to undergo a conformity assessment by a notified body. Before it can issue a CE certificate, the notified body must seek a scientific opinion from the EMA on the suitability of the companion diagnostic to the medicinal product concerned if the medicinal product falls exclusively within the scope of the centralized procedure for the authorization of medicines, or the medicinal product is already authorized through the centralized procedure, or a MMA for the medicinal product has been submitted through the centralized procedure. For other substances, the notified body can seek the opinion from a national competent authorities or the EMA.

The aforementioned EU rules are generally applicable in the EEA.

#### ***Other Healthcare Laws***

In addition to FDA restrictions on marketing of pharmaceutical and biological products, other U.S. federal and state and foreign healthcare regulatory laws restrict business practices in the pharmaceutical industry, which include, but are not limited to, state and federal anti-kickback, fraud & abuse, false claims, consumer fraud and transparency laws regarding drug pricing and payments or other transfers of value made to physicians and other licensed healthcare professionals. These laws may affect our sales, marketing and other promotional activities by limiting the kinds of financial arrangements we may have with physicians, customers and third party payors including discount practices, customer support, education and training programs, physician consulting and other service arrangements. In addition, manufacturers can be held liable under the False Claims Act even when they do not submit claims directly to government payors if they are deemed to “cause” the submission of false or fraudulent claims by, for example, providing

inaccurate billing or coding information to customers or promoting a product off label. These laws are broadly written, and it is often difficult to determine precisely how these laws will be applied to specific circumstances. Such laws include:

- The federal Anti-Kickback Statute, which prohibits, among other things, any person or entity from knowingly and willfully offering, paying, soliciting, receiving or providing any remuneration, directly or indirectly, overtly or covertly, to induce or in return for purchasing, leasing, ordering or arranging for or recommending the purchase, lease or order of any item or service reimbursable, in whole or in part, under Medicare, Medicaid or other federal healthcare programs. A person or entity does not need to have actual knowledge of the federal Anti-Kickback Statute or specific intent to violate it to have committed a violation;
- The federal false claims laws, including the False Claims Act, which prohibit any person or entity from, among other things, knowingly presenting, or causing to be presented, a false, fictitious or fraudulent claim for payment to, or approval by, the federal government or knowingly making, using or causing to be made or used a false record or statement material to a false or fraudulent claim to the federal government. In addition, the government may assert that 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 False Claims Act;
- The federal Health Insurance Portability and Accountability Act of 1996 (“HIPAA”), which prohibits, among other actions, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private third-party payors, knowingly and willfully embezzling or stealing from a healthcare benefit program, willfully obstructing a criminal investigation of a healthcare offense, and knowingly and willfully 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 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 to have committed a violation;
- The Physician Payments Sunshine Act, which imposed, among other things, new annual reporting requirements for covered manufacturers for certain payments and “transfers of value” provided to physicians (as defined by statute), certain non-physician practitioners including physician assistants and nurse practitioners, and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members; and
- Analogous state laws and regulations, such as state anti-kickback and false claims laws, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers.

If our operations are found to be in violation of any of such laws or any other governmental regulations that apply to us, we may be subject to penalties, including, without limitation, administrative, civil and criminal penalties, damages, fines, disgorgement, contractual damages, reputational harm, diminished profits and future earnings, the curtailment or restructuring of our operations, exclusion from participation in federal and state healthcare programs and individual imprisonment, any of which could adversely affect our ability to operate our business and our financial results.

To the extent that any of our product candidates, once approved, are sold in a foreign country, we may be subject to similar foreign laws and regulations, which may include, for instance, applicable post-marketing requirements, including safety surveillance, anti-fraud and abuse laws, and implementation of corporate compliance programs and reporting of payments or other transfers of value to healthcare professionals.

### **Coverage and Reimbursement**

Significant uncertainty exists as to the coverage and reimbursement status of any pharmaceutical or biological product for which we obtain regulatory approval. In the United States and markets in other countries, patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payors to reimburse all or part of the associated healthcare costs. Patients are unlikely to use our products unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of our products. Sales of any product candidates for which we receive regulatory approval for commercial sale will therefore depend, in part, on the availability of coverage and adequate reimbursement from third-party payors. Third-party payors include government authorities, managed care plans, private health insurers and other organizations.

The process for determining whether a third-party payor will provide coverage for a pharmaceutical or biological product typically is separate from the process for setting the price of such product or for establishing the reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the FDA-approved products for a particular indication. A decision by a third-party payor not to cover our product candidates could reduce physician utilization of our products once approved and have a material adverse effect on our sales, results of operations and financial condition. Moreover, a third-party payor's decision to provide coverage for a pharmaceutical or biological product does not imply that an adequate reimbursement rate will be approved. 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. In addition, coverage and reimbursement for new products can differ significantly from payor to payor. One third-party payor's decision to cover a particular medical product or service does not ensure that other payors will also provide coverage for the medical product or service, or will provide coverage at an adequate reimbursement rate. As a result, the coverage determination process will require us to provide scientific and clinical support for the use of our products to each payor separately and will be a time consuming process.

The containment of healthcare costs has become a priority of federal, state and foreign governments, and the prices of pharmaceutical or biological products have been a focus in this effort. Third-party payors are increasingly challenging the prices charged for medical products and services, examining the medical necessity and reviewing the cost-effectiveness of pharmaceutical products, biological products, medical devices and medical services, in addition to questioning safety and efficacy. If these third-party payors do not consider our product candidates to be cost-effective compared to other available therapies, they may not cover our products after FDA approval or, if they do, the level of payment may not be sufficient to allow us to sell our products at a profit.

### **Healthcare Reform**

A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and other third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medical products. For example, in March 2010, the Affordable Care Act, or ACA, was enacted, which, among other things, increased the minimum Medicaid rebates owed by most manufacturers under the Medicaid Drug Rebate Program; introduced a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected; extended the Medicaid Drug Rebate Program to utilization of prescriptions of individuals enrolled in Medicaid managed care plans; imposed mandatory discounts for certain Medicare Part D beneficiaries as a condition for manufacturers' outpatient drugs coverage under Medicare Part D; subjected drug manufacturers to new annual fees based on pharmaceutical companies' share of sales to federal healthcare programs, and created a new Patient Centered Outcomes Research Institute to oversee, identify priorities in and conduct comparative clinical effectiveness research, along with funding for such research.

Since its enactment, there have been judicial, executive and Congressional legislative challenges to certain aspects of the ACA. On June 17, 2021, the U.S. Supreme Court dismissed the most recent judicial challenge to the ACA brought by several states without specifically ruling on the constitutionality of the ACA. Prior to the Supreme Court's decision, President Biden issued an executive order to initiate a special enrollment period from February 15, 2021 through August 15, 2021 for purposes of obtaining health insurance coverage through the ACA marketplace. The

executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA.

In addition, the Budget Control Act of 2011 and the Bipartisan Budget Act of 2015 led to aggregate reductions of Medicare payments to providers of 2% per fiscal year that will remain in effect through 2030, with the exception of a temporary suspension from May 1, 2020 through March 31, 2022, unless additional Congressional action is taken. On January 2, 2013, the American Taxpayer Relief Act was signed into law, which, among other things, further reduced Medicare payments to several types of providers, including hospitals, imaging centers and cancer treatment centers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

Moreover, there has recently been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed and enacted legislation designed, among other things, to bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs and reform government program reimbursement methodologies for pharmaceutical products. In addition, individual states in the United States have also become increasingly active in implementing regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures and, in some cases, mechanisms to encourage importation from other countries and bulk purchasing. Furthermore, there has been increased interest by third party payors and governmental authorities in reference pricing systems and publication of discounts and list prices.

Similar political, economic and regulatory developments are occurring in the EU and may affect the ability of pharmaceutical companies to profitably commercialize their products. In addition to continuing pressure on prices and cost containment measures, legislative developments at the EU or member state level may result in significant additional requirements or obstacles. The delivery of healthcare in the EU, including the establishment and operation of health services and the pricing and reimbursement of medicines, is almost exclusively a matter for national, rather than EU, law and policy. National governments and health service providers have different priorities and approaches to the delivery of health care and the pricing and reimbursement of products in that context. In general, however, the healthcare budgetary constraints in most EU member states have resulted in restrictions on the pricing and reimbursement of medicines by relevant health service providers. Coupled with ever-increasing EU and national regulatory burdens on those wishing to develop and market products, this could restrict or regulate post-approval activities and affect the ability of pharmaceutical companies to commercialize their products. In international markets, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies

In the future, there may continue to be additional proposals relating to the reform of the U.S. healthcare system and international healthcare systems. 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 limited coverage and reimbursement and reduced demand for our products, once approved, or additional pricing pressures. Any reduction in reimbursement from Medicare or other government funded 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.

### **Data Privacy and Security**

Numerous state, federal and foreign laws, including consumer protection laws and regulations, govern the collection, dissemination, use, access to, confidentiality and security of personal information, including health-related information. In the United States, numerous federal and state laws and regulations, including data breach notification laws, health information privacy and security laws, including HIPAA, and federal and state consumer protection laws and regulations (e.g., Section 5 of the FTC Act), that govern the collection, use, disclosure, and protection of health-related and other personal information could apply to our operations or the operations of our partners. In addition, certain

state and non-U.S. laws, such as the California Consumer Privacy Act, or the CCPA, the California Privacy Rights Act, or the CPRA, and the EU General Data Protection Regulation, or the GDPR, govern the privacy and security of personal information, including health-related information in certain circumstances, some of which are more stringent than HIPAA and many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts. Failure to comply with these laws, where applicable, can result in the imposition of significant civil and/or criminal penalties and private litigation. Privacy and security laws, regulations, and other obligations are constantly evolving, may conflict with each other to complicate compliance efforts, and can result in investigations, proceedings, or actions that lead to significant civil and/or criminal penalties and restrictions on data processing.

### **Research and Development Expenses**

Our research and development expenses were \$29.1 million, \$31.8 million and \$38.0 million for the years ended December 31, 2021, 2020, and 2019, respectively. Please see “Management’s Discussion and Analysis of Financial Condition and Results of Operations-Research and Development Expenses” for additional detail regarding our research and development activities.

### **Environment**

Our third-party manufacturers are subject to inspections by the FDA for compliance with cGMP and other U.S. regulatory requirements, including U.S. federal, state and local regulations regarding environmental protection and hazardous and controlled substance controls, among others. Environmental laws and regulations are complex, change frequently and have tended to become more stringent over time. We have incurred, and may continue to incur, significant expenditures to ensure we are in compliance with these laws and regulations. We would be subject to significant penalties for failure to comply with these laws and regulations.

### **Human Capital Resources**

As of December 31, 2021, we had 28 total employees, all of whom were full-time and 21 of whom were primarily engaged in research and development activities.

Our human capital resources objectives include, as applicable, identifying, recruiting, retaining, incentivizing and integrating our existing and additional employees. We strive to attract and retain the most talented employees in the industry by offering competitive compensation and benefits that support their health, financial and emotional well-being. The principal purposes of our compensation plans are to attract, retain and motivate selected employees and directors. We use a combination of fixed and variable compensation including base salary, cash-based performance bonuses and stock-based compensation awards.

### **Facilities**

We currently lease a total of approximately 27,280 square feet of office and research and development facilities in Burlingame, California. 7,585 square feet are subleased to Angel Pharmaceuticals through February 2023. Our lease expires in 2025. We regularly explore alternatives which would provide us with additional space to accommodate our anticipated growth.

### **Corporate Information**

We were incorporated in Delaware on January 27, 2014 and began operations in November 2014. Our principal executive offices are located at 863 Mitten Road, Suite 102, Burlingame, California 94010, and our telephone number is (650) 900 4520. Our website address is <http://www.corvuspharma.com>. The information on our website is not incorporated by reference in this Annual Report on Form 10 K or in any other filings we make with the SEC.

We are a “smaller reporting company” as defined in the Exchange Act. We take advantage of certain of the scaled disclosures available to smaller reporting companies and will be able to take advantage of these scaled disclosures for so long as the market value of our voting and non-voting common stock held by non-affiliates is less than \$250 million measured on the last business day of our second fiscal quarter, or our annual revenue is less than \$100 million

during the most recently completed fiscal year and the market value of our voting and non-voting common stock held by non-affiliates is less than \$700 million measured on the last business day of our second fiscal quarter.

### **Financial Information about Segments**

We view our operations and manage our business as one reportable segment. See Note 2 to our audited consolidated financial statements included in this Annual Report on Form 10-K. Additional information required by this item is incorporated herein by reference to Part II, Item 6, “Selected Financial Data.”

### **Available Information**

We file electronically with the SEC our annual reports on Form 10-K, quarterly reports on Form 10-Q and current reports on Form 8-K pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended. We make available on our website at <http://www.corvuspharma.com>, free of charge, copies of these reports, as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC. The public may read or copy any materials we file with the SEC. The SEC maintains a website that contains reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC. The address of that website is [www.sec.gov](http://www.sec.gov). The information on or accessible through the SEC and our website is not incorporated into, and is not considered part of, this filing. Further, our references to the URLs for these websites are intended to be inactive textual references only.

### **Item 1A.**

#### **Risk Factors**

*Our business involves significant risks, some of which are described below. You should consider carefully the risks and uncertainties described below, together with all of the other information in this Annual Report on Form 10-K, including our audited consolidated financial statements and related notes included elsewhere in this Annual Report on Form 10-K and “Management’s Discussion and Analysis of Financial Condition and Results of Operations.” If any of the following risks are realized, our business, financial condition, results of operations and prospects could be materially and adversely affected. Many of the following risks and uncertainties are, and will be, exacerbated by the COVID-19 pandemic and any worsening of the global business and economic environment as a result. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also impair our business operations.*

#### **Risks Related to Our Limited Operating History, Financial Condition and Capital Requirements**

***We have a limited operating history, have incurred significant operating losses since our inception and expect to incur significant losses for the foreseeable future. We may never generate any revenue or become profitable or, if we achieve profitability, we may not be able to sustain it.***

We are a clinical-stage biopharmaceutical company with a limited operating history. Biopharmaceutical product development is a highly speculative undertaking and involves a substantial degree of risk. To date, we have focused primarily on developing our lead product candidates, mupadolimab, CPI-818 and ciforadenant, and researching additional product candidates. We have incurred significant operating losses since we were founded in January 2014 and have not yet generated any revenue from sales. If our product candidates are not approved, we may never generate any revenue. We incurred a net loss of \$43.2 million, \$6.0 million and \$46.7 million for the years ended December 31, 2021, 2020 and 2019, respectively. We had an accumulated deficit of \$266.4 million as of December 31, 2021. We expect to continue to incur losses for the foreseeable future, and we anticipate these losses will increase as we continue our development of, seek regulatory approval for and, if approved, begin to commercialize mupadolimab, CPI-818 and ciforadenant, and as we develop other product candidates. Even if we achieve profitability in the future, we may not be able to sustain it in subsequent periods. Our prior losses, combined with expected future losses, have had and will continue to have an adverse effect on our stockholders’ equity and results of operations.

***We will require substantial additional financing to achieve our goals, and a failure to obtain this necessary capital when needed on acceptable terms, or at all, could force us to delay, limit, reduce or terminate our product development, other operations or commercialization efforts.***

Since commencing our operations in 2014, the majority of our efforts have been focused on the research and development of mupadolimab, CPI-818 and ciforadenant. We believe that we will continue to expend substantial resources for the foreseeable future as we continue clinical development of, seek regulatory approval for and, if approved, prepare for the commercialization of ciforadenant, mupadolimab, and CPI-818, as well as product candidates under our other development programs. These expenditures will include costs associated with research and development, conducting preclinical studies and clinical trials, obtaining regulatory approvals, manufacturing and supply, sales and marketing and general operations. In addition, other unanticipated costs may arise. Because the outcome of any clinical trial and/or regulatory approval process is highly uncertain, we may not be able to accurately estimate the actual amounts necessary to successfully complete the development, regulatory approval process and commercialization of mupadolimab, CPI-818 and ciforadenant or any other product candidates.

As of December 31, 2021, we had capital resources consisting of cash, cash equivalents and marketable securities of \$69.5 million. We do not expect our existing capital resources to be sufficient to enable us to fund the completion of all of our ongoing and planned clinical trials and remaining development program of any of ciforadenant, mupadolimab or CPI-818 through commercialization. In addition, while Angel Pharmaceuticals has received outside investment of approximately \$41.0 million in connection with its formation and licensing of certain of our intellectual property, such cash is not available for our use. Our operating plan may change as a result of many factors, including those described below as well as others currently unknown to us, and we may need to seek additional funds sooner than planned, through public or private equity, including pursuant to the 2020 Sales Agreement and 2021 Sales Agreement with Jefferies, debt financings or other sources, such as strategic collaborations. Such financing would result in dilution to stockholders, imposition of debt covenants and repayment obligations or other restrictions that may affect our business. If we raise additional capital through strategic collaboration agreements, we may have to relinquish valuable rights to our product candidates, including possible future revenue streams. For example, in October 2020 we formed Angel Pharmaceuticals with a group of investors in China to create a new China-based biopharmaceutical company with a mission to bring innovative quality medicines to Chinese patients for treatment of serious diseases including cancer, autoimmune diseases and infectious diseases. We granted Angel Pharmaceuticals a license to rights to develop and commercialize our three clinical-stage candidates – mupadolimab, CPI-818 and ciforadenant – in greater China and Angel obtained global rights to our BTK inhibitor preclinical programs. In addition, additional funding may not be available to us on acceptable terms, or at all, and any additional fundraising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize our product candidates. Furthermore, even if we believe we have sufficient funds for our current or future operating plans, we may seek additional capital due to favorable market conditions or strategic considerations.

The amount and timing of any expenditures needed to implement our development and commercialization programs will depend on numerous factors, including, but not limited to:

- the type, number, scope, progress, expansions, results of and timing of our ongoing and planned clinical trials of mupadolimab, CPI-818 and ciforadenant and any of our planned preclinical studies and clinical trials of other product candidates which we are pursuing or may choose to pursue in the future;
- the impact of changes in the COVID-19 pandemic, including the impact of vaccines and therapeutic treatments;
- the need for, and the progress, costs and results of, any additional clinical trials of mupadolimab, CPI-818 and ciforadenant or any of our other product candidates we may initiate based on the results of our planned clinical trials or discussions with the United States Food and Drug Administration (“FDA”) or other regulatory agencies, including any additional trials the FDA or other regulatory agencies may require;
- the costs of obtaining, maintaining and enforcing our patents and other intellectual property rights;

- the costs and timing of obtaining or maintaining manufacturing for mupadolimab, CPI-818 and ciforadenant and our other product candidates, including commercial manufacturing if any product candidate is approved;
- the costs and timing of establishing sales and marketing capabilities;
- our ability to achieve sufficient market acceptance, coverage and reimbursement from third-party payors and adequate market share for our product candidates;
- the terms and timing of establishing collaborations, license agreements and other partnerships;
- whether the FDA or other regulatory agencies accepts data from any clinical trials of our product candidates conducted by Angel Pharmaceuticals in China;
- costs associated with any new product candidates that we may develop, in-license or acquire;
- Angel Pharmaceuticals' ability to develop and commercialize product candidates in China;
- general economic conditions, such as rising inflation;
- the effect of competing technological and market developments;
- our ability to attract, hire and retain qualified personnel;
- our ability to establish and maintain partnering arrangements for development; and
- the costs associated with being a public company.

Several of these factors are outside of our control and if we are unable to obtain funding on a timely basis, we will be unable to complete the clinical trials for mupadolimab, CPI-818 and ciforadenant and our other product candidates, and we may be required to significantly curtail some or all of our activities.

***The COVID-19 pandemic could adversely impact our business, including our clinical trials, and financial condition.***

The COVID-19 pandemic has spread to most countries, including the United States and European and Asia-Pacific countries, including countries in which we have planned or active clinical trial sites. As the COVID-19 pandemic continues to spread around the globe, we will likely 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 or interruption of clinical trial subject visits and study procedures, the occurrence of which could affect the integrity of clinical trial data;

- risk that participants enrolled in our clinical trials will contract COVID-19 while the clinical trial is ongoing, which could impact the results of the clinical trial, including by increasing the number of observed adverse events;
- 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 authorization from local regulatory authorities 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 pandemic which may require us to change the ways in which our clinical trials are conducted, which may result in unexpected costs, or to discontinue such clinical trials altogether;
- interruptions or delays in preclinical studies due to restricted or limited operations at our research and development laboratory facilities;
- 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 in affected geographies outside the United States.

In addition, the spread of the COVID-19 pandemic has had an impact and may continue to severely impact the trading price of shares of our common stock and could further severely impact our ability to raise additional capital on a timely basis or at all.

The COVID-19 pandemic continues to rapidly evolve. The extent to which the COVID-19 pandemic may impact our business, including our clinical trials, and financial condition 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 pandemic, 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.

#### **Risks Related to the Discovery and Development of Our Product Candidates**

***Our product candidates are in various stages of development and may fail or suffer delays that materially and adversely affect their commercial viability. If we are unable to advance our product candidates through clinical development, obtain regulatory approval and ultimately commercialize such product candidates, or experience significant delays in doing so, our business will be materially harmed.***

We have invested a significant portion of our efforts and financial resources in the development of our most advanced product candidates, mupadolimab, ciforadenant and CPI-818. We have no products on the market and our ability to achieve and sustain profitability depends on obtaining regulatory approvals for and successfully commercializing our product candidates, either alone or with third parties. Before obtaining regulatory approval for the commercial distribution of our product candidates, we or our collaborator must conduct extensive preclinical tests and clinical trials to demonstrate sufficient safety and efficacy of our product candidates in patients.

As a result, we may not have the financial resources to continue development of, or to modify existing or enter into new collaborations for, a product candidate if we experience any issues that delay or prevent regulatory approval of, or our ability to commercialize, product candidates, including:

- negative or inconclusive results from our clinical trials, the clinical trials of our collaborators, including Angel Pharmaceuticals, or the clinical trials of others for product candidates similar to ours, leading to a decision or requirement to conduct additional preclinical testing or clinical trials or abandon a program;
- changes in the COVID-19 pandemic, including the impact of vaccines and therapeutic treatments;
- product-related side effects experienced by participants in our clinical trials, the clinical trials of our collaborators or by individuals using drugs or therapeutic biologics similar to our product candidates;
- the extent to which the COVID-19 pandemic may impact our clinical trials;
- delays in submitting Investigational New Drug applications (“INDs”) or comparable foreign applications or delays or failure in obtaining the necessary approvals from regulators 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 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 product candidate components or materials or other supplies necessary for the conduct of our clinical trials or the clinical trials of our collaborators;
- greater than anticipated clinical trial costs;
- delay in the development, approval or certification of companion diagnostic tests for our product candidates;
- 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, policy 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.

We could find that the product candidates we or our collaborators pursue are not safe or effective. Furthermore, if one or more of our product candidates generally prove to be ineffective, unsafe or commercially unviable, the development of our entire platform and pipeline could be delayed, potentially permanently. Any of these occurrences may materially and adversely affect our business, financial condition, results of operations and prospects.

Of the large number of drugs in development in the pharmaceutical industry, only a small percentage result in the submission of a NDA or BLA to the FDA or comparable marketing applications to foreign regulatory authorities, and even fewer are approved for commercialization. Furthermore, even if we do receive regulatory approval to market ciforadenant, mupadolimab or CPI-818, any such approval may be subject to limitations on the indicated uses for which we may market the product. Accordingly, even if we are able to obtain the requisite financing to continue to fund our

development programs, we cannot assure our stockholders that ciforadenant, mupadolimab or CPI-818 will be successfully developed or commercialized. If we or any of our existing or potential future collaborators are unable to develop, or obtain regulatory approval for, or, if approved, successfully commercialize ciforadenant, mupadolimab or CPI-818, we may not be able to generate sufficient revenue to continue our business.

***Clinical drug development involves a lengthy and expensive process with an uncertain outcome, and the results of preclinical studies and early clinical trials are not necessarily predictive of future results. Any product candidate we or any of our existing or potential future collaborators advance into clinical trials, including mupadolimab, CPI-818 and ciforadenant, may not have favorable results in later clinical trials, if any, or receive regulatory approval.***

Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. The results of preclinical studies and early clinical trials of our product candidates may not be predictive of the results of later-stage clinical trials. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy traits despite having progressed through preclinical studies and initial clinical trials. 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, notwithstanding promising results in earlier trials.

Furthermore, our ongoing and planned clinical trials will need to demonstrate sufficient safety and efficacy for approval by regulatory authorities in larger patient populations. Since the initiation of our Phase 1/1b clinical trial in January 2016, ciforadenant has been administered to more than 300 cancer patients and, while it has generally been well tolerated, there have been possibly drug-related or drug-related serious adverse events observed during the trial, and limited information is available concerning long-term safety and efficacy. It remains possible that patients enrolled in our Phase 1/1b clinical trial or our amended Phase 1b/2 clinical trial for ciforadenant could respond in unexpected ways. Our Phase 1/1b and our amended Phase 1b/2 clinical trials are conducted in patients with advanced cancers who have failed other approved therapies for their disease, and as such, it may be difficult to establish safety and efficacy in this type of patient population. Furthermore, a portion of our Phase 1/1b clinical trial, our amended Phase 1b/2 clinical trial and Genentech's Phase 1b/2 clinical trial under our collaboration agreement, includes the administration of ciforadenant in combination with Genentech's cancer immunotherapy, Tecentriq, which could exacerbate immune system related adverse events, cause increased toxicity or otherwise lead to unexpected adverse events. As a result, there can be no assurance that the results of historical clinical studies of ciforadenant conducted by third parties or the results of our clinical studies to-date will be indicative of the ongoing results of our Phase 1/1b clinical trial or amended Phase 1b/2 clinical trial, Genentech's Phase 1b/2 clinical trial or any future clinical trial of ciforadenant.

In March 2018, we began enrolling patients in our Phase 1/1b trial evaluating mupadolimab in cancer patients. The trial is designed to enroll successive cohorts of patients with advanced cancers who will receive increasing doses of mupadolimab both alone, or in combination with ciforadenant and/or pembrolizumab. As of February 15, 2022, mupadolimab has been generally well tolerated in the clinical trial at doses up to 24 mg/kg. However, CD73 is involved in several physiological systems and the administration of anti-CD73 antibodies such as mupadolimab could result in unforeseen safety issues. Similar to our Phase 1/1b clinical trial of ciforadenant, it is possible that patients enrolled in our Phase 1/1b clinical trial for mupadolimab could respond in unexpected ways and that the administration of mupadolimab in combination with ciforadenant and pembrolizumab could exacerbate immune system related adverse events. As a result, there can be no assurance that we will be able to generate favorable safety and efficacy data for mupadolimab or that we will be able to successfully complete our Phase 1/1b clinical trial.

In March 2019, we initiated a multi-center Phase 1/1b clinical trial evaluating CPI-818 in patients with various malignant T-cell lymphomas. Similar to our clinical trials of ciforadenant and mupadolimab, it is possible that patients enrolled in our Phase 1/1b clinical trial for CPI-818 could respond in unexpected ways.

Under our collaboration with Angel Pharmaceuticals, it will be responsible for the clinical development and commercialization, including all related expenses, of the licensed pipeline programs in greater China, and for the pre-clinical BTK program globally. It plans to initiate clinical trials in greater China for mupadolimab, CPI-818 and ciforadenant in the next 12 to 18 months and such trials will be subject to many of the same risks as our ongoing clinical programs.

For the foregoing reasons, we cannot be certain that our ongoing or planned clinical trials or any other future clinical trials will be successful. Any safety concerns observed in any one of our clinical trials in our targeted indications could limit the prospects for regulatory approval of our product candidates in those and other indications, which could have a material adverse effect on our business, financial condition and results of operations.

In addition, the FDA's and other regulatory authorities' policies with respect to clinical trials may change and additional government regulations may be enacted. For instance, the regulatory landscape related to clinical trials in the European Union ("EU") recently evolved. The EU Clinical Trials Regulation ("CTR") which was adopted in April 2014 and repeals the EU Clinical Trials Directive, became applicable on January 31, 2022. While the Clinical Trials Directive required a separate clinical trial application ("CTA") to be submitted in each member state, to both the competent national health authority and an independent ethics committee, the CTR introduces a centralized process and only requires the submission of a single application to all member states concerned. The CTR allows sponsors to make a single submission to both the competent authority and an ethics committee in each member state, leading to a single decision per member state. The assessment procedure of the CTA has been harmonized as well, including a joint assessment by all member states concerned, and a separate assessment by each member state with respect to specific requirements related to its own territory, including ethics rules. Each member state's decision is communicated to the sponsor via the centralized EU portal. Once the CTA is approved, clinical study development may proceed. The CTR foresees a three-year transition period. The extent to which ongoing and new clinical trials will be governed by the CTR varies. For clinical trials whose CTA was made under the Clinical Trials Directive before January 31, 2022, the Clinical Trials Directive will continue to apply on a transitional basis for three years. Additionally, sponsors may still choose to submit a CTA under either the Clinical Trials Directive or the CTR until January 31, 2023 and, if authorized, those will be governed by the Clinical Trials Directive until January 31, 2025. By that date, all ongoing trials will become subject to the provisions of the CTR. Compliance with the CTR requirements by us and our third-party service providers, such as clinical research organizations ("CROs"), may impact our developments plans.

If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies governing clinical trials, our development plans may also be impacted.

***Any termination or suspension of, or delays in the commencement or completion of, our planned clinical trials could result in increased costs to us, delay or limit our ability to generate revenue and adversely affect our commercial prospects.***

Before we can initiate clinical trials in the United States or in foreign countries for any of our product and development candidates, we must submit the results of preclinical testing to the FDA or foreign regulatory authorities along with other information, including information about product candidate chemistry, manufacturing and controls and our proposed clinical trial protocol, as part of an IND or similar application. In addition, we may rely in part on preclinical, clinical and quality data generated by CROs and other third parties for regulatory submissions for our product candidates. If these third parties do not make timely regulatory submissions for our product candidates, it will delay our plans for our clinical trials. If those third parties do not make this data available to us, we will likely have to develop all necessary preclinical and clinical data on our own, which will lead to significant delays and increase development costs of the product candidate. In addition, the FDA or foreign regulatory authorities may require us to conduct additional preclinical testing for any product candidate before it allows us to initiate clinical testing under any IND or similar, which may lead to additional delays and increase the costs of our preclinical development. Delays in the completion of our planned clinical trials for product candidates could significantly affect our product development costs.

While we initiated our Phase 1/1b clinical trial for ciforadenant in January 2016, our Phase 1/1b clinical trial for mupadolimab in cancer in March 2018 and our Phase 1/1b clinical trial for CPI-818 in March 2019, we do not know whether any of our other planned trials, including a planned Phase 2 clinical trial evaluating mupadolimab as a potential first-line therapy in NSCLC patients and a planned Phase 2 clinical trial evaluating ciforadenant as a potential first-line therapy in RCC patients, will begin on time in the future or whether any of our trials will be completed on schedule, if at

all. The commencement and completion of clinical trials can be delayed for a number of reasons, including delays related to:

- the FDA or foreign regulatory authorities failing to grant permission to proceed or placing a clinical trial on hold;
- subjects failing to enroll or remain in our trial at the rate we expect;
- subjects choosing an alternative treatment for the indication for which we are developing mupadolimab, CPI-818 and ciforadenant or other product candidates, or participating in competing clinical trials;
- lack of adequate funding to continue the clinical trial;
- subjects experiencing severe or unexpected drug-related adverse effects;
- a facility manufacturing mupadolimab, CPI-818 and ciforadenant, any of our other product candidates or any of their components being ordered by the FDA or other regulatory authorities to temporarily or permanently shut down due to violations of good manufacturing practice (“cGMP”) regulations or other applicable requirements, or infections or cross-contaminations of product candidates in the manufacturing process;
- any changes to our manufacturing process that may be necessary or desired;
- any failure or delay in reaching an agreement with CROs and clinical trial sites;
- third-party clinical investigators losing the licenses or permits necessary to perform our clinical trials, not performing our clinical trials on our anticipated schedule or consistent with the clinical trial protocol, good clinical practices (“GCP”) or regulatory requirements or other third parties not performing data collection or analysis in a timely or accurate manner;
- third-party contractors becoming debarred or suspended or otherwise penalized by the FDA or other government or regulatory authorities for violations of regulatory requirements, in which case we may need to find a substitute contractor, and we may not be able to use some or all of the data produced by such contractors in support of our marketing applications;
- one or more Institutional Review Boards (“IRBs”) or other reviewing bodies refusing to approve, suspending or terminating the trial at an investigational site, precluding enrollment of additional subjects, or withdrawing its approval of the trial; or
- patients failing to complete a trial or return for post-treatment follow-up.

In addition, disruptions caused by the COVID-19 pandemic may increase the likelihood that we encounter such difficulties or delays in initiating, enrolling, conducting or completing our planned and ongoing clinical trials. We could also encounter delays if a clinical trial is suspended or terminated by us, by the IRBs of the institutions in which such trials are being conducted, by the Data Safety Monitoring Board for such trial or by the FDA or other regulatory authorities. Such authorities may impose such a suspension or termination due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a drug, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. In addition, changes in regulatory requirements and policies may occur, and we may need to amend clinical trial protocols to comply with these changes. Amendments may require us to resubmit our clinical trial protocols to IRBs or other reviewing bodies for reexamination, which may impact the costs, timing or successful completion of a clinical trial.

If we experience delays in the completion of, or termination of, any clinical trial of our product candidates, the commercial prospects of our product candidates will be harmed, and our ability to generate product revenues from any of these product candidates will be delayed. In addition, any delays in completing our clinical trials will increase our costs, slow down our product candidate development and approval process and jeopardize our ability to commence product sales and generate revenues. See also the risk factor below titled “If we encounter difficulties enrolling subjects in our clinical trials, our clinical development activities could be delayed or otherwise adversely affected.”

In addition, many of the factors that cause, or lead to, termination or suspension of, or a delay in the commencement or completion of, clinical trials may also ultimately lead to the denial of regulatory approval of a product candidate. For example, if we make manufacturing or formulation changes to our product candidates, we may need to conduct additional studies to bridge our modified product candidates to earlier versions. Further, if one or more clinical trials are delayed, our competitors may be able to bring products to market before we do, and the commercial viability of mupadolib, CPI-818 and ciforadenant or other product candidates could be significantly reduced. Any of these occurrences may harm our business, financial condition and prospects significantly.

***Interim “top-line” and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data.***

From time to time, we may publicly disclose interim, top-line or preliminary data from our clinical trials, which is based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the top-line or preliminary results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Top-line or preliminary data also remain subject to audit and verification procedures that may result in the final data being materially different from the top-line or preliminary data we previously published. As a result, top-line and preliminary data should be viewed with caution until the final data are available.

From time to time, we may also disclose interim data from our preclinical studies and clinical trials. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Adverse differences between interim data and final data could significantly harm our business prospects. Further, disclosure of interim data by us or by our competitors could result in volatility in the price of our common stock.

Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular product candidate or product and our company in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is material or otherwise appropriate information to include in our disclosure.

If the interim, top-line or preliminary data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, our product candidates may be harmed, which could harm our business, operating results, prospects or financial condition.

***Our product candidates are subject to extensive regulation, compliance with which is costly and time consuming, and such regulation may cause unanticipated delays or prevent the receipt of the required approvals to commercialize our product candidates.***

The clinical development, manufacturing, labeling, storage, record-keeping, advertising, promotion, import, export, marketing and distribution of our product candidates are subject to extensive regulation by the FDA in the United States and by comparable authorities in foreign markets. In the United States, we are not permitted to market our product

candidates until we receive regulatory approval from the FDA. The process of obtaining regulatory approval is expensive, often takes many years and can vary substantially based upon the type, complexity and novelty of the product candidates involved, as well as the target indications and patient population. Approval policies or regulations may change, and the FDA and comparable authorities have substantial discretion in the drug approval process, including the ability to delay, limit or deny approval of a product candidate for many reasons. Despite the time and expense invested in clinical development of product candidates, regulatory approval is never guaranteed.

The FDA or comparable foreign regulatory authorities, including in China, can delay, limit or deny approval of a product candidate for many reasons, including:

- such authorities may disagree with the design or implementation of our or any of our existing or potential future collaborators' clinical trials;
- we or any of our existing or potential future collaborators may be unable to demonstrate to the satisfaction of the FDA or other regulatory authorities that a product candidate is safe and effective for any indication;
- such authorities may not accept clinical data from trials which are conducted at clinical facilities or in countries where the standard of care is potentially different from that of the United States;
- we or any of our existing or potential future collaborators may be unable to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;
- such authorities may disagree with our interpretation of data from preclinical studies or clinical trials;
- approval may be granted only for indications that are significantly more limited than what we apply for and/or with other significant restrictions on distribution and use;
- such authorities may find deficiencies in the manufacturing processes or facilities of third-party manufacturers with which we or any of our existing or potential future collaborators contract for clinical and commercial supplies; or
- the approval policies or regulations of such authorities may significantly change in a manner rendering our or any of our existing or potential future collaborators' clinical data insufficient for approval.

With respect to foreign markets, approval procedures vary among countries and, in addition to the foregoing risks, may involve additional product testing, administrative review periods and agreements with pricing authorities. In addition, events raising questions about the safety of certain marketed pharmaceuticals may result in increased cautiousness by the FDA and comparable foreign regulatory authorities, including in China, in reviewing new drugs based on safety, efficacy or other regulatory considerations and may result in significant delays in obtaining regulatory approvals. Any delay in obtaining, or inability to obtain, applicable regulatory approvals would prevent us or any of our existing or potential future collaborators from commercializing our product candidates.

***We are conducting clinical trials for mupadolimab, CPI-818 and ciforadenant, and we and Angel Pharmaceuticals may in the future, conduct additional clinical trials of product candidates, at sites outside the United States, and the FDA may not accept data from trials conducted in foreign locations.***

We are conducting oncology clinical trials with mupadolimab, CPI-818, and ciforadenant in North America, Australia and South Korea. In addition, Angel Pharmaceuticals has initiated a clinical trial in China for CPI-818 and plans to initiate clinical trials for mupadolimab and ciforadenant and we expect its clinical trial activity in China to be part of our planned global pivotal study for ciforadenant. The acceptance of study data from clinical trials conducted outside the U.S. or another jurisdiction by the FDA or comparable foreign regulatory authority may be subject to certain conditions or may not be accepted at all. In cases where data from foreign clinical trials are intended to serve as the sole basis for marketing approval in the U.S., the FDA will generally not approve the application on the basis of foreign data

alone unless (i) the data are applicable to the U.S. population and U.S. medical practice; (ii) the trials were performed by clinical investigators of recognized competence and pursuant to GCP regulations; and (iii) the data may be considered valid without the need for an on-site inspection by the FDA, or if the FDA considers such inspection to be necessary, the FDA is able to validate the data through an on-site inspection or other appropriate means. In addition, even where the foreign study data are not intended to serve as the sole basis for approval, the FDA will not accept the data as support for an application for marketing approval unless the study is well-designed and well-conducted in accordance with GCP requirements and the FDA is able to validate the data from the study through an onsite inspection if deemed necessary. Many foreign regulatory authorities have similar approval requirements. In addition, such foreign trials would be subject to the applicable local laws of the foreign jurisdictions where the trials are conducted. There can be no assurance that the FDA or any comparable foreign regulatory authority will accept data from trials conducted outside of the U.S. or the applicable jurisdiction. If the FDA or such foreign regulatory authority does not accept the data from our or Angel Pharmaceuticals' clinical trials for ciforadenant, mupadolimab or CPI-818, or any other product candidates, it would likely result in the need for additional trials, which would be costly and time-consuming and delay or permanently halt our development of mupadolimab, CPI-818 and ciforadenant or any other product candidates.

***If we are required by the FDA or similar regulatory authorities to obtain approval, clearance or certification of a companion diagnostic device in connection with approval of one of our product candidates, and we do not obtain or face delays in obtaining approval, clearance or certification of a companion diagnostic device, we will not be able to commercialize the product candidate and our ability to generate revenue will be materially impaired.***

According to FDA guidance, if the FDA determines that a companion diagnostic device is essential to the safe and effective use of a novel therapeutic product or indication, the FDA generally will not approve the therapeutic product or new therapeutic product indication if the companion diagnostic is not also approved or cleared for that indication. We plan to collaborate with patient diagnostic companies during our clinical trial enrollment process to help identify patients with tumor gene alterations that we believe are most likely to respond to our product candidates. If a satisfactory companion diagnostic is not commercially available, we may be required to create or obtain one that would be subject to regulatory approval requirements. The process of obtaining or creating such diagnostic is time consuming and costly.

Companion diagnostics are developed in conjunction with clinical programs for the associated product and are subject to regulation as medical devices by the FDA and comparable foreign regulatory authorities, and, to date, the FDA has required premarket approval of all companion diagnostics for cancer therapies. Generally, when a companion diagnostic is essential to the safe and effective use of a therapeutic product, the FDA requires that the companion diagnostic be approved before or concurrent with approval of the therapeutic product and before a product can be commercialized. The approval of a companion diagnostic as part of the therapeutic product's labeling limits the use of the therapeutic product to only those patients who express the specific genetic alteration that the companion diagnostic was developed to detect.

If the FDA or a comparable foreign regulatory authority requires approval, certification or clearance of a companion diagnostic for any of our product candidates, whether before or after the product candidate obtains marketing approval, we and/ or third-party collaborators may encounter difficulties in developing and obtaining approval, clearance or certification for these companion diagnostics. Any delay or failure by us or third-party collaborators to develop or obtain regulatory approval, clearance or certification of a companion diagnostic could delay or prevent approval or continued marketing of our related product candidates. We may also experience delays in developing a sustainable, reproducible and scalable manufacturing process for the companion diagnostic or in transferring that process to commercial partners or negotiating insurance reimbursement plans, all of which may prevent us from completing our clinical trials or commercializing our product candidates, if approved, on a timely or profitable basis, if at all.

Approval, clearance or certification of companion diagnostics may be subject to further legislative or regulatory reforms notably in the EU. On May 25, 2017, the new In Vitro Medical Devices Regulation ("IVDR") entered into force. The IVDR repeals and replaces the EU In Vitro Diagnostic Medical Devices Directive. Unlike directives, which must be implemented into the national laws of the EU member states, regulations are directly applicable, i.e., without the need for adoption of EU member states laws implementing them, in all EU member states and are intended to eliminate current differences in the regulation of medical devices among EU member states. The IVDR, among other things, is

intended to establish a uniform, transparent, predictable and sustainable regulatory framework across the EU for medical devices and ensure a high level of safety and health while supporting innovation. The IVDR will, however, only become applicable in May 2022, and on October 14, 2021, the European Commission proposed a “progressive” roll-out of the IVDR to prevent disruption in the supply of in vitro diagnostic medical devices. The European Parliament and Council voted to adopt the proposed regulation on December 15, 2021 and the regulation entered into force on January 2022. The IVDR will fully apply on May 26, 2022 but there will be a tiered system extending the grace period for many devices (depending on their risk classification) before they have to be fully compliant with the regulation..

The regulation of companion diagnostics will be subject to further requirements once the IVDR becomes applicable as it introduces a new classification system for companion diagnostics which are now specifically defined as diagnostic tests that support the safe and effective use of a specific medicinal product, by identifying patients that are suitable or unsuitable for treatment. Companion diagnostics will have to undergo a conformity assessment by a notified body. Before it can issue a CE certificate, the notified body must seek a scientific opinion from the EMA on the suitability of the companion diagnostic to the medicinal product concerned if the medicinal product falls exclusively within the scope of the centralized procedure for the authorization of medicines, or the medicinal product is already authorized through the centralized procedure, or a marketing authorization application for the medicinal product has been submitted through the centralized procedure. For other substances, the notified body can seek the opinion from a national competent authorities or the EMA.

These modifications may make it more difficult and costly for us to obtain regulatory clearances, approvals or certification for our companion diagnostics or to manufacture, market or distribute our products after clearance or approval is obtained.

***If we encounter difficulties enrolling subjects in our clinical trials, our clinical development activities could be delayed or otherwise adversely affected.***

Subject enrollment, a significant factor in the timing of clinical trials, is affected by many factors including the size and nature of the patient population, the proximity of patients to clinical sites, the eligibility criteria for the trial, the design of the clinical trial, the risk that enrolled patients will not complete a clinical trial, our ability to recruit clinical trial investigators with the appropriate competencies and experience, competing clinical trials and clinicians’ and patients’ perceptions as to the potential advantages of the product candidate being studied in relation to other available therapies, including any new drugs that may be approved for the indications we are investigating. We will be required to identify and enroll a sufficient number of subjects for each of our clinical trials. Potential subjects for any planned clinical trials may not be adequately diagnosed or identified with the diseases which we are targeting or may not meet the entry criteria for our studies. We also may encounter difficulties in identifying and enrolling subjects with a stage of disease appropriate for our planned clinical trials. We may not be able to initiate or continue clinical trials if we are unable to locate a sufficient number of eligible subjects to participate in the clinical trials required by the FDA or other foreign regulatory agencies. In addition, the process of finding and diagnosing subjects may prove costly.

We are enrolling patients with NSCLC and HNSCC in our Phase 1/1b clinical trial of mupadolimab and patients with T-cell lymphomas in our Phase 1/1b clinical trial of CPI-818 and plan to enroll patients with NSCLC in our planned Phase 2 clinical trial of mupadolimab and patients with RCC in our planned Phase 2 clinical trial of ciforadenant. If patients are unwilling to participate in our studies for any reason, including the existence of competitive clinical trials for similar patient populations, the availability of approved therapies or negative perceptions of the safety or efficacy of our product candidates, the timeline for recruiting subjects, conducting studies and obtaining regulatory approval of our product candidates may be delayed. Our inability to enroll a sufficient number of subjects for any of our future clinical trials would result in significant delays or may require us to abandon one or more clinical trials altogether.

We believe we have appropriately considered the above factors in our trials when determining expected clinical trial timelines, but we cannot assure our stockholders that our assumptions are correct or that we will not experience delays in enrollment, which would result in the delay of completion of such trials beyond our expected timelines. Furthermore, the COVID-19 pandemic could significantly affect enrollment in our future and planned clinical trials to an extent that we have not considered within our expected timelines.

***The occurrence of serious complications or side effects in connection with use of our product candidates, either in clinical trials or post-approval, could lead to discontinuation of our clinical development programs, refusal of regulatory authorities to approve our product candidates or, post-approval, revocation of marketing authorizations or refusal to approve new indications, which could severely harm our business, prospects, operating results and financial condition.***

During the conduct of clinical trials, patients report changes in their health, including illnesses, injuries and discomforts, to their study doctor. Often, it is not possible to determine whether or not the product candidate being studied caused these conditions. It is possible that as we test our product candidates in larger, longer and more extensive clinical programs with different dosing regimens and in combination with other immunotherapies, or as use of these product candidates becomes more widespread if they receive regulatory approval, illnesses, injuries, discomforts and other adverse events that were observed in earlier trials, as well as conditions that did not occur or went undetected in previous trials, will be reported by subjects. For example, possibly drug-related or drug-related serious adverse events have been observed during our Phase 1/1b clinical trial and our amended Phase 1b/2 clinical trial in patients receiving combination therapy with ciforadenant and Tecentriq include hemolytic anemia, encephalitis, hepatitis, pneumonitis, mucositis, myocarditis and dermatitis. Other toxicities observed during our Phase 1/1b clinical trial and our amended Phase 1b/2 clinical trial were mild and are commonly seen in patients with advanced cancers, such as nausea, vomiting, fatigue, rash, diarrhea, fever, abdominal pain, cough, constipation and decreased appetite. Other immune-oncology drugs also have been found occasionally to induce immune related toxicities such as colitis, hepatitis, pneumonitis, meningitis, myocarditis and various endocrine diseases.

Many times side effects are only detectable after investigational products are tested in large-scale, Phase 3 clinical trials or, in some cases, after they are made available to patients on a commercial scale after approval. Results of our current clinical trials and any future clinical trials we undertake could reveal a high and unacceptable severity and prevalence of these or other side effects. In such an event, our trials could be suspended or terminated, and the FDA or comparable foreign regulatory authorities could order us to cease further development of or deny approval of our product candidates for any or all targeted indications. Drug-related side effects could affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. Any of these occurrences may harm our business, financial condition and prospects significantly.

In addition, if one or more of our product candidates receives marketing approval, and we or others later identify undesirable side effects caused by such products, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw approvals of such product;
- regulatory authorities may require additional warnings on the label;
- 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; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of the particular product candidate, if approved, and could significantly harm our business, results of operations and prospects.

***We may not be successful in our efforts to identify or discover additional product candidates.***

The success of our business depends primarily upon our ability to develop and commercialize mupadolimab, CPI-818 and ciforadenant. Although mupadolimab, CPI-818 and ciforadenant are currently in clinical development, our research programs may fail to identify other potential product candidates, or advance them into and through clinical

development for a number of reasons. Our research methodology may be unsuccessful in identifying other potential product candidates or our other potential product candidates may be shown to have harmful side effects or may have other characteristics that may make the products unmarketable or unlikely to receive marketing approval. It may also take greater human and financial resources to identify additional therapeutic opportunities for our product candidates or to develop suitable potential product candidates through our research programs than we will possess, thereby limiting our ability to diversify and expand our product candidate portfolio.

#### **Risks Related to Our Reliance on Third Parties**

***We rely, and expect to continue to rely, on third parties to conduct our clinical trials. If these third parties do not meet our deadlines or otherwise conduct the trials as required, our clinical development programs could be delayed or unsuccessful and we may not be able to obtain regulatory approval for or commercialize our product candidates when expected, or at all.***

We do not have the ability to conduct all aspects of our preclinical testing or clinical trials ourselves. As a result, we are dependent on third parties to conduct our ongoing and planned clinical trials for mupadolimab, CPI-818 and ciforadenant and expect to continue to be dependent on third parties to conduct any additional future clinical trials of mupadolimab, CPI-818 and ciforadenant and preclinical and clinical trials for our other product candidates. The timing of the initiation and completion of these trials will therefore be controlled by such third parties and may occur at times substantially different from our estimates. Specifically, we use and rely on medical institutions, clinical investigators, CROs and consultants to conduct our trials in accordance with our clinical protocols and regulatory requirements. Such CROs, investigators and other third parties play a significant role in the conduct of these trials and subsequent collection and analysis of data, and we will control only certain aspects of their activities. Nevertheless, we are responsible for ensuring that each of our studies is conducted in accordance with the applicable protocol and legal, regulatory and scientific standards, and our reliance on the CROs and other third parties does not relieve us of our regulatory responsibilities. We and our CROs are required to comply with GCP requirements, which are regulations and guidelines enforced by the FDA, the Competent Authorities of the member states of the European Union and comparable foreign regulatory authorities for all of our product candidates in clinical development.

Regulatory authorities enforce these GCPs through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of our CROs or trial sites fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable, and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. In addition, our clinical trials must be conducted with product produced under cGMP or similar regulations. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process.

There is no guarantee that any such CROs, investigators or other third parties will devote adequate time and resources to such trials or perform as contractually required. If any of these third parties fail to meet expected deadlines, adhere to our clinical protocols or meet regulatory requirements, or otherwise performs in a substandard manner, our clinical trials may be extended, delayed or terminated. These difficulties may be exacerbated as a result of the ongoing COVID-19 pandemic.

If any of our clinical trial sites terminates for any reason, including as a result of the COVID-19 pandemic, we may experience the loss of follow-up information on subjects enrolled in such clinical trials unless we are able to transfer those subjects to another qualified clinical trial site, which may be difficult or impossible.

In addition, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and may receive cash or equity compensation in connection with such services. If these relationships and any related compensation result in perceived or actual conflicts of interest, or the FDA concludes that the financial relationship may have affected the interpretation of the study, the integrity of the data generated at the applicable clinical trial site may be questioned and the utility of the clinical trial itself may be jeopardized, which could result in the delay or rejection of any NDA, BLA or other applications we submit by the FDA or foreign regulatory authorities. Any such delay or rejection could prevent us from commercializing mupadolimab, CPI-818 and ciforadenant or our other product candidates.

***We rely on third parties to conduct some or all aspects of our manufacturing, research and preclinical and clinical testing, and these third parties may not perform satisfactorily.***

We do not expect to independently conduct all aspects of our manufacturing, research and preclinical and clinical testing. We currently rely, and expect to continue to rely, on third parties with respect to these items. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our studies in accordance with regulatory requirements or our stated study plans and protocols, we may not be able to complete, or may be delayed in completing, the preclinical and clinical studies required to support future IND or other submissions and approval of our product candidates. These difficulties may be exacerbated as a result of the ongoing COVID-19 pandemic. Furthermore, any of these third parties may terminate its engagement with us at any time. If we need to enter into alternative arrangements, it could delay our product development activities, and we may not be able to negotiate alternative arrangements on commercially reasonable terms, or at all.

***We and our contract manufacturers are subject to significant regulation with respect to manufacturing our products and the contract manufacturers on which we rely may not continue to meet regulatory requirements.***

We do not currently have nor do we plan to acquire the infrastructure or internal capability to manufacture our clinical drug supplies for use in the conduct of our trials, and we lack the resources and the capability to manufacture any of our product candidates on a clinical or commercial scale. We currently rely on several different manufacturers who supply different parts of the ciforadenant and CPI-818 molecules, on one manufacturer for mupadolimab drug substance and on other third-party manufacturers to produce our other product candidates.

All entities involved in the preparation of therapeutics for clinical studies or commercial sale, including our existing contract manufacturers for our product candidates, are subject to extensive regulation. Components of a finished therapeutic product approved for commercial sale or used in late-stage clinical studies must be manufactured in accordance with cGMP requirements. These regulations govern manufacturing processes and procedures, including record keeping, and the implementation and operation of quality systems to control and assure the quality of investigational products and products approved for sale. Poor control of production processes can lead to the introduction of adventitious agents or other contaminants, or to inadvertent changes in the properties or stability of our product candidates that may not be detectable in final product testing. We or our contract manufacturers must supply all necessary documentation in support of an NDA or BLA on a timely basis and must adhere to the FDA's Good Laboratory Practice regulations and cGMP regulations enforced by the FDA through its facilities inspection program. Our facilities and quality systems and the facilities and quality systems of some or all of our third-party contractors must pass a pre-approval inspection for compliance with the applicable regulations as a condition of regulatory approval of our product candidates or any of our other potential products. In addition, the regulatory authorities may, at any time, audit or inspect our manufacturing facilities or those of our third-party contractors involved with the preparation of our product candidates or the associated quality systems for compliance with the regulations applicable to the activities being conducted. We do not control the manufacturing process of, and are completely dependent on, our contract manufacturing partners for compliance with cGMPs.

The regulatory authorities also may, at any time following approval of a product for sale, audit the manufacturing facilities of our third-party contractors. If any such inspection or audit identifies a failure to comply with applicable regulations or if a violation of our product specifications or applicable regulations occurs independent of such an inspection or audit, we or the relevant regulatory authority may require remedial measures that may be costly and/or time-consuming for us or a third party to implement and that may include the temporary or permanent suspension of a clinical study or commercial sales or the temporary or permanent closure of a facility. Such violations could also result in civil and/or criminal penalties, and the FDA may impose regulatory sanctions including, among other things, refusal to approve a pending application for a new drug product or biologic product, revocation of a pre-existing approval or closing one or more manufacturing facilities.

In addition, if supply from an approved manufacturer is interrupted, there could be a significant disruption in commercial supply. An alternative manufacturer would need to be qualified through an NDA or BLA supplement which could result in further delay. The regulatory agencies may also require additional studies if a new manufacturer is relied

upon for commercial production. Changing manufacturers may involve substantial costs and is likely to result in a delay in our desired clinical and commercial timelines.

***We, or our third-party manufacturers, may be unable to successfully scale-up manufacturing of our product candidates in sufficient quality and quantity, which would delay or prevent us from developing our product candidates and commercializing approved products, if any.***

In order to conduct clinical trials of our product candidates, we will need to manufacture them in large quantities. We, or any manufacturing partners, may be unable to successfully increase the manufacturing capacity for any of our product candidates in a timely or cost-effective manner, or at all. In addition, quality issues may arise during scale-up activities. If we or any manufacturing partners are unable to successfully scale up the manufacture of our product candidates in sufficient quality and quantity, the development, testing and clinical trials of that product candidate may be delayed or become infeasible, and regulatory approval or commercial launch of any resulting product may be delayed or not obtained, which could significantly harm our business.

In addition, the supply chain for the manufacturing of our product candidates is complicated and can involve several parties. If we were to experience any supply chain issues, including as a result of the COVID-19 pandemic, our product supply could be seriously disrupted. We expect that the logistical challenges associated with our supply chain will grow more complex as we expand enrollment in our clinical trials for mupadolimab and CPI-818 and as we commence any clinical trials for additional product candidates.

***Our reliance on third parties requires us to share our trade secrets, which increases the possibility that a competitor will discover them or that our trade secrets will be misappropriated or disclosed.***

Because we rely on third parties to research and develop and to manufacture our product candidates, we must share trade secrets with them. We seek to protect our proprietary technology in part by entering into confidentiality agreements and, if applicable, material transfer agreements, consulting agreements or other similar agreements with our advisors, employees, third-party contractors and consultants prior to beginning research or disclosing proprietary information. These agreements typically limit the rights of the third parties to use or disclose our confidential information, including our trade secrets. Despite the contractual provisions employed when working with third parties, the need to share trade secrets and other confidential information increases the risk that such trade secrets become known by our competitors, are inadvertently incorporated into the technology of others, or are disclosed or used in violation of these agreements. Given that our proprietary position is based, in part, on our know-how and trade secrets, a competitor's independent discovery of our trade secrets or other unauthorized use or disclosure would impair our competitive position and may have a material adverse effect on our business.

In addition, these agreements typically restrict the ability of our advisors, employees, third-party contractors and consultants to publish data potentially relating to our trade secrets, although our agreements may contain certain limited publication rights. For example, any academic institution that we may collaborate with in the future will likely expect to be granted rights to publish data arising out of such collaboration. In the future we may also conduct joint research and development programs that may require us to share trade secrets under the terms of our research and development or similar agreements. Despite our efforts to protect our trade secrets, our competitors may discover our trade secrets, either through breach of our agreements with third parties, independent development or publication of information by any of our third-party collaborators. A competitor's discovery of our trade secrets would impair our competitive position and have an adverse impact on our business.

#### **Risks Related to Commercialization of Our Product Candidates**

***If we are unable to commercialize our product candidates or if we experience significant delays in obtaining regulatory approval for, or commercializing, any or all of our product candidates, our business will be materially and adversely affected.***

Our ability to generate product revenue will depend heavily on our ability to successfully develop and commercialize our product candidates. We do not expect that such commercialization of any of our product candidates

will occur for at least the next several years, if ever. Our ability to commercialize our product candidates effectively will depend on several factors, including the following:

- successful completion of preclinical studies and clinical trials, including the ability to demonstrate safety and efficacy of our product candidates;
- managing the complexity of our clinical trial designs;
- receipt of marketing approvals from the FDA and similar foreign regulatory authorities;
- establishing commercial manufacturing capabilities by making arrangements with third-party manufacturers;
- successfully launching commercial sales of any approved products, whether alone or in collaboration with others;
- acceptance of any approved products by patients, the medical community and third-party payors;
- establishing market share while competing with other therapies;
- a continued acceptable safety profile of any approved products;
- maintaining compliance with post-approval regulation and other requirements; and
- qualifying for, identifying, registering, maintaining, enforcing and defending intellectual property rights and claims covering our product candidates.

If we experience significant delays or an inability to commercialize our product candidates, our business, financial condition and results of operations will be materially adversely affected.

***If we do not achieve our projected development goals in the time frames we announce and expect, the commercialization of our products may be delayed and, as a result, our stock price may decline.***

We estimate the timing of the accomplishment of various scientific, clinical, regulatory and other product development goals, which we sometimes refer to as milestones. These milestones may include the commencement or completion of scientific studies and clinical trials and the submission of regulatory filings. From time to time, we may publicly announce the expected timing of some of these milestones. All of these milestones will be based on a variety of assumptions, and the actual timing of these milestones can vary dramatically compared to our estimates, in some cases for reasons beyond our control. For example, the COVID-19 pandemic has had a significant impact on the ability of biopharmaceutical companies to conduct clinical trials and, while we have not yet experienced delays resulting from the pandemic, there can be no assurance that we will be able to avoid such delays in the future. If we do not meet these milestones as publicly announced, the commercialization of our products may be delayed and, as a result, our stock price may decline.

***Any approved products could be subject to restrictions or withdrawal from the market, and we may be subject to penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our product candidates, when and if any of them are approved.***

Following potential approval of any of our product candidates, the FDA or foreign regulatory authorities may impose significant restrictions on a product's indicated uses or marketing or impose ongoing requirements for potentially costly and time consuming post-approval studies, post-market surveillance or clinical trials. Following approval, if any, of mupadolimab, CPI-818 and ciforadenant or any other product candidate, such candidate will also be subject to ongoing FDA or foreign regulatory authorities requirements governing the labeling, packaging, storage, distribution,

safety surveillance, advertising, promotion, recordkeeping and reporting of safety and other post-market information. If we or a regulatory agency discovers previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, a regulatory agency may impose restrictions on that product, the manufacturing facility or us, including requesting recall or withdrawal of the product from the market or suspension of manufacturing.

If we or the manufacturing facilities for mupadolimab, CPI-818 and ciforadenant or any other product candidate that may receive regulatory approval, if any, fail to comply with applicable regulatory requirements, a regulatory agency may:

- issue warning letters or untitled letters;
- seek an injunction or impose civil or criminal penalties or monetary fines;
- suspend or withdraw regulatory approval;
- suspend any ongoing clinical trials;
- refuse to approve pending applications or supplements or applications filed by us;
- suspend or impose restrictions on operations, including costly new manufacturing requirements; or
- seize or detain products, refuse to permit the import or export of product or request that we initiate a product recall.

The occurrence of any event or penalty described above may inhibit our ability to commercialize our product candidates and generate revenue.

The FDA has the authority to require a risk evaluation and mitigation strategy (“REMS”) as part of an NDA or BLA or after approval, which may impose further requirements or restrictions on the distribution or use of an approved drug, 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. Similar risk exist in foreign jurisdictions.

In addition, if mupadolimab, CPI-818 and ciforadenant or any of our other product candidates is approved, our product labeling, advertising and promotion will be subject to regulatory requirements and continuing regulatory review. The FDA and foreign regulatory authorities strictly regulates the promotional claims that may be made about prescription products. In particular, a product may not be promoted for uses that are not approved by the FDA or foreign regulatory authorities as reflected in the product’s approved labeling. If we receive marketing approval for a product candidate, physicians may nevertheless prescribe it to their patients in a manner that is inconsistent with the approved label. If we are found to have promoted such off-label uses, we may become subject to significant liability. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant sanctions. The federal government has levied large civil and criminal fines against companies for alleged improper promotion and has enjoined several companies from engaging in off-label promotion. The FDA has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response, and could generate negative publicity. Any failure to comply with ongoing regulatory requirements may significantly and adversely affect our ability to commercialize our product candidates.

Further, 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.

We also cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. 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 be subject to enforcement action and we may not achieve or sustain profitability.

***Disruptions at the FDA and other government agencies caused by funding shortages or global health concerns could hinder their ability to hire, retain or deploy key leadership and other personnel, or otherwise prevent new or modified products from being developed, approved or commercialized in a timely manner or at all, which could negatively impact our business.***

The ability of the FDA and foreign regulatory authorities to review and/or approve new products can be affected by a variety of factors, including government budget and funding levels, statutory, regulatory, and policy changes, the FDA's or foreign regulatory authorities' ability to hire and retain key personnel and accept the payment of user fees, and other events that may otherwise affect the FDA's or foreign regulatory authorities' ability to perform routine functions. Average review times at the FDA and foreign regulatory authorities have fluctuated in recent years as a result. In addition, government funding of other government agencies that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA and other agencies such as the EMA, following its relocation to Amsterdam and resulting staff changes, may also slow the time necessary for new drugs and biologics or modifications to approved drugs or biologics to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical FDA employees and stop critical activities.

Separately, in response to the COVID-19 pandemic, in March 2020, the FDA announced its intention to postpone most inspections of foreign manufacturing facilities, and on March 18, 2020, the FDA temporarily postponed routine surveillance inspections of domestic manufacturing facilities. Subsequently, in July 2020, the FDA resumed certain on-site inspections of domestic manufacturing facilities subject to a risk-based prioritization system. The FDA utilized this risk-based assessment system to assist in determining when and where it was safest to conduct prioritized domestic inspections. Additionally, on April 15, 2021, the FDA issued a guidance document in which the FDA described its plans to conduct voluntary remote interactive evaluations of certain drug manufacturing facilities and clinical research sites, among other facilities. According to the guidance, the FDA may request such remote interactive evaluations where the FDA determines that remote evaluation would be appropriate based on mission needs and travel limitations. In May 2021, the FDA outlined a detailed plan to move toward a more consistent state of inspectional operations, and in July 2021, the FDA resumed standard inspectional operations of domestic facilities and was continuing to maintain this level of operation as of September 2021. More recently, the FDA has continued to monitor and implement changes to its inspectional activities to ensure the safety of its employees and those of the firms it regulates as it adapts to the evolving COVID-19 pandemic. Regulatory authorities outside the United States have adopted similar restrictions or other policy measures in response to the COVID-19 pandemic. If a prolonged government shutdown occurs, or if global health concerns continue to prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews, or other regulatory activities, it could significantly impact the ability of the FDA or other regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

***Even if we receive regulatory approval we still may not be able to successfully commercialize mupadolimab, CPI-818 and ciforadenant or any other product candidate, and the revenue that we generate from sales, if any, could be limited.***

Even if mupadolimab, CPI-818 and ciforadenant or any of our other product candidates receive regulatory approval, they may not gain market acceptance among physicians, patients, healthcare payors or the medical community. The degree of market acceptance of our product candidates will depend on a number of factors, including:

- demonstration of clinical efficacy and safety compared to other more-established products;
- the indications for which our product candidates are approved;

- the limitation of our targeted patient population and other limitations or warnings contained in any FDA-approved labeling;
- acceptance of a new formulation by healthcare providers and their patients;
- our ability to obtain and maintain sufficient third-party coverage and reimbursement from government healthcare programs, including Medicare and Medicaid, private health insurers and other third-party payors;
- the willingness of patients to pay out-of-pocket in the absence of third-party coverage and reimbursement;
- the prevalence and severity of any adverse effects;
- pricing and cost-effectiveness;
- the timing of market introduction of our product candidates as well as competitive drugs;
- the effectiveness of our or any of our existing or potential future collaborators' sales and marketing strategies; and
- unfavorable publicity relating to the product candidate.

If any product candidate is approved but does not achieve an adequate level of acceptance by physicians, hospitals, healthcare payors or patients, we may not generate sufficient revenue from that product candidate and may not become or remain profitable. Our efforts to educate the medical community and third-party payors regarding the benefits of mupadolimab, CPI-818 and ciforadenant or any of our other product candidates may require significant resources and may never be successful.

***Failure to obtain or maintain adequate coverage and reimbursement for our product candidates, if approved, could limit our ability to market those products and decrease our ability to generate revenue.***

Successful commercial sales of any approved products will depend on the availability of adequate coverage and reimbursement from government health administration authorities, private health insurers and other third-party payors. Each third-party payor separately decides which products it will cover and establishes the reimbursement level, and there is no guarantee that any of our product candidates that may be approved for marketing by regulatory authorities will receive adequate coverage or reimbursement levels. Obtaining and maintaining coverage approval for a product candidate is time-consuming, costly and may be difficult. We may be required to conduct expensive pharmacoeconomic studies to justify coverage and reimbursement or the level of coverage and reimbursement relative to other therapies. If coverage and adequate reimbursement are not available or limited, we may not be able to successfully commercialize any product candidate for which we obtain marketing approval. Government authorities and third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for drugs and biologics. Even if we obtain coverage for a given product, the resulting reimbursement rates may be inadequate and may affect the demand for, or the price of, any product candidate for which we obtain marketing approval.

***Recently enacted legislation, future legislation and healthcare reform measures may increase the difficulty and cost for us to obtain marketing approval for and commercialize our product candidates and affect the prices we may obtain.***

In the United States and some foreign jurisdictions, there have been, and we expect there will continue to be, a number of legislative and regulatory changes to the healthcare system, including cost-containment measures that may

reduce or limit coverage and reimbursement for newly approved drugs and biologics and affect our ability to profitably sell any product candidates for which we obtain marketing approval.

For example, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, collectively referred to as the ACA, was enacted with a goal of reducing the cost of healthcare and substantially changing the way healthcare is financed by both governmental and private insurers. The ACA, among other things, subjected biological products to potential competition by lower-cost biosimilars; addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected; increased the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program; extended the rebate program to individuals enrolled in Medicaid managed care organizations; established annual fees and taxes on manufacturers of certain prescription drugs; created a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D; and established a new Patient-Centered Outcomes Research Institute to oversee, identify priorities and conduct comparative clinical effectiveness research, along with funding for such research.

Since its enactment, there have been judicial, executive and Congressional challenges to certain aspects of the ACA. For example, the Tax Cuts and Jobs Act was enacted, which, among other things, removes penalties for not complying with the ACA's individual mandate to carry health insurance. On December 14, 2018, a U.S. District Court Judge in the Northern District of Texas, ruled that the individual mandate is a critical and inseparable feature of the ACA, and therefore, because it was repealed as part of the Tax Act, the remaining provisions of the ACA are invalid as well. On December 18, 2019, the U.S. Court of Appeals for the 5th Circuit upheld the District Court's decision that the individual mandate was unconstitutional but remanded the case back to the District Court to determine whether the remaining provisions of the ACA are invalid as well. The U.S. Supreme Court is currently reviewing the case, although it is unclear when a decision will be made or how the Supreme Court will rule. In addition, there may be other efforts to challenge, replace, modify, repeal, or otherwise invalidate the ACA. We are continuing to monitor any changes to the ACA that, in turn, may potentially impact our business in the future.

In addition, other legislative changes have been proposed and adopted in the United States since the Affordable Care Act was enacted. These new laws, among other things, included aggregate reductions of Medicare payments to providers of 2% per fiscal year that will remain in effect through 2030, with the exception of a temporary suspension from May 1, 2020 through March 31, 2021, unless additional Congressional action is taken. In addition, in January 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several types of providers, including hospitals, imaging centers and cancer treatment centers. Recently there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed bills designed to, among other things, reform government program reimbursement methodologies. Additionally, individual states in the United States have also become increasingly active in passing legislation and implementing regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

We expect that the ACA, these new laws and other healthcare reform measures that may be adopted in the future may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies and additional downward pressure on the price that we receive for any approved product. 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, if approved.

In the EU, similar political, economic and regulatory developments may affect our ability to profitably commercialize our product candidates, if approved. In addition to continuing pressure on prices and cost containment measures, legislative developments at the EU or member state level may result in significant additional requirements or obstacles that may increase our operating costs. The delivery of healthcare in the EU, including the establishment and

operation of health services and the pricing and reimbursement of medicines, is almost exclusively a matter for national, rather than EU, law and policy. National governments and health service providers have different priorities and approaches to the delivery of health care and the pricing and reimbursement of products in that context. In general, however, the healthcare budgetary constraints in most EU member states have resulted in restrictions on the pricing and reimbursement of medicines by relevant health service providers. Coupled with ever-increasing EU and national regulatory burdens on those wishing to develop and market products, this could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to commercialize our product candidates, if approved. In markets outside of the United States and EU, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies.

We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action in the United States, the EU or any other jurisdiction. If we or any third parties we may engage are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we or such third parties are not able to maintain regulatory compliance, our product candidates may lose any regulatory approval that may have been obtained and we may not achieve or sustain profitability.

***Any product candidates for which we intend to seek approval as biologic products may face competition sooner than anticipated.***

The ACA includes a subtitle called the Biologics Price Competition and Innovation Act of 2009 (“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 twelve years from the date on which the reference product was first licensed. During this twelve-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 its product. The law is complex and is still being interpreted and implemented by the FDA. Any processes adopted by the FDA to implement the BPCIA could have a material adverse effect on the future commercial prospects for our biological products.

Mupadolibab, which we are evaluating in a Phase 1/1b oncology clinical trial is a biological product. We believe that mupadolibab and any of our future product candidates, if approved as a biological product under a BLA, should qualify for the twelve-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 product 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. Jurisdictions in addition to the United States have established abbreviated pathways for regulatory approval of biological products that are biosimilar to earlier approved reference products. For example, the EU has had an established regulatory pathway for biosimilars since 2006. Moreover, the extent to which a biosimilar, once approved, could be substituted for any one of our reference products in a way that is similar to traditional generic substitution for non-biological products will depend on a number of marketplace and regulatory factors that are still developing.

***We may fail to obtain orphan drug designations from the FDA for our product candidates, and even if we obtain such designations, we may be unable to maintain the benefits associated with orphan drug designation, including the potential for market exclusivity.***

Under the Orphan Drug Act, the FDA may grant orphan drug designation to a drug or biologic intended to treat a rare disease or condition, which is defined as one occurring in 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 or biologic 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 product that has orphan drug designation subsequently receives the first FDA approval for the disease for which it has such designation, the product is entitled to orphan drug

exclusivity, which means that the FDA may not approve any other applications, including a full NDA or BLA, to market the same drug or biologic for the same disease or condition for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity or where the manufacturer is unable to assure sufficient product quantity.

While we have not obtained nor have we sought to obtain orphan designation for any product candidate, we believe many of the potential indications of our product candidates, could qualify for orphan drug designation. As a result, we may seek to obtain orphan drug designation for our product candidates in the future. Even if we obtain such designations, we may not be the first to obtain marketing approval of our product candidate for the orphan-designated 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 can be approved for the same condition. Even after an orphan product is approved, the FDA can subsequently approve the same drug for the same condition if the FDA concludes 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 drug, nor gives the drug any advantage in the regulatory review or approval process. In addition, while we may seek orphan drug designation for our product candidates, we may never receive such designations.

***We may expend our limited resources to pursue a particular product candidate and fail to capitalize on product candidates that may be more profitable or for which there is a greater likelihood of success.***

Because we have limited financial and managerial resources, we focus on specific product candidates, including mupadolimab, CPI-818 and ciforadenant. As a result, we may forgo or delay pursuit of opportunities with other product candidates that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable product candidates. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate.

***We may not be successful in establishing and maintaining development or other strategic collaborations, which could adversely affect our ability to develop and commercialize product candidates.***

In connection with our Phase 1/1b clinical trial for ciforadenant, we entered into a clinical trial collaboration agreement with Genentech in October 2015. Pursuant to the agreement, Genentech provides access to, and supplies of, its cancer immunotherapy, Tecentriq, to be used in combination with ciforadenant during the clinical trial. The collaboration operates under a joint development committee with equal representation from both companies. In May 2017, we signed a second clinical trial collaboration agreement with Genentech. Under this second agreement, ciforadenant administered in combination with Tecentriq is being evaluated in a Phase 1b/2 randomized, controlled clinical study as second-line therapy in patients with non-small cell lung cancer who are resistant and/or refractory to prior therapy with an anti-PD-(L)1 antibody. However, we and Genentech each have the right to terminate the respective collaboration agreements due to material breach by either party, for safety considerations, if directed by a regulatory authority or if development of ciforadenant or Tecentriq is discontinued. If we fail to maintain these strategic collaborations with Genentech (1) the development of ciforadenant in combination with Tecentriq may be terminated or delayed; (2) our cash expenditures related to development of ciforadenant could increase significantly, and we may need to seek additional financing; (3) we may be required to hire additional employees or otherwise develop expertise for which we have not budgeted; (4) we will bear all of the risk related to the development of ciforadenant as a combination therapy; and (5) we will need to seek collaborations with other companies that have anti-PD-1 or anti-PD-L1 antibodies, which will significantly delay our development program and could have a material adverse effect on our business, financial condition and results of operations.

***We may form strategic alliances and collaborative partnerships in the future, and we may not realize the benefits of such alliances.***

In addition to our collaboration agreements with Genentech, we may form additional strategic alliances, create joint ventures or collaborations or enter into licensing arrangements with third parties that we believe will complement or augment our existing business, including for the continued development or commercialization of our product candidates. These relationships may result in or include non-recurring and other charges, increased near- and long-term expenditures, the issuance of securities that dilute our existing stockholders or disruptions to our management and business. In addition, we face significant competition in seeking appropriate strategic partners, and the negotiation process is time-consuming and complex. Moreover, we may not be successful in our efforts to establish a strategic partnership or other alternative arrangements for our product candidates because third parties may view the risk of failure in future clinical trials as too significant or the commercial opportunity for our product candidates as too limited. We cannot be certain that, following a strategic transaction or license, we will achieve the revenue or specific net income that justifies such transaction.

Even if we are successful in our efforts to establish strategic alliances or collaborative partnerships, the terms that we agree upon may not be favorable to us, and we may not be able to maintain such strategic alliances or collaborative partnerships if, for example, development or approval of a product candidate is delayed, the safety of a product candidate is questioned or sales of an approved product candidate are unsatisfactory. In addition, any existing or potential future strategic alliances or collaborative partnerships may be terminable by our strategic partners, and we may not be able to adequately protect our rights under these agreements. Furthermore, strategic partners may negotiate for certain rights to control decisions regarding the development and commercialization of our product candidates, if approved, and may not conduct those activities in the same manner as we do. Any termination of strategic alliances or collaborative partnerships we enter into in the future, or any delay in entering into collaborative partnership agreements related to our product candidates, could delay the development and commercialization of our product candidates and reduce their competitiveness if they reach the market, which could have a material adverse effect on our business, financial condition and results of operations.

In October 2020, we formed Angel Pharmaceuticals with a group of investors in China to create a new China-based biopharmaceutical company with a mission to bring innovative quality medicines to Chinese patients for treatment of serious diseases including cancer, autoimmune diseases and infectious diseases. We granted Angel Pharmaceuticals a license to rights to develop and commercialize our three clinical-stage candidates – mupadolimab, CPI-818 and ciforadenant – in greater China and obtained global rights to our BTK inhibitor preclinical programs. While certain of our executive officers and directors will initially be on the board of directors of Angel Pharmaceuticals, we have limited control over it and so we will be subject to many of the same risks set forth above with respect to all collaborations. Additionally, any actions taken by the Chinese government to implement trade policy changes, financial restrictions, or increased regulatory scrutiny on U.S. companies could negatively impact Angel Pharmaceuticals. For instance, China has previously taken or threatened to take trade and other actions in retaliation against U.S. policies, and is likely to continue to do so. Past or future developments in this regard may have a material adverse effect on the economies, financial markets, and currency exchange rates in China and the United States. Tensions between the United States and China have increased over the past few years as a result of disputes in areas including trade policy, intellectual property, cybersecurity and data privacy, as well as due to geopolitical conflicts such as the war between Ukraine and Russia. Our interests in Angel Pharmaceuticals could be harmed if relations between the United States and China worsen or if either government imposes additional policies, tariffs or sanctions and our business could encounter increased regulatory scrutiny in China, as well as adverse media or public attention in China, as a result of the deteriorating bilateral relationship.

Angel Pharmaceuticals will also be subject to many of the same risks that are set forth in this “Risk Factors” section pertaining to operations, government regulation, and intellectual property, which may adversely affect Angel Pharmaceuticals’ ability to develop and commercialize products.

***We face competition from entities that have developed or may develop product candidates for cancer, including companies developing novel treatments and technology platforms. If these companies develop technologies or product candidates more rapidly than we do or their technologies are more effective, our ability to develop and successfully commercialize product candidates may be adversely affected.***

Our competitors have developed, are developing or will develop product candidates and processes competitive with our product candidates. Competitive therapeutic treatments include those that have already been approved and accepted by the medical community and any new treatments that enter the market. We believe that a significant number of products are currently under development, and may become commercially available in the future, for the treatment of conditions for which we may attempt to develop product candidates. In particular, there is intense and rapidly evolving competition in the immunoregulatory therapeutics field. Our competitors include larger and better funded pharmaceutical, biopharmaceutical, biotechnological and therapeutics companies. Moreover, we also compete with universities and other research institutions that may be active in oncology research and could be in direct competition with us. We also compete with these organizations to recruit management, scientists and clinical development personnel, which could negatively affect our level of expertise and our ability to execute our business plan. We will also face competition in establishing clinical trial sites, registering subjects for clinical trials and in identifying and in-licensing new product candidates. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies.

Kyowa Hakko Kirin has approval in Japan and the US for istradefylline, an A2A antagonist, in Parkinson's disease. Within oncology, Novartis has announced an exclusive licensing agreement with Palobiofarma SL and is conducting a Phase 1 trial with an A2A antagonist. AstraZeneca plc is conducting clinical trials with an A2A antagonist for use in cancer therapy. Merck KgaA has entered into a pre-clinical collaboration with Domain Therapeutics Inc. to develop programs targeting the adenosine pathway. In addition, Redoxtherapies, Inc., which was acquired by Juno Therapeutics and subsequently by Celgene, and Arcus Biosciences, Inc. are developing A2A receptor antagonists for cancer. Astra Zeneca, Bristol-Myers Squibb, and Novartis in partnership with Surface Oncology, Inc. have initiated clinical trials with anti-CD73 antibodies in cancer patients. Recently, Astra Zeneca reported positive results in a phase 2 clinical trial in Stage 3 NSCLC with the combination of durvalumab and their anti CD73 antibody, oleclumab. More generally, in the field of immunoncology, there are large pharmaceutical companies with approved products or products in late-stage development that target other immune checkpoints, including PD-1, PD-L1 or CTLA-4. These companies include Bristol-Myers Squibb (nivolumab, ipilimumab), Merck (pembrolizumab), Genentech (atezolizumab) and AstraZeneca (durvalumab, tremelimumab).

Many of our competitors have significantly greater financial, technical, manufacturing, marketing, sales and supply resources or experience than we do. If we successfully obtain approval for any product candidate, we will face competition based on many different factors, including the safety and effectiveness of our products, the ease with which our products can be administered and the extent to which patients accept relatively new routes of administration, the timing and scope of regulatory approvals for these products, the availability and cost of manufacturing, marketing and sales capabilities, price, reimbursement coverage and patent position. 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 product candidates.

***The market opportunities for our product candidates may be limited to those patients who are ineligible for or have failed prior treatments and may be small.***

Cancer therapies are sometimes characterized as first-line, second-line or third-line, and the FDA often approves new therapies initially only for third-line use. When cancer is detected early enough, first line therapy is sometimes adequate to cure the cancer or prolong life without a cure. Whenever first-line therapy, usually chemotherapy, hormone therapy, surgery or a combination of these, proves unsuccessful, second-line therapy may be administered. Second-line therapies often consist of more chemotherapy, radiation, antibody drugs, tumor targeted small molecules or a combination of these. Third-line therapies can include bone marrow transplantation, antibody and small molecule targeted therapies, more invasive forms of surgery and new technologies. In markets with approved therapies, we expect to initially seek approval of our product candidates as a later stage therapy for patients who have failed other approved

treatments. Subsequently, for those drugs that prove to be sufficiently beneficial, if any, we would expect to seek approval as a second-line therapy and potentially as a first-line therapy, but there is no guarantee that our product candidates, even if approved, would be approved for second-line or first-line therapy. In addition, we may have to conduct additional clinical trials prior to gaining approval for second-line or first-line therapy.

Our projections of both the number of people who have the cancers we are targeting, as well as the subset of people with these cancers in a position to receive later stage therapy and who have the potential to benefit from treatment with our product candidates, are based on our beliefs and estimates. These estimates have been derived from a variety of sources, including scientific literature, surveys of clinics, patient foundations or market research and may prove to be incorrect. Further, new studies may change the estimated incidence or prevalence of these cancers. The number of patients may turn out to be lower than expected. In addition, the potentially addressable patient population for our product candidates may be limited or may not be amenable to treatment with our product candidates. Even if we obtain significant market share for our product candidates, we may never achieve profitability without obtaining regulatory approval for additional indications, including use as a first or second-line therapy.

***We have no sales, marketing or distribution capabilities, and we may have to invest significant resources to develop these capabilities.***

We have no internal sales, marketing or distribution capabilities. If mupadolimab, CPI-818 and ciforadenant or any of our other product candidates ultimately receives regulatory approval, we may not be able to effectively market and distribute the product candidate. We may have to seek collaborators or invest significant amounts of financial and management resources to develop internal sales, distribution and marketing capabilities, some of which will be committed prior to any confirmation that mupadolimab, CPI-818 and ciforadenant or any of our other product candidates will be approved, if at all. We may not be able to enter into collaborations or hire consultants or external service providers to assist us in sales, marketing and distribution functions on acceptable financial terms or at all. Even if we determine to perform sales, marketing and distribution functions ourselves, we could face a number of additional related risks, including:

- we may not be able to attract and build an effective marketing department or sales force;
- the cost of establishing a marketing department or sales force may exceed our available financial resources and the revenue generated by mupadolimab, CPI-818 and ciforadenant or any other product candidates that we may develop, in-license or acquire; and
- our direct sales and marketing efforts may not be successful.

***Governments may impose price controls, which may adversely affect our future profitability.***

We intend to seek approval to market our product candidates in both the United States and in foreign jurisdictions. In some foreign countries, particularly in the EU, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product candidate. To obtain reimbursement or pricing approval in some countries, we may be required to conduct clinical trials to compare the cost-effectiveness of our product candidates to other available therapies, which is time-consuming and costly. If reimbursement of our future products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, we may be unable to achieve or sustain profitability.

## Risks Related to Our Business Operations

***Our operating results may fluctuate significantly, which makes our future operating results difficult to predict and could cause our operating results to fall below expectations or any guidance we may provide.***

Our quarterly and annual operating results may fluctuate significantly, which makes it difficult for us to predict our future operating results. These fluctuations may occur due to a variety of factors, many of which are outside of our control, including, but not limited to:

- the timing and cost of, and level of investment in, research, development and commercialization activities relating to our product candidates, which may change from time to time;
- coverage and reimbursement policies with respect to our product candidates, if approved, and potential future drugs that compete with our product candidates;
- the cost of manufacturing our product candidates, which may vary depending on the quantity of production and the terms of our agreements with manufacturers;
- expenditures that we may incur to acquire, develop or commercialize additional product candidates and technologies;
- the level of demand for any approved products, which may vary significantly;
- future accounting pronouncements or changes in our accounting policies; and
- the timing and success or failure of clinical trials for our product candidates or competing product candidates, or any other change in the competitive landscape of our industry, including consolidation among our competitors or partners.

The cumulative effects of these factors could result in large fluctuations and unpredictability in our quarterly and annual operating results. As a result, comparing our operating results on a period-to-period basis may not be meaningful. Investors should not rely on our past results as an indication of our future performance.

This variability and unpredictability could also result in our failing to meet the expectations of industry or financial analysts or investors for any period. If our revenue or operating results fall below the expectations of analysts or investors or below any forecasts we may provide to the market, or if the forecasts we provide to the market are below the expectations of analysts or investors, the price of our common stock could decline substantially. Such a stock price decline could occur even when we have met any previously publicly stated revenue or earnings guidance we may provide.

***We are dependent on the services of our President and Chief Executive Officer, Richard A. Miller, M.D., and other key executives, and if we are not able to retain these members of our management or recruit additional management, clinical and scientific personnel, our business will suffer.***

We are dependent on the principal members of our management and scientific staff. The loss of service of any of our management could harm our business. In addition, we are dependent on our continued ability to attract, retain and motivate highly qualified management, clinical and scientific personnel. If we are not able to retain our management, particularly our President and Chief Executive Officer, Dr. Miller, and to attract, on acceptable terms, additional qualified personnel necessary for the continued development of our business, we may not be able to sustain our operations or grow. Although we have executed employment agreements with each member of our current executive management team, including Dr. Miller, these agreements are terminable at will with or without notice and, therefore, we may not be able to retain their services as expected.

We will need to expand and effectively manage our managerial, operational, financial and other resources in order to successfully pursue our clinical development and commercialization efforts. We may not be able to attract or retain qualified management and scientific and clinical personnel in the future due to the intense competition for qualified personnel among pharmaceutical, biotechnology and other businesses, particularly in the San Francisco Bay Area. Our industry has experienced a high rate of turnover of management personnel in recent years. If we are not able to attract, integrate, retain and motivate necessary personnel to accomplish our business objectives, we may experience constraints that will significantly impede the achievement of our development objectives, our ability to raise additional capital and our ability to implement our business strategy.

In addition, we do not currently maintain “key person” life insurance on the lives of our executives or any of our employees. This lack of insurance means that we may not have adequate compensation for the loss of the services of these individuals.

***We may encounter difficulties in managing our growth and expanding our operations successfully.***

We will need to grow our organization substantially to continue development and pursue the potential commercialization of mupadolimab, CPI-818 and ciforadenant and our other product candidates. As we seek to advance mupadolimab, CPI-818 and ciforadenant and other product candidates, we will need to expand our financial, development, regulatory, manufacturing, marketing and sales capabilities or contract with third parties to provide these capabilities for us. As our operations expand, we expect that we will need to manage additional relationships with various strategic partners, suppliers and other third parties. Our future financial performance and our ability to commercialize our product candidates and to compete effectively will depend, in part, on our ability to manage any future growth effectively.

***We are subject to various federal and state healthcare laws and regulations, and our failure to comply with these laws and regulations could harm our results of operations and financial condition.***

Although we do not currently have any products on the market, if we obtain FDA or foreign approval for any of our product candidates and begin commercializing those products in the United States or abroad, our operations may be directly, or indirectly through our customers and third-party payors, subject to various U.S. federal, state and foreign healthcare laws and regulations. These laws will affect our operations, sales and marketing practices, and our relationships with physicians and other customers and third-party payors. Such laws include:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons or entities from knowingly and willfully soliciting, offering, receiving or providing remuneration, 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, any good or service, for which payment may be made under a federal healthcare program such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the federal Anti-Kickback Statute or specific intent to violate it to have committed a violation;
- the 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, claims for payment that are false or fraudulent 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 that 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 federal False Claims Act;
- the federal Health Insurance Portability and Accountability Act of 1996 (“HIPAA”), which imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters. 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 to have committed a violation;

- the federal Physician Payment Sunshine Act, which requires manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children’s Health Insurance Program (with certain exceptions) to report annually to the government information related to payments or other “transfers of value” made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain non-physician practitioners (physician assistants, nurse practitioners, clinical nurse specialists, certified registered nurse anesthetists, anesthesiology assistants and certified nurse midwives) and teaching hospitals, and requires applicable manufacturers and group purchasing organizations to report annually to the government ownership and investment interests held by the physicians described above and their immediate family members. Manufacturers are required to submit reports to the government by the 90th day of each calendar year; and
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry’s voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government; and state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures and pricing information.

Ensuring that our internal operations and 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 such laws or any other governmental laws and regulations that may apply to us, we may be subject to significant penalties, including civil, criminal and administrative penalties, damages, fines, exclusion from U.S. government funded healthcare programs, such as Medicare and Medicaid, disgorgement, individual imprisonment, contractual damages, reputational harm, diminished profits and the curtailment or restructuring of our operations.

***We and our current and any existing or future collaborators, third-party manufacturers and suppliers will or may use biological materials and may use hazardous materials, and any claims relating to improper handling, storage or disposal of these materials could be time consuming or costly.***

We and our current and any existing or future collaborators, third-party manufacturers or suppliers will or may use biological materials and may use hazardous materials, including chemicals and biological agents and compounds that could be dangerous to human health and safety of the environment. Our operations and the operations of our third-party manufacturers and suppliers also produce hazardous waste products. Federal, state and local laws and regulations govern the use, generation, manufacture, storage, handling and disposal of these materials and wastes. Compliance with applicable environmental laws and regulations may be expensive, and current or future environmental laws and regulations may impair our product development efforts. In addition, we cannot eliminate the risk of accidental injury or contamination from these materials or wastes. We do not carry specific biological or hazardous waste insurance coverage, and our property, casualty and general liability insurance policies specifically exclude coverage for damages and fines arising from biological or hazardous waste exposure or contamination. In the event of contamination or injury, we could be held liable for damages or be penalized with fines in an amount exceeding our resources, and our clinical trials or regulatory approvals could be suspended.

***If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of mupadolimab, CPI-818 and ciforadenant or our other product candidates.***

We face an inherent risk of product liability as a result of the clinical testing of mupadolimab, CPI-818 and ciforadenant, and the planned clinical testing of our other product candidates and will face an even greater risk if we commercialize our product candidates. For example, we may be sued if mupadolimab, CPI-818 and ciforadenant or our other product candidates allegedly cause injury or are found to be otherwise unsuitable during product testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product candidate, negligence, strict liability and a breach of warranties. Claims could also be asserted under state consumer protection acts.

If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit or cease the commercialization of our product candidates. Even a successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in:

- decreased demand for mupadolimab, CPI-818 and ciforadenant or our other product candidates;
- injury to our reputation;
- withdrawal of clinical trial participants;
- costs to defend the related litigation;
- a diversion of management's time and our resources;
- substantial monetary awards to trial participants or patients;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- loss of revenue;
- the inability to commercialize mupadolimab, CPI-818 and ciforadenant or our other product candidates; and
- a decline in our stock price.

We have product liability insurance coverage in an amount and on terms and conditions that are customary for similarly situated companies and that are satisfactory to our board of directors. Our inability to retain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of mupadolimab, CPI-818 and ciforadenant or our other product candidates. Although we plan to maintain such insurance, any claim that may be brought against us could result in a court judgment or settlement in an amount that is not covered, in whole or in part, by our insurance or that is in excess of the limits of our insurance coverage. Our insurance policies will also have various exclusions, and we may be subject to a product liability claim for which we have no coverage. We may have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts.

***We and any of our existing or potential future collaborators will be required to report to regulatory authorities if any products that may be approved in the future cause or contribute to adverse medical events, and any failure to do so would result in sanctions that would materially harm our business.***

If we and any of our existing or potential future collaborators are successful in commercializing our products, the FDA and foreign regulatory authorities would require that we and any of our existing or potential future collaborators report certain information about adverse medical events if those products may have caused or contributed to those adverse events. The timing of our obligation to report would be triggered by the date we become aware of the adverse event as well as the nature of the event. We and any of our existing or potential future collaborators or CROs may fail to report adverse events within the prescribed timeframe. If we or any of our existing or potential future collaborators or CROs fail to comply with such reporting obligations, the FDA or a foreign regulatory authority could take action, including criminal prosecution, the imposition of civil monetary penalties, seizure of our products or delay in approval or clearance of future products.

***Our employees, independent contractors, principal investigators, CROs, consultants and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements.***

We are exposed to the risk that our employees, independent contractors, principal investigators, CROs, consultants and vendors may engage in misconduct or other illegal activity. Misconduct by these parties could include intentional, reckless and/or negligent conduct involving the improper use or misrepresentation of information obtained in the course of clinical trials, the creation of fraudulent data in our preclinical studies or clinical trials or illegal misappropriation of drug product, which could result in regulatory sanctions and cause serious harm to our reputation. It is not always possible to identify and deter misconduct by employees and other third parties, 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 or regulations. In addition, we are subject to the risk that a person or government could allege such fraud or other misconduct, even if none occurred. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of fines and other sanctions.

**Risks Related to Our Intellectual Property**

***Our rights to develop and commercialize our product candidates are subject in part to the terms and conditions of licenses granted to us by other companies. The patent protection, prosecution and enforcement for some of our product candidates may be dependent on third parties.***

We currently are heavily reliant upon licenses of certain patent rights and proprietary technology from third parties that is important or necessary to the development of our technology and products, including technology related to our product candidates. For example, we rely on our license agreement with Vernalis for rights with respect to the intellectual property covering ciforadenant and certain development candidates under our A2B receptor antagonist program. Further, we rely on our license agreement with The Scripps Research Institute for rights related to our lead development candidate for our anti-CD73 program, mupadolimab. These and other licenses we may enter into in the future may not provide adequate rights to use such intellectual property and technology in all relevant fields of use or in all territories in which we may wish to develop or commercialize our technology and products in the future. As a result, we may not be able to develop and commercialize our technology and products in fields of use and territories for which we are not granted rights pursuant to such licenses.

Licenses to additional third-party technology that may be required for our development programs may not be available in the future or may not be available on commercially reasonable terms, which could have a material adverse effect on our business and financial condition.

In some circumstances, we may not have the right to control the preparation, filing, prosecution and enforcement of patent applications, or to maintain the patents, covering technology that we license from third parties. In addition, some of our agreements with our licensors require us to obtain consent from the licensor before we can enforce patent rights, and our licensor may withhold such consent or may not provide it on a timely basis. Therefore, we cannot be certain that our licensors or collaborators will prosecute, maintain, enforce and defend such intellectual property rights in a manner consistent with the best interests of our business, including by taking reasonable measures to protect the confidentiality of know-how and trade secrets, or by paying all applicable prosecution and maintenance fees related to intellectual property registrations for any of our product candidates. We also cannot be certain that our licensors have drafted or prosecuted the patents and patent applications licensed to us in compliance with applicable laws and regulations, which may affect the validity and enforceability of such patents or any patents that may issue from such applications. If they fail to do so, this could cause us to lose rights in any applicable intellectual property that we in-license, and as a result our ability to develop and commercialize products or product candidates may be adversely affected and we may be unable to prevent competitors from making, using and selling competing products.

***Our success depends on our ability to protect our intellectual property and our proprietary technologies.***

Our commercial success depends in part on our ability to obtain and maintain patent protection and trade secret protection for our product candidates, proprietary technologies and their uses as well as our ability to operate without infringing upon the proprietary rights of others. We generally seek to protect our proprietary position by filing patent applications in the United States and abroad related to our product candidates, proprietary technologies and their uses that are important to our business. There can be no assurance that our patent applications or those of our licensors will result in additional patents being issued or that issued patents will afford sufficient protection against competitors with similar technology, nor can there be any assurance that the patents issued will not be infringed, designed around or invalidated by third parties. Even issued patents may later be found invalid or unenforceable or may be modified or revoked in proceedings instituted by third parties before various patent offices or in courts. The degree of future protection for our proprietary rights is uncertain. Only limited protection may be available and may not adequately protect our rights or permit us to gain or keep any competitive advantage. This failure to properly protect the intellectual property rights relating to our product candidates could have a material adverse effect on our financial condition and results of operations.

While we have rights to an issued composition-of-matter patent in the United States and corresponding issued patents in certain foreign territories covering citoradenant, we cannot be certain that the claims in any of our patent applications covering composition-of-matter of our other product candidates will be considered patentable by the United States Patent and Trademark Office (“USPTO”), courts in the United States or by the patent offices and courts in foreign countries, nor can we be certain that the claims in our issued composition-of-matter patents will not be found invalid or unenforceable if challenged.

The patent application process is subject to numerous risks and uncertainties, and there can be no assurance that we or any of our existing or potential future collaborators will be successful in protecting our product candidates by obtaining and defending patents. These risks and uncertainties include the following:

- the USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent process, the noncompliance with which can result in abandonment or lapse of a patent or patent application, and partial or complete loss of patent rights in the relevant jurisdiction;
- patent applications may not result in any patents being issued;
- patents that may be issued or in-licensed may be challenged, invalidated, modified, revoked, circumvented, found to be unenforceable or otherwise may not provide any competitive advantage;
- our competitors, many of whom have substantially greater resources than we do and many of whom have made significant investments in competing technologies, may seek or may have already obtained patents that will limit, interfere with or eliminate our ability to make, use and sell our potential product candidates;
- there may be significant pressure on the U.S. government and international governmental bodies to limit the scope of patent protection both inside and outside the United States for disease treatments that prove successful, as a matter of public policy regarding worldwide health concerns; and
- countries other than the United States may have patent laws less favorable to patentees than those upheld by U.S. courts, allowing foreign competitors a better opportunity to create, develop and market competing product candidates.

The patent prosecution process is also expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Although we enter into non-disclosure and confidentiality agreements with parties who have access to

patentable aspects of our research and development output, such as our employees, corporate collaborators, outside scientific collaborators, CROs, contract manufacturers, consultants, advisors and other third parties, any of these parties may breach such agreements and disclose such output before a patent application is filed, thereby jeopardizing our ability to seek patent protection.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our patents, if issued, or the patent rights that we license from others, may be challenged in the courts or patent offices in the United States and abroad. Such challenges may result in loss of exclusivity or in patent claims being narrowed, invalidated or held unenforceable, which could limit our ability to stop others from using or commercializing similar or identical products, or limit the duration of the patent protection of our products and product candidates. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our intellectual property may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

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

In addition, we rely on the protection of our trade secrets, including unpatented know-how, technology and other proprietary information to maintain our competitive position. Although we have taken steps to protect our trade secrets and unpatented know-how, including entering into confidentiality agreements with third parties, and confidential information and inventions agreements with employees, consultants and advisors. Despite these efforts, we cannot provide any assurances that all such agreements have been duly executed, and any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets. Moreover, third parties may still obtain this information or may come upon this or similar information independently, and we would have no right to prevent them from using that technology or information to compete with us. If any of these events occurs or if we otherwise lose protection for our trade secrets, the value of this information may be greatly reduced and our competitive position would be harmed. If we do not apply for patent protection prior to such publication or if we cannot otherwise maintain the confidentiality of our proprietary technology and other confidential information, then our ability to obtain patent protection or to protect our trade secret information may be jeopardized.

***Our commercial success depends significantly on our ability to operate without infringing the patents and other proprietary rights of third parties. Claims by third parties that we infringe their proprietary rights may result in liability for damages or prevent or delay our developmental and commercialization efforts.***

Our commercial success depends in part on our avoiding infringement of the patents and proprietary rights of third parties. Other entities may have or obtain patents or proprietary rights that could limit our ability to make, use, sell, offer for sale or import our product candidates and future approved products or impair our competitive position. There is a substantial amount of litigation, both within and outside the United States, involving patent and other intellectual property rights in the biotechnology and pharmaceutical industries, including patent infringement lawsuits, interferences, oppositions, reexaminations, inter partes review (“IPR”) proceedings and post-grant review (“PGR”) proceedings before the USPTO and/or corresponding foreign patent offices. Numerous third-party U.S. and foreign issued patents and pending patent applications exist in the fields in which we are developing product candidates. There may be third-party patents or patent applications with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our product candidates. For example, we are aware of an issued patent in Australia that may be relevant to commercialization of ciforadenant in that country. That Australian patent is expected to expire in 2022. Our ability to commercialize ciforadenant in Australia prior to 2022 could be adversely affected if we do not obtain a license under such patent. We are also aware of a corresponding patent application that has been issued in the United States and which is expected to expire in 2023. However, to the extent that any claims of this patent may be interpreted to cover our potential uses of ciforadenant, we do not believe that such claims would be valid and enforceable if asserted. We have filed a PGR petition challenging the patentability of certain claims of the patent and the

patentee subsequently disclaimed every challenged claim. As the biotechnology industry expands and more patents are issued, the risk increases that our product candidates may be subject to claims of infringement of the patent rights of third parties. Because patent applications are maintained as confidential for a certain period of time, until the relevant application is published we may be unaware of third-party patent applications that, if issued as patents, may be infringed by commercialization of mupadolimab, CPI-818 and ciforadenant or our other product candidates, and cannot be certain that we were the first to file a patent application related to a product candidate or technology. Moreover, because patent applications can take many years to issue, there may be currently-pending patent applications that may later result in issued patents that our product candidates may infringe. In addition, identification of third-party patent rights that may be relevant to our technology is difficult because patent searching is imperfect due to differences in terminology among patents, incomplete databases and the difficulty in assessing the meaning of patent claims. Any claims of patent infringement asserted by third parties would be time consuming and could:

- result in costly litigation;
- divert the time and attention of our technical personnel and management;
- cause development delays;
- prevent us from commercializing mupadolimab, CPI-818 and ciforadenant or our other product candidates until the asserted patent expires or is held finally invalid or not infringed in a court of law;
- require us to develop non-infringing technology, which may not be possible on a cost-effective basis; or
- require us to enter into royalty or licensing agreements, which may not be available on commercially reasonable terms, or at all.

Although no third party has asserted a claim of patent infringement against us as of the date of this report, others may hold proprietary rights that could prevent mupadolimab, CPI-818 and ciforadenant or our other product candidates from being marketed. Any patent-related legal action against us claiming damages and seeking to enjoin commercial activities relating to our product candidates or processes could subject us to potential liability for damages, including treble damages if we were determined to willfully infringe, and require us to obtain a license to manufacture or market mupadolimab, CPI-818 and ciforadenant or our other product candidates.

Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. We cannot predict whether we would prevail in any such actions or that any license required under any of these patents would be made available on commercially acceptable terms, if at all. Moreover, even if we or our future strategic partners were able to obtain a license, the rights may be nonexclusive, which could result in our competitors gaining access to the same intellectual property. In addition, we cannot be certain that we could redesign our product candidates or processes to avoid infringement, if necessary. Accordingly, an adverse determination in a judicial or administrative proceeding, or the failure to obtain necessary licenses, could prevent us from developing and commercializing mupadolimab, CPI-818 and ciforadenant or our other product candidates, which could harm our business, financial condition and operating results. In addition, intellectual property litigation, regardless of its outcome, may cause negative publicity and could prohibit us from marketing or otherwise commercializing our product candidates and technology.

***We may be involved in lawsuits to protect or enforce our patents or the patents of our licensors, which could be expensive, time consuming, and unsuccessful. Further, our issued patents could be found invalid or unenforceable if challenged in court.***

Competitors may infringe our intellectual property rights or those of our licensors. To prevent infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming. In addition, in a patent infringement proceeding, a court may decide that a patent we own or in-license is not valid, is unenforceable and/or is not infringed. If we or any of our existing or potential future collaborators were to initiate legal

proceedings against a third party to enforce a patent directed at one of our product candidates, the defendant could counterclaim that our patent is invalid and/or unenforceable in whole or in part. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge include an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness or non-enablement. Grounds for an unenforceability assertion could include an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO or made a misleading statement during prosecution. Third parties may also raise similar claims before the USPTO, even outside the context of litigation. The outcome following legal assertions of invalidity and unenforceability is unpredictable, and prior art could render our patents or those of our licensors invalid. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, we would lose at least part, and perhaps all, of the patent protection on such product candidate. Such a loss of patent protection would have a material adverse impact on our business.

Interference proceedings provoked by third parties or brought by us or declared by the USPTO may be necessary to determine the priority of inventions with respect to our patents or patent applications or those of our licensors. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. Our defense of litigation or interference proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees. In addition, the uncertainties associated with litigation could have a material adverse effect on our ability to raise the funds necessary to continue our clinical trials, continue our research programs, license necessary technology from third parties or enter into development or manufacturing partnerships that would help us bring our product candidates to market.

Even if resolved in our favor, litigation or other legal proceedings relating to our intellectual property rights may cause us to incur significant expenses, and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could compromise our ability to compete in the marketplace.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of our common stock.

***Recent patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents.***

On September 16, 2011, the Leahy-Smith America Invents Act (“Leahy-Smith Act”) was signed into law. The Leahy-Smith Act includes a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications will be prosecuted and may also affect patent litigation. In particular, under the Leahy-Smith Act, the United States transitioned in March 2013 to a “first to file” system in which the first inventor to file a patent application will be entitled to the patent. Third parties are allowed to submit prior art before the issuance of a patent by the USPTO, and may become involved in post-grant proceedings including opposition, derivation, reexamination, inter-partes review or interference proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope or enforceability of, or invalidate, our patent rights, which could adversely affect our competitive position.

***We may not be successful in obtaining or maintaining necessary rights to our product candidates through acquisitions and in-licenses.***

We currently have rights to the intellectual property, through licenses from third parties and under patents that we own, to develop our product candidates. Because our programs may require the use of proprietary rights held by third parties, the growth of our business will depend in part on our ability to acquire, in-license or use these proprietary rights. For example, our product candidates may require specific formulations to work effectively and efficiently and the rights to these formulations may be held by others. We may be unable to acquire or in-license any compositions, methods of use, processes or other third-party intellectual property rights from third parties that we identify as necessary for our product candidates. The licensing and acquisition of third-party intellectual property rights is a competitive area, and a number of more established companies are also pursuing strategies to license or acquire third-party intellectual property rights that we may consider attractive. These established companies may have a competitive advantage over us due to their size, cash resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment.

We have collaborated with U.S. academic institutions and may in the future collaborate with U.S. and foreign academic institutions to accelerate our preclinical research or development under written agreements with these institutions. These institutions may provide us with an option to negotiate a license to any of the institution's rights in technology resulting from the collaboration. Regardless of such option, we may be unable to negotiate a license within the specified timeframe or under terms that are acceptable to us. If we are unable to do so, the institution may offer the intellectual property rights to other parties, potentially blocking our ability to pursue our program.

If we are unable to successfully obtain rights to required third-party intellectual property rights or maintain the existing intellectual property rights we have, we may have to abandon development of that program and our business and financial condition could suffer.

***We may fail to comply with any of our obligations under existing agreements pursuant to which we license or have otherwise acquired intellectual property rights or technology, which could result in the loss of rights or technology that are material to our business.***

Licensing of intellectual property is of critical importance to our business and involves complex legal, business and scientific issues. We are party to various agreements that we depend on for rights to use various technologies that are material to our business, including intellectual property rights covering citoradenant and methods relating to its use and manufacture. In each of these cases, our rights to use the licensed intellectual property are subject to the continuation of and our compliance with the terms of these agreements. Disputes may arise regarding our rights to intellectual property licensed to us from a third party, including but not limited to:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- the sublicensing of patent and other rights;
- our diligence obligations under the license agreement and what activities satisfy those diligence obligations;
- the ownership of inventions and know-how resulting from the creation or use of intellectual property by us, alone or with our licensors and collaborators;
- the scope and duration of our payment obligations;

- our rights upon termination of such agreement; and
- the scope and duration of exclusivity obligations of each party to the agreement.

If disputes over intellectual property and other rights that we have licensed or acquired from third parties prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates. If we fail to comply with our obligations under current or future licensing agreements, these agreements may be terminated or the scope of our rights under them may be reduced and we might be unable to develop, manufacture or market any product that is licensed under these agreements.

***We may be subject to claims that we have wrongfully hired an employee from a competitor or that we or our employees have wrongfully used or disclosed alleged confidential information or trade secrets of their former employers.***

As is common in the pharmaceutical industry, in addition to our employees, we engage the services of consultants to assist us in the development of our product candidates. Many of these consultants, and many of our employees, were previously employed at, or may have previously provided or may be currently providing consulting services to, other pharmaceutical companies including our competitors or potential competitors. We may become subject to claims that we, our employees or a consultant inadvertently or otherwise used or disclosed trade secrets or other information proprietary to their former employers or their former or current clients. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, which could adversely affect our business. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to our management team.

***We may be subject to claims challenging the inventorship or ownership of our patents and other intellectual property.***

We may also be subject to claims that former employees, collaborators or other third parties have an ownership interest in our patents or other intellectual property. Litigation may be necessary to defend against these and other claims challenging inventorship or ownership. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and distraction to management and other employees.

***If we do not obtain patent term extension for our product candidates, our business may be materially harmed.***

Depending upon the timing, duration and specifics of potential FDA marketing approval of ciforadenant, mupadolimab, CPI-818 or other product candidates, one or more of our U.S. patents may be eligible for limited patent term restoration under the Drug Price Competition and Patent Term Restoration Act of 1984 (“Hatch-Waxman Amendments”). The Hatch-Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, we may not be granted an extension because of, for example, 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 restoration or the term of any such extension is less than we request, our competitors may obtain approval of competing products following our patent expiration, and our revenue could be reduced, possibly materially.

***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 adversely affected.***

Our registered or unregistered trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names, which we need to build name recognition among potential partners or customers in our markets of interest. At times, competitors may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name

or trademark infringement claims brought by owners of other registered trademarks or trademarks that incorporate variations of our registered or unregistered trademarks or trade names. Over the long term, if we are unable to establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively and our business may be adversely affected. Our efforts to enforce or protect our proprietary rights related to trademarks, trade secrets, domain names, copyrights or other intellectual property may be ineffective and could result in substantial costs and diversion of resources and could adversely affect our financial condition or results of operations.

***Changes in U.S. patent law could diminish the value of patents in general, thereby impairing our ability to protect our product candidates.***

As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involve a high degree of technological and legal complexity. Therefore, obtaining and enforcing biopharmaceutical patents is costly, time consuming and inherently uncertain. In addition, Congress may pass patent reform legislation that is unfavorable to us. The Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by Congress, the federal courts and the USPTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents we might obtain in the future.

***We may not be able to protect our intellectual property rights throughout the world.***

While we have issued patents directed at ciforadenant in the United States and certain foreign territories, and pending patent applications directed at mupadolimab, CPI-818, ciforadenant and other product candidates in the United States and other countries, filing, prosecuting and defending patents on mupadolimab, CPI-818, ciforadenant and our other product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection but enforcement is not as strong as that in the United States. These products may compete with our product candidates, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

The legal systems of many foreign countries do not favor the enforcement of patents and other intellectual property protection, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

***Intellectual property rights do not necessarily address all potential threats to our competitive advantage.***

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations, and may not adequately protect our business or permit us to maintain our competitive advantage. For example:

- others may be able to make adenosine antagonists that are similar to our product candidates but that are not covered by the claims of the patents that we own or have exclusively licensed;
- we or our licensors or future collaborators might not have been the first to make the inventions covered by the issued patent or pending patent application that we own or have exclusively licensed;
- we or our licensors or future collaborators might not have been the first to file patent applications covering certain of our inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights;
- it is possible that our pending patent applications will not lead to issued patents;
- issued patents that we own or have exclusively licensed may be held invalid or unenforceable, as a result of legal challenges by our competitors;
- our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we may not develop additional proprietary technologies that are patentable; and
- the patents of others may have an adverse effect on our business.

Should any of these events occur, they could significantly harm our business, results of operations and prospects.

**Risks Related to Our Common Stock**

***An active, liquid and orderly market for our common stock may not be sustained.***

Although our common stock is listed on The Nasdaq Global Market (“Nasdaq”), an active trading market for our common stock may not be sustained on Nasdaq or any other exchange in the future. The lack of an active market may impair our stockholders’ ability to sell their shares at the time they wish to sell them or at a price that they consider reasonable. If an active market for our common stock is not sustained, it may also be difficult for our stockholders to sell shares without depressing the market price for the shares or at all. An inactive market may also impair our ability to raise capital by selling shares and may impair our ability to acquire other businesses, applications or technologies using our shares as consideration, which, in turn, could materially adversely affect our business. In any event, we have a limited public float and, as a result, our common stock has been and will likely continue to be less liquid than many other listed companies and trading may be adversely affected.

***The trading price of the shares of our common stock could be highly volatile, and investors in our common stock could incur substantial losses.***

Our stock price has been volatile. The stock market in general and the market for stock of pharmaceutical companies in particular have experienced extreme volatility that has often been unrelated to the operating performance

of particular companies. The market price for our common stock may be influenced by those factors discussed in this “Risk Factors” section and many others, including:

- our ability to enroll subjects in our planned clinical trials;
- results of the clinical trials, and the results of trials of our competitors or those of other companies in our market sector;
- regulatory approval of mupadolimab, CPI-818, ciforadenant and our other product candidates, or limitations to specific label indications or patient populations for its use, or changes or delays in the regulatory review process;
- Angel Pharmaceuticals’ ability to develop and commercialize product candidates in China;
- regulatory developments in the United States and foreign countries; including changes in the policies of the U.S. or Chinese governments resulting in sanctions instituted by either government;
- changes in the structure of healthcare payment systems, especially in light of current reforms to the U.S. healthcare system;
- the success or failure of our efforts to acquire, license or develop additional product candidates;
- innovations or new products developed by us or our competitors;
- announcements by us or our competitors of significant acquisitions, strategic partnerships, joint ventures or capital commitments;
- manufacturing, supply or distribution delays or shortages;
- any changes to our relationship with any manufacturers, suppliers, collaborators or other strategic partners;
- achievement of product sales and profitability;
- variations in our financial results or those of companies that are perceived to be similar to us;
- market conditions in the pharmaceutical sector and issuance of securities analysts’ reports or recommendations;
- the impact of political instability, natural disasters, war and/or events of terrorism, such as the military conflict between Ukraine and Russia, and the corresponding tensions created from such conflict between Russia, the United States and countries in Europe as well as other countries such as China;
- trading volume of our common stock;
- an inability to obtain additional funding;
- sales of our stock by insiders and stockholders;
- general economic, industry and market conditions other events or factors, many of which are beyond our control, including recession or depression resulting from the current COVID-19 pandemic;
- additions or departures of key personnel; and

- intellectual property, product liability or other litigation against us.

As a result of this volatility, investors may experience losses on their investment in our common stock.

In addition, in the past, stockholders have initiated class action lawsuits against pharmaceutical companies following periods of volatility in the market prices of these companies' stock. Such litigation, if instituted against us, could cause us to incur substantial costs and divert management's attention and resources, which could have a material adverse effect on our business, financial condition and results of operations.

***Our failure to meet the continued listing requirements of Nasdaq could result in a delisting of our common stock.***

If we fail to satisfy the continued listing requirements of Nasdaq, such as the corporate governance requirements or the minimum closing bid price requirement, Nasdaq may take steps to delist our common stock. Such a delisting would likely have a negative effect on the price of our common stock and would impair our stockholders' ability to sell or purchase our common stock when they wish to do so. In the event of a delisting, we can provide no assurance that any action taken by us to restore compliance with listing requirements would allow our common stock to become listed again, stabilize the market price or improve the liquidity of our common stock, prevent our common stock from dropping below the Nasdaq minimum bid price requirement or prevent future non-compliance with Nasdaq's listing requirements.

***Because a small number of our existing stockholders own a majority of our voting stock, a stockholder's ability to influence corporate matters will be limited.***

As of December 31, 2021, our executive officers, directors and greater than 5% stockholders, in the aggregate, owned approximately 46% of our outstanding common stock. As a result, such persons, acting together, have the ability to control our management and affairs and substantially all matters submitted to our stockholders for approval, including the election and removal of directors and approval of any significant transaction. This concentration of ownership may have the effect of delaying, deferring or preventing a change in control, impeding a merger, consolidation, takeover or other business combination involving us, or discouraging a potential acquiror from making a tender offer or otherwise attempting to obtain control of our business, even if such a transaction would benefit other stockholders.

***We do not currently intend to pay dividends on our common stock, and, consequently, our stockholders' ability to achieve a return on their investment will depend on appreciation, if any, in the price of our common stock.***

We have never declared or paid any cash dividend on our common stock. We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. Any return to stockholders will therefore be limited to the appreciation of their stock. There is no guarantee that shares of our common stock will appreciate in value or even maintain the price at which stockholders have purchased their shares.

To the extent that we raise additional capital by issuing equity securities, the share ownership of existing stockholders will be diluted. For example, on April 3, 2017, we filed a Registration Statement on Form S-3 (File No. 333-217102), covering the offering of up to \$250 million of shares of common stock, preferred stock, warrants and units. In March 2018, we sold 8,117,647 shares of our common stock for net proceeds of \$64.9 million in an underwritten public offering pursuant to our Registration Statement on Form S-3 (File No. 333-217102). On March 9, 2020 we filed a Registration Statement on Form S-3 (File No. 333-237040), covering the offering of up to \$200 million of shares of common stock, preferred stock, warrants and units and entered into a Sales Agreement ("2020 Sales Agreement") with Jefferies to sell shares of our common stock, from time to time, with aggregate gross sales proceeds of up to \$50,000,000, through an at-the-market equity offering program under which Jefferies will act as our sales agent. As of December 31, 2021, we had sold 6,920,339 shares of common stock pursuant for gross proceeds of \$31.1 million under the 2020 Sales Agreement. On November 1, 2021 we entered into another Sales Agreement ("2021 Sales Agreement") with Jefferies to sell shares of our common stock, from time-to-time, with aggregate gross sales proceeds of up to \$40,000,000. As of December 31, 2021, \$18.9 million remained for sale under the 2020 Sales Agreement and \$40.0 million remained for sale under the 2021 Sales Agreement.

***Sales of a substantial number of shares of our common stock by our existing stockholders in the public market could cause our stock price to fall.***

Sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock. Moreover, certain holders of shares of our common stock have rights, subject to certain conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. We have registered and intend to continue to register all shares of common stock that we may issue under our equity compensation plans. Once we register these shares, they can be freely sold in the public market upon issuance, subject to volume limitations applicable to affiliates.

***We are a smaller reporting company and the reduced reporting requirements applicable to smaller reporting companies may make our common stock less attractive to investors.***

We are a smaller reporting company, which allows us to take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not smaller reporting companies, including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, as amended, reduced disclosure obligations regarding executive compensation in our Annual Report and our periodic reports and proxy statements and providing only two years of audited financial statements in our Annual Report and our periodic reports. We will remain an smaller reporting company until (a) the aggregate market value of our outstanding common stock held by non-affiliates as of the last business day our most recently completed second fiscal quarter exceeds \$250 million or (b) (1) we have over \$100 million in annual revenues and (2) the aggregate market value of our outstanding common stock held by non-affiliates as of the last business day our most recently completed second fiscal quarter exceeds \$700 million. We cannot predict whether investors will find our common stock less attractive if we rely on certain or all of these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile and may decline.

***If we fail to maintain proper and effective internal control over financial reporting, our ability to produce accurate and timely consolidated financial statements could be impaired, investors may lose confidence in our financial reporting and the trading price of our common stock may decline.***

Pursuant to Section 404 of Sarbanes-Oxley, if we are an accelerated filer, our independent registered public accounting firm will be required to attest to the effectiveness of our internal control over financial reporting. The rules governing the standards that must be met for management to assess our internal control over financial reporting are complex and require significant documentation, testing and possible remediation. To continue to comply with the requirements of being a reporting company under the Exchange Act, as we continue to grow, we will need to upgrade our systems including information technology; implement additional financial and management controls, reporting systems and procedures; and hire additional accounting and finance staff. If we or, if required, our auditors are unable to conclude that our internal control over financial reporting is effective, investors may lose confidence in our financial reporting and the trading price of our common stock may decline.

We cannot assure our stockholders that there will not be material weaknesses or significant deficiencies in our internal control over financial reporting in the future. Any failure to maintain internal control over financial reporting could severely inhibit our ability to accurately report our financial condition, results of operations or cash flows. If we are unable to conclude that our internal control over financial reporting is effective, or if our independent registered public accounting firm determines we have a material weakness or significant deficiency in our internal control over financial reporting once that firm begin its Section 404 reviews, investors may lose confidence in the accuracy and completeness of our financial reports, the market price of our common stock could decline, and we could be subject to sanctions or investigations by Nasdaq, the SEC or other regulatory authorities. Failure to remedy any material weakness in our internal control over financial reporting, or to implement or maintain other effective control systems required of public companies, could also restrict our future access to the capital markets.

***Provisions in our charter documents and under Delaware law could discourage a takeover that stockholders may consider favorable and may lead to entrenchment of management.***

Our amended and restated certificate of incorporation and amended and restated bylaws contain provisions that could significantly reduce the value of our shares to a potential acquiror or delay or prevent changes in control or changes in our management without the consent of our board of directors. The provisions in our charter documents include the following:

- a classified board of directors with three-year staggered terms, which may delay the ability of stockholders to change the membership of a majority of our board of directors;
- no cumulative voting in the election of directors, which limits the ability of minority stockholders to elect director candidates;
- the exclusive right of our board of directors, unless the board of directors grants such right to the stockholders, to elect a director to fill a vacancy created by the expansion of the board of directors or the resignation, death or removal of a director, which prevents stockholders from being able to fill vacancies on our board of directors;
- the required approval of at least 66 2/3% of the shares entitled to vote to remove a director for cause, and the prohibition on removal of directors without cause;
- the ability of our board of directors to authorize the issuance of shares of preferred stock and to determine the price and other terms of those shares, including preferences and voting rights, without stockholder approval, which could be used to significantly dilute the ownership of a hostile acquiror;
- the ability of our board of directors to alter our amended and restated bylaws without obtaining stockholder approval;
- the required approval of at least 66 2/3% of the shares entitled to vote to adopt, amend or repeal our amended and restated bylaws or repeal the provisions of our amended and restated certificate of incorporation regarding the election and removal of directors;
- a prohibition on stockholder action by written consent, which forces stockholder action to be taken at an annual or special meeting of our stockholders;
- an exclusive forum provision providing that the Court of Chancery of the State of Delaware will be the exclusive forum for certain actions and proceedings;
- the requirement that a special meeting of stockholders may be called only by the board of directors, which may delay the ability of our stockholders to force consideration of a proposal or to take action, including the removal of directors; and
- advance notice procedures that stockholders must comply with in order to nominate candidates to our board of directors or to propose matters to be acted upon at a stockholders' meeting, which may discourage or deter a potential acquiror from conducting a solicitation of proxies to elect the acquiror's own slate of directors or otherwise attempting to obtain control of us.

We are also subject to the anti-takeover provisions contained in Section 203 of the Delaware General Corporation Law. Under Section 203, a corporation may not, in general, engage in a business combination with any holder of 15% or more of its capital stock unless the holder has held the stock for three years or, among other exceptions, the board of directors has approved the transaction.

***Our amended and restated certificate of incorporation and amended and restated bylaws provide that the Court of Chancery of the State of Delaware is the exclusive forum for substantially all disputes between us and our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.***

Our amended and restated certificate of incorporation and amended and restated bylaws provide that the Court of Chancery of the State of Delaware is the exclusive forum for any derivative action or proceeding brought on our behalf, any action asserting a breach of fiduciary duty, any action asserting a claim against us arising pursuant to the Delaware General Corporation Law, our amended and restated certificate of incorporation or our amended and restated bylaws, or any action asserting a claim against us that is governed by the internal affairs doctrine. This provision may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees, which may discourage such lawsuits against us and our directors, officers and other employees. Alternatively, if a court were to find this provision in our amended and restated certificate of incorporation and amended and restated bylaws to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could adversely affect our business and financial condition. This provision would not apply to suits brought to enforce a duty or liability created by the Exchange Act or any other claim for which the U.S. federal courts have exclusive jurisdiction.

### **General Risks**

***Our future growth may depend, in part, on our ability to operate in foreign markets, where we would be subject to additional regulatory burdens and other risks and uncertainties.***

Our future growth may depend, in part, on our ability to develop and commercialize our product candidates in foreign markets. We are not permitted to market or promote any of our product candidates before we receive regulatory approval from applicable regulatory authorities in foreign markets, and we may never receive such regulatory approvals for any of our product candidates. To obtain separate regulatory approval in many other countries we must comply with numerous and varying regulatory requirements regarding safety and efficacy and governing, among other things, clinical trials, commercial sales, pricing and distribution of our product candidates. If we obtain regulatory approval of our product candidates and ultimately commercialize our product candidates in foreign markets, we would be subject to additional risks and uncertainties, including the burden of complying with complex and changing foreign regulatory, tax, accounting and legal requirements and the reduced protection of intellectual property rights in some foreign countries.

***Recent U.S. tax legislation and future changes to applicable U.S. or foreign tax laws and regulations may have a material adverse effect on our business, financial condition and results of operations.***

We are subject to income and other taxes in the U.S. and foreign jurisdictions. Changes in laws and policy relating to taxes or trade may have an adverse effect on our business, financial condition and results of operations. For example, the U.S. government recently enacted significant tax reform, and certain provisions of the new law may adversely affect us. Changes include, but are not limited to, a federal corporate tax rate decrease from 35% to 21% for tax years beginning after December 31, 2017, the transition of U.S. international taxation from a worldwide tax system to a more generally territorial system, and a one-time transition tax on the mandatory deemed repatriation of foreign earnings. The legislation is unclear in many respects and could be subject to potential amendments and technical corrections, and will be subject to interpretations and implementing regulations by the Treasury and Internal Revenue Service, any of which could mitigate or increase certain adverse effects of the legislation. In addition, it is unclear how these U.S. federal income tax changes will affect state and local taxation. Generally, future changes in applicable U.S. or foreign tax laws and regulations, or their interpretation and application could have an adverse effect on our business, financial conditions and results of operations.

***Our information technology systems, or those of any of our existing or potential future collaborators, CROs or other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our product development programs.***

We maintain sensitive company data on our information technology systems, including our intellectual property

and proprietary business information. We face a number of threats to our networks from unauthorized access, security breaches and other system disruptions. Despite the implementation of security measures, our information technology and other internal computer systems and those of our current and any future CROs and other contractors, consultants and collaborators are vulnerable to damage from cyberattacks, “phishing” attacks, computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. Attacks upon information technology systems are increasing in their frequency, levels of persistence, sophistication and intensity, and are being conducted by sophisticated and organized groups and individuals with a wide range of motives and expertise. Furthermore, because the techniques used to obtain unauthorized access to, or to sabotage or disrupt, systems change frequently and often are not recognized until launched against a target, we may be unable to anticipate these techniques or implement adequate preventative measures. We may also experience security breaches that may remain undetected for an extended period. Even if identified, we may be unable to adequately investigate or remediate incidents or breaches due to attackers increasingly using tools and techniques that are designed to circumvent controls, to avoid detection, and to remove or obfuscate forensic evidence. As a result of the COVID-19 pandemic, we may also face increased cybersecurity risks due to our reliance on internet technology and the number of our and our service providers’ employees who are working remotely, which may create additional opportunities for cybercriminals to exploit vulnerabilities.

We and certain of our service providers are from time to time, subject to cyberattacks and security incidents. While we do not believe that we have experienced any significant system failure, accident or security breach to date, any such security breach may compromise information stored on our networks, or those of our vendors, and may result in significant data losses or theft of our intellectual property or proprietary business information. Further, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our development programs and our business operations, whether due to a loss of our trade secrets or other similar disruptions. For example, the loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. In addition, such a breach may require notification to governmental agencies, or affected individuals pursuant to applicable data privacy and security laws. We would also be exposed to a risk of loss, including financial assets or litigation and potential liability, which could materially adversely affect our business, reputation, financial condition, results of operations and prospects. We also rely on third parties to manufacture our product candidates, and similar events relating to their computer systems could also have a material adverse effect on our business. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development and commercialization of our product candidates could be delayed.

***Changes in and failures to comply with U.S. and foreign privacy and data protection laws, regulations and standards may adversely affect our business, operations and financial performance.***

We are subject to or affected by numerous federal, state and foreign laws and regulations, as well as regulatory guidance, governing the collection, use, disclosure, retention, and security of personal data, such as information that we collect about patients and healthcare providers in connection with clinical trials in the United States and abroad. The global data protection landscape is rapidly evolving, and implementation standards and enforcement practices are likely to remain uncertain for the foreseeable future. This evolution may create uncertainty in our business, affect our or our collaborators’, service providers’ and contractors’ ability to operate in certain jurisdictions or to collect, store, transfer use and share personal information, necessitate the acceptance of more onerous obligations in our contracts, result in liability or impose additional costs on us. In the United States, numerous federal and state laws and regulations could apply to our operations or the operations of our partners, including state data breach notification laws, state health information privacy laws, and federal and state consumer protection laws and regulations (e.g. Section 5 of the FTC Act), that govern the collection, use, disclosure, and protection of health-related and other personal information. In addition, we may obtain health information from third parties (including research institutions from which we obtain clinical trial data) that are subject to privacy and security requirements under HIPAA. Depending on the facts and circumstances, we could be subject to criminal penalties if we knowingly obtain, use, or disclose individually identifiable health information that was provided to us by a HIPAA-covered entity in a manner that is not authorized or permitted by HIPAA.

Further, California enacted the CCPA, on June 28, 2018, which went into effect on January 1, 2020. The CCPA

gives California residents expanded rights to access and delete their personal information, opt out of certain personal information sharing, and receive detailed information about how their personal information is used. The CCPA provides for civil penalties for violations, as well as a private right of action for data breaches that is expected to increase data breach litigation. Although there are limited exemptions for health-related information, including clinical trial data, the CCPA may increase our compliance costs and potential liability. Further, the CPRA, recently passed in California, which significantly amends the CCPA and will impose additional data protection obligations on covered businesses, including additional consumer rights processes, limitations on data uses, new audit requirements for higher risk data, and opt outs for certain uses of sensitive data. It will also create a new California data protection agency authorized to issue substantive regulations and could result in increased privacy and information security enforcement. The majority of the provisions will go into effect on January 1, 2023, and additional compliance investment and potential business process changes may be required. Similar laws have been proposed in other states and at the federal level, and if passed, such laws may have potentially conflicting requirements that would make compliance challenging.

Our operations abroad may also be subject to increased scrutiny or attention from data protection authorities. Many countries in these regions have established or are in the process of establishing privacy and data security legal frameworks with which we, our collaborators, service providers, including our CRO, and contractors must comply. For example, the GDPR, which went into effect in May 2018, imposes strict requirements for processing the personal data of individuals within the EEA, including clinical trial data. The GDPR has and will continue to increase compliance burdens on us, including by mandating potentially burdensome documentation requirements and granting certain rights to individuals to control how we collect, use, disclose, retain and process information about them. The processing of sensitive personal data, such as physical health condition, may impose heightened compliance burdens under the GDPR and is a topic of active interest among foreign regulators. Further, recent legal developments in Europe have created complexity and uncertainty regarding transfers of personal data from the EEA to the United States, e.g. on July 16, 2020, the Court of Justice of the European Union, or the CJEU invalidated the EU-US Privacy Shield Framework, or the Privacy Shield under which personal data could be transferred from the EEA to US entities who had self-certified under the Privacy Shield scheme. While the CJEU upheld the adequacy of the standard contractual clauses, or SCCs, it made clear that reliance on them alone may not necessarily be sufficient in all circumstances. The European Commission issued revised SCCs on June 4, 2021 to account for the decision of the CJEU and recommendations made by the European Data Protection Board. The revised SCCs must be used for relevant new data transfers from September 27, 2021; existing standard contractual clauses arrangements must be migrated to the revised clauses by December 27, 2022. The new SCCs apply only to the transfer of personal data outside of the EEA and not the UK; the UK's Information Commissioner's Office launched a public consultation on its draft revised data transfers mechanisms in August 2021 and laid its proposal before Parliament, with the UK SCCs expected to come into force in March 2022, with a two-year grace period. As supervisory authorities issue further guidance on personal data export mechanisms, including circumstances where the standard contractual clauses cannot be used, and/or start taking enforcement action, we could suffer additional costs, complaints and/or regulatory investigations or fines, and/or if we are otherwise unable to transfer personal data between and among countries and regions in which we operate, it could affect the manner in which we provide our services, the geographical location or segregation of our relevant systems and operations, and could adversely affect our financial results. In addition, the GDPR provides for robust regulatory enforcement and fines of up to €20 million or 4% of the annual global revenue of the noncompliant company, whichever is greater. Further, from January 1, 2021, we have to comply with the GDPR and the United Kingdom ("UK") GDPR, which, together with the amended UK Data Protection Act 2018, retains the GDPR in UK national law, the latter regime having the ability to separately fine up to the greater of £17.5 million or 4% of global turnover. The relationship between the United Kingdom and the EU in relation to certain aspects of data protection law remains unclear, and it is unclear how United Kingdom data protection laws and regulations will develop in the medium to longer term, and how data transfers to and from the United Kingdom will be regulated in the long term. The European Commission has adopted an adequacy decision in favor of the UK, enabling data transfers from EU member states to the UK without additional safeguards. However, the UK adequacy decision will automatically expire in June 2025 unless the European Commission re-assesses and renews or extends that decision and remains under review by the Commission during this period. In September 2021, the UK government launched a consultation on its proposals for wide-ranging reform of UK data protection laws following Brexit. There is a risk that any material changes which are made to the UK data protection regime could result in the European Commission reviewing the UK adequacy decision, and the UK losing its adequacy decision if the European Commission deems the UK to no longer provide adequate protection for personal data. The relationship between the UK and the EU in relation to certain aspects of data protection law remains uncertain, and it is unclear how UK data protection laws and

regulations will develop in the medium to longer term.

As we expand into other foreign countries and jurisdictions, we may be subject to additional laws and regulations that may affect how we conduct business. The cost of compliance with these laws, regulations and standards is high and is likely to increase in the future. Any failure or perceived failure by us or our collaborators, service providers and contractors to comply with federal, state or foreign laws or regulation, our internal policies and procedures or our contracts governing processing of personal information could result in negative publicity, diversion of management time and effort and proceedings against us by governmental entities or others. In many jurisdictions, enforcement actions and consequences for noncompliance are rising.

Our operations could be subject to earthquakes, power shortages, telecommunications failures, water shortages, floods, hurricanes, typhoons, fires, extreme weather conditions, medical epidemics and pandemics, such as the COVID-19 pandemic, and other natural or manmade disasters or business interruptions, for which we are predominantly self-insured. We currently rely on several different manufacturers who supply different parts of the ciforadenant molecule and CPI-818 molecule, on one manufacturer for mupadolimab drug substance and on other third-party manufacturers to produce our other product candidates. Our ability to obtain clinical supplies of mupadolimab, CPI-818 and ciforadenant or our other product candidates could be disrupted if the operations of these suppliers were affected by a man-made or natural disaster or other business interruption. The occurrence of any of these business disruptions could seriously harm our operations and financial condition and increase our costs and expenses.

In response to the COVID-19 pandemic, we have limited the use of our physical facilities and many of our employees work remotely. We intend to make full use of our physical facilities after national, state and local authorities have indicated that it is safe to do so. In the event of a continuation of shelter-in-place orders or mandated local travel restrictions, our employees conducting research and development activities may not be able to access our facilities and our activities may be significantly limited or curtailed, possibly for an extended period of time. Furthermore, it is possible that over the long term our operational efficiency may be decreased if our employees and third-party collaborators are unable to meet and work in the same physical location.

***Our ability to use net operating loss carryforwards and other tax attributes may be limited.***

We have incurred substantial losses during our history and do not expect to become profitable in the near future, and we may never achieve profitability. To the extent that we continue to generate taxable losses, unused losses will carry forward to offset future taxable income, if any, until such unused losses expire. As of December 31, 2021, we had federal net operating loss (“NOL”) carryforwards of approximately \$212.6 million and state NOL carryforwards of approximately \$246.3 million available to offset future taxable income. If not utilized, the federal and state NOL carryforwards will begin to expire in various years beginning in 2034. As of December 31, 2021, we also had \$7.9 million of federal and \$4.5 million of state research and development tax credit carryforwards available to reduce future income taxes. The federal research and development tax credits will begin to expire in 2035, if not utilized. The state research and development tax credits have no expiration date. Utilization of NOL carryforwards and credits may be subject to an annual limitation due to the “ownership change” provisions under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended. An “ownership change” is generally defined as a cumulative change in the ownership interest of significant stockholders over a rolling three-year period in excess of 50 percentage points. Similar provisions under state tax law may also apply. If finalized, Treasury Regulations currently proposed under Section 382 of the Code may further limit our ability to utilize our pre-change NOLs or credits if we undergo a future ownership change. We may experience an ownership change in the future as a result of subsequent shifts in our stock ownership, some of which changes are outside our control. Such ownership changes could result in the expiration of our NOL carryforwards and other tax attributes before they can be utilized and, if we are profitable, our future cash flows could be adversely affected due to our increased tax liability.

Additionally, under the Tax Cut and Jobs Act (the “Tax Act”), as modified by the Coronavirus Aid, Relief, and Economic Security Act (the “CARES Act”), NOL carryforwards arising in tax years beginning after December 31, 2020 are limited to 80% of taxable income. Under the Tax Act, federal NOL carryforwards arising in tax years beginning after December 31, 2017 may be carried forward indefinitely. Under the CARES Act, federal NOL carryforwards arising in tax years beginning after December 31, 2017 and before January 1, 2021 may be carried back to each of the five tax

years preceding the tax year of such loss. The changes in the carryforward and carryback periods as well as the limitation on use of NOL carryforwards may significantly impact our ability to use NOL carryforwards, particularly for tax years beginning after December 31, 2020, as well as the timing of any such use, and could adversely affect our results of operations.

***If securities or industry analysts do not publish research or reports or publish unfavorable research or reports about our business, our stock price and trading volume could decline.***

The trading market for our common stock is influenced by the research and reports that industry or securities analysts publish about us or our business. If any of the analysts who cover us issue an adverse or misleading opinion regarding us, our business model, our intellectual property or our stock performance, or if our target studies and operating results fail to meet the expectations of analysts, our stock price would likely decline. If one or more of these analysts cease coverage of us or fail to publish reports on us regularly, we could lose visibility in the financial markets, which in turn could cause our stock price or trading volume to decline.

***Our business could be negatively impacted by corporate citizenship and ESG matters and or our reporting of such matters.***

Institutional, individual, and other investors, proxy advisory services, regulatory authorities, consumers and other stakeholders are increasingly focused on environmental, social and governance (ESG) practices of companies. As we look to respond to evolving standards for identifying, measuring, and reporting ESG metrics, our efforts may result in a significant increase in costs and may nevertheless not meet investor or other stakeholder expectations and evolving standards or regulatory requirements, which may negatively impact our financial results, our reputation, our ability to attract or retain employees, our attractiveness as an investment or business partner, or expose us to government enforcement actions, private litigation, and actions by stockholders or stakeholders.

#### **Item 1B. Unresolved Staff Comments**

None

#### **Item 2. Properties**

We currently lease approximately 27,280 square feet of office and research and development facilities in Burlingame, California. Approximately 7,585 square feet are subleased to Angel Pharmaceuticals through February 2023. Our lease expires in 2025. We frequently explore alternatives that would provide us with additional space to accommodate our anticipated growth.

#### **Item 3. Legal Proceedings**

We are not currently a party to any material litigation or legal proceedings; however, we may from time to time be involved in various legal proceedings incident to the ordinary course of our business.

#### **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 for Common Stock

Our common stock has been listed on The Nasdaq Global Market under the symbol “CRVS” since March 23, 2016. Prior to that there was no public trading market for our common stock. The following table sets forth for the indicated periods the high and low sales prices per share for our common stock on the Nasdaq stock market.

	Price Range	
	High	Low
<b>2021</b>		
First Quarter	\$ 4.77	\$ 2.86
Second Quarter	\$ 3.14	\$ 2.46
Third Quarter	\$ 8.53	\$ 1.89
Fourth Quarter	\$ 5.31	\$ 2.34
<b>2020</b>		
First Quarter	\$ 6.35	\$ 1.01
Second Quarter	\$ 4.24	\$ 1.91
Third Quarter	\$ 6.88	\$ 2.51
Fourth Quarter	\$ 5.74	\$ 3.64

#### Holders of Record

As of March 10, 2022, there were approximately 19 stockholders of record of our common stock. The actual number of stockholders is greater than this number of record holders, and includes stockholders who are beneficial owners, but whose shares are held in street name by brokers and other nominees. This number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

#### Dividend Policy

We currently intend to retain future earnings, if any, for use in operation of our business and to fund future growth. We have never declared or paid any cash dividends on our capital stock and do not anticipate paying any cash dividends in the foreseeable future. Payment of cash dividends, if any, in the future will be at the discretion of our board of directors and will depend on then-existing conditions, including our financial condition, operating results, contractual restrictions, capital requirements, business prospects and other factors our board of directors may deem relevant.

#### Securities Authorized for Issuance Under Equity Compensation Plans

The information required by this Item regarding equity compensation plans is incorporated by reference to the information set forth in PART III Item 12 of this Annual Report on Form 10-K.

#### Use of Proceeds from Registered Securities

None.

#### Recent Sales of Unregistered Equity Securities

In November 2019, we entered into an exchange agreement (the “Exchange Agreement”) with entities affiliated with Biotechnology Value Fund, L.P. (the “Exchanging Stockholders”), pursuant to which we exchanged an aggregate of 1,458,000 shares of our common stock owned by the Exchanging Stockholders for warrants (the “Exchange

Warrants”) to purchase an aggregate of 1,458,000 shares of common stock (subject to adjustment in the event of stock splits, recapitalizations and other similar events affecting common stock), with an exercise price of \$0.0001 per share. The Exchange Warrants were issued without registration under the Securities Act of 1933, as amended (the “Securities Act”), in reliance on the exemption from registration contained in Section 3(a)(9) of the Securities Act. The Exchanging Stockholders exercised the Exchange Warrants pursuant to a cashless exercise on September 20, 2021 and we issued an aggregate of 1,457,947 shares of common stock to such Exchanging Stockholders.

#### Issuer Purchases of Equity Securities by the Issuer and Affiliated Purchasers

None.

#### Item 6. Selected Financial Data

You should read the following selected financial data together with the information under “Item 7. Management’s Discussion and Analysis of Financial Condition and Results of Operations” and our consolidated financial statements and related notes included in Part II, Item 8 of this Annual Report on Form 10-K. The selected consolidated statement of operations data for each of the years ended December 31, 2021, 2020 and 2019 and the consolidated balance sheet data as of December 31, 2021 and 2020 are derived from our audited consolidated financial statements included elsewhere in this Annual Report on Form 10-K. The consolidated statement of operations data for the years ended December 31, 2018 and 2017 and the consolidated balance sheet data as of December 31, 2019, 2018 and 2017 are derived from our audited consolidated financial statements which are not included in this Annual Report on Form 10-K. Our historical results of any prior periods are not necessary indicative of results to be expected in any future period.

Consolidated Statements of Operations and Comprehensive Loss Data:	Year Ended December 31,				
	2021	2020	2019	2018	2017
	(In thousands, except share and per share amounts)				
Operating expenses:					
Research and development	\$ 29,115	\$ 31,830	\$ 37,975	\$ 38,586	\$ 46,305
General and administrative	9,515	11,930	10,879	10,636	10,219
Total operating expenses	38,630	43,760	48,854	49,222	56,524
Loss from operations	(38,630)	(43,760)	(48,854)	(49,222)	(56,524)
Interest income and other expense, net.	(15)	540	2,182	2,283	861
Gain on deconsolidation of Angel Pharmaceuticals	—	37,459	—	—	—
Sublease income - related party	235	—	—	—	—
Loss from equity method investment	(4,831)	(234)	—	—	—
Net loss	\$ (43,241)	\$ (5,995)	\$ (46,672)	\$ (46,939)	\$ (55,663)
Net loss per share, basic and diluted	\$ (1.03)	\$ (0.20)	\$ (1.59)	\$ (1.71)	\$ (2.72)
Shares used to compute net loss per share, basic and diluted	41,854,110	29,478,878	29,349,810	27,509,960	20,488,506
Other comprehensive income (loss):					
Unrealized gain (loss) on marketable securities	(7)	(25)	63	7	(2)
Cumulative foreign currency translation adjustment	1,872	—	—	—	—
Comprehensive loss	\$ (41,376)	\$ (6,020)	\$ (46,609)	\$ (46,932)	\$ (55,665)

Consolidated Balance Sheet Data:	Year Ended December 31,				
	2021	2020	2019	2018	2017
	(In thousands)				
Cash, cash equivalents and marketable securities	\$ 69,451	\$ 44,259	\$ 77,982	\$ 114,597	\$ 90,055
Working capital	61,620	33,187	69,119	108,562	82,265
Total assets	109,455	85,529	83,646	118,232	94,775
Convertible preferred stock	—	—	—	—	—
Total stockholders’ equity	\$ 97,162	\$ 72,148	\$ 71,111	\$ 110,336	\$ 84,835

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

*The following discussion should be read in conjunction with the consolidated financial statements and notes thereto included elsewhere in this Annual report on Form 10-K. This Annual Report on Form 10-K, including the following sections, contains forward-looking statements within the meaning of the federal securities laws. These statements are subject to risks and uncertainties that could cause actual results and events to differ materially from those expressed or implied by such forward-looking statements. For a detailed discussion of these risks and uncertainties, see the “Risk Factors” section in Item 1A of this Annual Report on Form 10-K. We caution the reader not to place undue reliance on these forward-looking statements, which reflect management’s analysis only as of the date of this Form 10-K. We undertake no obligation to update forward-looking statements, which reflect events or circumstances occurring after the date of this Form 10-K.*

### Overview

We are a clinical stage biopharmaceutical company. Our strategy is to focus our efforts on the development of immune modulator product candidates with the potential to treat solid cancers, T-cell lymphomas, autoimmune diseases and infectious diseases. We have built a pipeline of five programs, three of which are in clinical development.

Our lead product candidate is mupadolimab (formerly CPI-006), a humanized monoclonal antibody that is designed to react with a specific site on CD73. In both preclinical and in vivo studies in cancer patients and patients with COVID-19, mupadolimab has demonstrated binding to various immune cells and the enhancement of immune responses by activating B cells. We believe mupadolimab has the potential to be an important new therapeutic agent with a novel mechanism of action for the treatment of a broad range of cancers and infectious diseases.

Our next product candidate, CPI-818, is a selective, covalent inhibitor of ITK and is in a multi-center Phase 1/1b clinical trial in patients with various malignant T-cell lymphomas. CPI-818 is designed to inhibit the proliferation of certain malignant T-cells, and we believe it also has the potential to regulate the growth of abnormal T cells involved in autoimmunity and allergy.

Our third product candidate, ciforadenant (formerly CPI-444), is an oral, small molecule antagonist of the A2A receptor for adenosine with which we completed a Phase 2 expansion protocol in combination with Genentech, Inc.’s cancer immunotherapy, Tecentriq® (atezolizumab) for patients with either advanced or refractory renal cell cancer (“RCC”). Ciforadenant is designed to disable a tumor’s ability to subvert attack by the immune system by blocking the binding of immunosuppressive adenosine in the tumor microenvironment to the A2A receptor.

Our molecularly targeted product candidates are designed to exhibit a high degree of specificity, which we believe has the potential to provide greater safety compared to other cancer therapies and may facilitate their development either as monotherapies or in combination with other cancer therapies such as immune checkpoint inhibitors or chemotherapy.

We believe the breadth and status of our pipeline demonstrates our management team’s expertise in understanding and developing immunology focused assets as well as in identifying product candidates that can be in-licensed and further developed internally to treat many types of cancer.

Our diverse and versatile product candidates have also enabled us to address opportunities in foreign markets. In October 2020, we announced the formation and launch of Angel Pharmaceuticals Co., Ltd. (“Angel Pharmaceuticals”), a new China based biopharmaceutical company with a mission to bring innovative quality medicines to Chinese patients for treatment of serious diseases including cancer, autoimmune diseases and infectious diseases. We formed Angel Pharmaceuticals as a wholly owned subsidiary and it launched with a post-money valuation of approximately \$106.0 million, based on an approximate \$41.0 million cash investment from a Chinese investor group that includes funds associated with Tigermed and Betta Pharmaceuticals, Hisun Pharmaceuticals and Zhejiang Puissance Capital. Such cash is not available for our use. Contemporaneously with the financing, Angel Pharmaceuticals licensed the rights to develop and commercialize our three clinical-stage candidates – mupadolimab, CPI-818 and ciforadenant – in greater China and obtained global rights to our BTK inhibitor preclinical programs. Under the collaboration, we currently have a 49.7% equity interest in Angel Pharmaceuticals, excluding 7% of Angel’s equity reserved for issuance

under the Employee Stock Ownership Plan (“ESOP”), and are entitled to designate three individuals on Angel’s five-person Board of Directors.

To date, the majority of our efforts have been focused on the research, development and advancement of mupadolimab, CPI-818 and ciforadenant, and we have not generated any revenue from product sales and, as a result, we have incurred significant losses. We expect to continue to incur significant research and development and general and administrative expenses related to our operations. Our net loss for the years ended December 31, 2021 and 2020 was \$43.2 million and \$6.0 million, respectively. As of December 31, 2021, we had an accumulated deficit of \$266.4 million. We expect to continue to incur losses for the foreseeable future, and we anticipate these losses will increase as we continue our development of, seek regulatory approval for and begin to commercialize mupadolimab, CPI-818 and ciforadenant, and as we develop other product candidates. Even if we achieve profitability in the future, we may not be able to sustain profitability in subsequent periods.

Since our inception and through December 31, 2021, we have funded our operations primarily through the sale and issuance of stock, including through our initial public offering (“IPO”) in March 2016, in which we raised net proceeds of approximately \$70.6 million, a follow-on offering of our common stock in March 2018, in which we raised net proceeds of approximately \$64.9 million and a follow on offering in February 2021, in which we raised net proceeds of approximately \$32.0 million, in each case net of underwriting discounts and commissions and offering expenses. Immediately prior to the consummation of the IPO, all of our outstanding shares of convertible preferred stock were converted into 14.3 million shares of our common stock.

In March 2020, we entered into an open market sale agreement (the “2020 Sales Agreement”) with Jefferies LLC (“Jefferies”) to sell shares of the Company’s common stock, from time-to-time, with aggregate gross sales proceeds of up to \$50,000,000, through an at-the-market equity offering program under which Jefferies will act as our sales agent. In November 2021, we entered into another Sale Agreement (“2021 Sales Agreement”) with Jefferies to sell shares of our common stock from time-to-time, with aggregate gross sales proceeds of up to \$40,000,000. Jefferies is entitled to compensation for its services equal to up to 3.0% of the gross proceeds of any shares of common stock sold through Jefferies under the 2020 Sales Agreement and 2021 Sales Agreement.

During the year ended December 31, 2021, we sold 6,609,605 shares under our at-the-market offering program resulting in net proceeds of \$29.0 million. As of December 31, 2021, \$18.9 million remained for sale under the 2020 Sales Agreement and \$40.0 million remained for sale under the 2021 Sales Agreement.

As of December 31, 2021, we had capital resources consisting of cash, cash equivalents and marketable securities of approximately \$69.5 million. While we believe that our current cash, cash equivalents and short-term marketable securities will be sufficient to fund our planned operations for at least 12 months from the date of the issuance of these financial statements, we do not expect our existing capital resources to be sufficient to enable us to fund the completion of all of our ongoing or planned clinical trials and remaining development program of any of mupadolimab, CPI-818 or ciforadenant through commercialization. In addition, our operating plan may change as a result of many factors, including those described in the section of this report entitled “Risk Factors” and others currently unknown to us, and we may need to seek additional funds sooner than planned, through public or private equity, debt financings or other sources, such as strategic collaborations. Such financing would result in dilution to stockholders, imposition of debt covenants and repayment obligations or other restrictions that may affect our business. If we raise additional capital through strategic collaboration agreements, we may have to relinquish valuable rights to our product candidates, including possible future revenue streams. In addition, additional funding may not be available to us on acceptable terms or at all and any additional fundraising efforts may divert our management from its day-to-day activities, which may adversely affect our ability to develop and commercialize our product candidates. Furthermore, even if we believe we have sufficient funds for our current or future operating plans, we may seek additional capital due to favorable market conditions or strategic considerations.

We currently have no manufacturing capabilities and do not intend to establish any such capabilities. We have no commercial manufacturing facilities for our product candidates. As such, we are dependent on third parties to supply our product candidates according to our specifications, in sufficient quantities, on time, in compliance with appropriate regulatory standards and at competitive prices.

## **Impact of COVID-19**

COVID-19 has placed strains on the providers of healthcare services, including the healthcare institutions where we conduct our clinical trials. These strains have resulted in institutions prohibiting the initiation of new clinical trials, enrollment in existing clinical trials and restricting the on-site monitoring of clinical trials. We also follow FDA guidance on clinical trial conduct during the COVID-19 pandemic, including the remote monitoring of clinical data.

In alignment with public health guidance designed to slow the spread of COVID-19, as of mid-March 2020, we implemented a reduced onsite staffing model and transitioned to a remote work plan for all employees other than those providing essential services, such as our laboratory staff. In July 2021, we started transitioning back to office work for employees not providing essential services. For our onsite employees, we have implemented heightened health and safety measures designed to comply with applicable federal, state and local guidelines in response to the COVID-19 pandemic. We are further supporting all of our employees by leveraging virtual meeting technology and encouraging employees to follow local health authority guidance. We may need to undertake additional actions that could impact our operations if required by applicable laws or regulations or if we determine such actions to be in the best interests of our employees.

## **Components of Results of Operations**

### ***Revenue***

To date, we have not generated any revenues. We do not expect to receive any revenues from any product candidates that we develop unless and until we obtain regulatory approval and commercialize our products or enter into revenue-generating collaboration agreements with third parties.

### **Research and Development Expenses**

Our research and development expenses consist primarily of costs incurred to conduct research and development of our product candidates. We record research and development expenses as incurred. Research and development expenses include:

- employee-related expenses, including salaries, benefits, travel and non-cash stock-based compensation expense;
- external research and development expenses incurred under arrangements with third parties, such as contract research organizations, preclinical testing organizations, contract manufacturing organizations, academic and non-profit institutions and consultants;
- costs to acquire technologies to be used in research and development that have not reached technological feasibility and have no alternative future use;
- license fees; and
- other expenses, which include direct and allocated expenses for laboratory, facilities and other costs.

We plan to increase our research and development expenses substantially as we continue the development and potential commercialization of our product candidates. Our current planned research and development activities include the following:

- enrollment and completion of our Phase 1/1b clinical trial of mupadolimab in patients with NSCLC and advanced, HPV+ head and neck cancer;
- enrollment and completion of our ongoing Phase 1/1b clinical trial of CPI-818;

- enrollment and completion of our Phase 2 clinical trial of mupadolimab;
- process development and manufacturing of drug supply of mupadolimab, CPI-818 and ciforadenant; and
- preclinical studies under our other programs in order to select development product candidates.

In addition to our product candidates that are in clinical development, we believe it is important to continue substantial investment in potential new product candidates to build the value of our product candidate pipeline and our business.

Our expenditures on current and future preclinical and clinical development programs are subject to numerous uncertainties related to timing and cost to completion. The duration, costs and timing of clinical trials and development of product candidates will depend on a variety of factors, including many of which are beyond our control. The process of conducting the necessary clinical research to obtain regulatory approval is costly and time consuming, and the successful development of our product candidates is uncertain. The risks and uncertainties associated with our research and development projects are discussed more fully in “Part I, Item 1A—Risk Factors.” As a result of these risks and uncertainties, we are unable to determine with any degree of certainty the duration and completion costs of our research and development projects or if, when or to what extent we will generate revenues from the commercialization and sale of any of our product candidates that obtain regulatory approval. We may never succeed in achieving regulatory approval for any of our product candidates.

### General and Administrative Expenses

General and administrative expenses include personnel costs, expenses for outside professional services and allocated expenses. Personnel costs consist of salaries, benefits and stock-based compensation. Outside professional services consist of legal, accounting and audit services and other consulting fees. Allocated expenses consist of rent expense related to our office and research and development facility.

We expect that our general and administrative expenses will increase in the future as we increase our headcount to support our continued research and development and potential commercialization of one or more of our product candidates.

### Results of Operations

*Comparison of the periods below as indicated (in thousands):*

	Year ended December 31,			Change 2020 to 2021	Change 2019 to 2020
	2021	2020	2019		
Operating expenses:					
Research and development	\$ 29,115	\$ 31,830	\$ 37,975	\$ (2,715)	\$ (6,145)
General and administrative	9,515	11,930	10,879	(2,415)	1,051
Total operating expenses	38,630	43,760	48,854	(5,130)	(5,094)
Loss from operations	(38,630)	(43,760)	(48,854)	5,130	5,094
Interest income and other expense, net	(15)	540	2,182	(555)	(1,642)
Gain on deconsolidation of Angel Pharmaceuticals	—	37,459	—	(37,459)	37,459
Sublease income - related party	235	—	—	235	—
Loss from equity method investment	(4,831)	(234)	—	(4,597)	(234)
Net loss	\$ (43,241)	\$ (5,995)	\$ (46,672)	\$ (37,246)	\$ 40,677

### Research and Development Expenses

Research and development expenses for the years ended December 31, 2021 and 2020, consisted of the following costs by program (specific program costs consist solely of external costs):

	Year ended December 31,			Change	Change
	2021	2020	2019	2020 to 2021	2019 to 2020
Ciforadenant (formerly CPI-444)	\$ 1,532	\$ 3,784	\$ 5,750	\$ (2,252)	\$ (1,966)
Mupadolimab (formerly CPI-006)	14,145	8,956	6,774	5,189	2,182
CPI-818	934	2,734	6,577	(1,800)	(3,843)
Other programs	57	645	981	(588)	(336)
Unallocated employee and overhead costs	12,447	15,711	17,893	(3,264)	(2,182)
	<u>\$ 29,115</u>	<u>\$ 31,830</u>	<u>\$ 37,975</u>	<u>\$ (2,715)</u>	<u>\$ (6,145)</u>

For the year ended December 31, 2021, the decrease in ciforadenant costs of \$2.3 million as compared to the year ended December 31, 2020, primarily consisted of a decrease of \$1.9 million in clinical trial expenses and a decrease of \$0.5 million in other outside services, partially offset by an increase of \$0.1 million in drug manufacturing costs.

For the year ended December 31, 2021, the increase in mupadolimab costs of \$5.2 million as compared to the year ended December 31, 2020, primarily consisted of an increase of \$3.1 million in clinical trial expenses, an increase of \$1.8 million in drug manufacturing costs as well as an increase of \$0.3 million in other outside services.

For the year ended December 31, 2021, the decrease in CPI-818 costs of \$1.8 million as compared to the year ended December 31, 2020, primarily consisted of a decrease of \$1.0 million in clinical trial expenses, a decrease of \$0.1 million in other outside services and a decrease of \$0.1 million in drug manufacturing costs. Additionally, \$0.6 million in drug manufacturing costs, which were expensed in prior years, were billed to Angel Pharmaceuticals during the year ended December 31, 2021.

For the year ended December 31, 2021, the decrease in costs related to other programs of \$0.6 million as compared to the year ended December 31, 2020, primarily consisted of a decrease of \$0.5 million in manufacturing costs and a decrease of \$0.1 million in other outside services.

For the year ended December 31, 2021, the decrease in unallocated costs of \$3.3 million as compared to the year ended December 31, 2020, primarily consisted of a decrease of \$2.7 million in personnel and related costs and a decrease of \$0.6 million in outside services.

For the year ended December 31, 2020, the decrease in ciforadenant costs of \$2.0 million as compared to the year ended December 31, 2019, primarily consisted of a decrease of \$1.5 million in clinical trial expenses, a decrease of \$0.2 million in drug manufacturing costs and a decrease of \$0.3 million in other outside services.

For the year ended December 31, 2020, the increase in mupadolimab costs of \$2.2 million as compared to the year ended December 31, 2019, primarily consisted of an increase of \$3.5 million in clinical trial expenses as well as an increase of \$0.4 million in other outside services, partially offset by a decrease of \$1.7 million in drug manufacturing costs.

For the year ended December 31, 2020, the decrease in CPI-818 costs of \$3.8 million as compared to the year ended December 31, 2019, primarily consisted of a decrease of \$2.7 million in drug manufacturing costs, a decrease of \$0.4 million in clinical trial expenses and a decrease of \$0.7 million in other outside services.

For the year ended December 31, 2020, the decrease in costs related to other programs of \$0.3 million as compared to the year ended December 31, 2019, primarily consisted of a decrease of \$0.6 million in outside services, partially offset by an increase of \$0.3 million in drug manufacturing costs.

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For the year ended December 31, 2020, the decrease in unallocated costs of \$2.2 million as compared to the year ended December 31, 2019, primarily consisted of a decrease of \$1.5 million in outside services and a decrease of \$0.7 million in personnel and related costs.

### *General and Administrative Expenses*

For the year ended December 31, 2021, the decrease in general and administrative expenses of \$2.4 million as compared to the year ended December 31, 2020, primarily consisted of an increase of \$1.3 million in outside professional services and an increase of \$1.1 million in personnel and related costs.

For the year ended December 31, 2020, the increase in general and administrative expenses of \$1.1 million as compared to the year ended December 31, 2019, primarily consisted of an increase of \$1.9 million in outside professional services, which was partially offset by a decrease of \$0.8 million in personnel and related costs.

### *Interest Income and Other Expense, net*

For the year ended December 31, 2021, the decrease in interest income and other expense, net of \$0.6 million as compared to the year ended December 31, 2020, primarily consisted of a decrease in interest income earned due to a decrease in interest rates.

For the year ended December 31, 2020, the decrease in interest income and other expense, net of \$1.6 million as compared to the year ended December 31, 2019, primarily consisted of a decrease in interest income earned due to a decrease in cash equivalents and marketable securities and a decrease in interest rates.

### *Gain on deconsolidation of Angel Pharmaceuticals*

For the year ended December 31, 2020, the gain on deconsolidation of Angel Pharmaceuticals of \$37.5 million represents the fair value of our investment in Angel Pharmaceuticals at the date Angel Pharmaceuticals was deconsolidated from our financial statements.

### *Sublease income – related party*

For the year ended December 31, 2021, the sublease income – related party of \$0.2 million represents rent payments made by Angel Pharmaceuticals pursuant to the facility sublease entered into in August 2021.

### *Loss from equity method investment*

For the year ended December 31, 2021, the increase in loss from equity method investment of \$4.6 million as compared to the year ended December 31, 2020, primarily consisted of an increase in our share of Angel Pharmaceutical's loss for the year ended December 31, 2021.

For the year ended December 31, 2020, the loss from equity method investment of \$0.2 million represents our share of Angel Pharmaceutical's loss for the period from deconsolidation of our investment in Angel Pharmaceuticals through December 31, 2020.

## **Liquidity and Capital Resources**

### ***Sources of Liquidity***

As of December 31, 2021, we had cash, cash equivalents and marketable securities of \$69.5 million and an accumulated deficit of \$266.4 million, compared to cash, cash equivalents and marketable securities of \$44.3 million and an accumulated deficit of \$223.1 million as of December 31, 2020. We have financed our operations primarily through sales of our common stock and convertible preferred stock.

Since our inception and through December 31, 2021, we have funded our operations primarily through the sale and issuance of stock, including through our IPO in March 2016, in which we raised net proceeds of approximately \$70.6 million, a follow-on offering of our common stock in March 2018, in which we raised net proceeds of approximately \$64.9 million and a follow on offering in February 2021, in which we raised net proceeds of approximately \$32.0 million, in each case net of underwriting discounts and commissions and offering expenses. Immediately prior to the consummation of the IPO, all of our outstanding shares of convertible preferred stock were converted into 14.3 million shares of our common stock.

In March 2020, we entered into the 2020 Sales Agreement with Jefferies to sell shares of the Company's common stock, from time-to-time, with aggregate gross sales proceeds of up to \$50,000,000, through an at-the-market equity offering program under which Jefferies will act as our sales agent. In November 2021, we entered into the 2021 Sales Agreement with Jefferies to sell shares of our common stock from time-to-time, with aggregate gross sales proceeds of up to \$40,000,000. Jefferies is entitled to compensation for its services equal to up to 3.0% of the gross proceeds of any shares of common stock sold through Jefferies under the 2020 Sales Agreement and 2021 Sales Agreement.

During the year ended December 31, 2021, we sold 6,609,605 shares under its at-the-market offering program resulting in net proceeds of \$29.0 million. As of December 31, 2021, \$18.9 million remained for sale under the 2020 Sales Agreement and \$40.0 million remained for sale under the 2021 Sales Agreement.

We believe our current cash, cash equivalents and marketable securities will be sufficient to fund our planned expenditures and meet our obligations through at least the next twelve months from the issuance of our consolidated financial statements as of and for year ended December 31, 2021. The amounts and timing of our actual expenditures depend on numerous factors, including:

- the progress, timing, costs and results of clinical trials for mupadolimab, CPI-818 and ciforadenant;
- the extent to which the COVID-19 pandemic may impact our business, including our clinical trials and financial condition;
- the timing, progress, costs and results of preclinical and clinical development activities for our other product candidates;
- the number and scope of preclinical and clinical programs we decide to pursue;
- the costs involved in prosecuting, maintaining and enforcing patent and other intellectual property rights;
- the cost and timing of regulatory approvals;
- our efforts to enhance operational systems and hire additional personnel, including personnel to support development of our product candidates and satisfy our obligations as a public company; and
- other factors described in the section of this report entitled "Risk Factors."

We expect to increase our spending in connection with the development and commercialization of our product candidates. Until such time, if ever, as we can generate substantial revenue from product sales, we expect to fund our operations and capital funding needs through equity and/or debt financings. We may also enter into additional collaboration arrangements or selectively partner for clinical development and commercialization. The sale of additional equity would result in dilution to our stockholders. The incurrence of debt financing would result in debt service obligations and the governing documents would likely include operating and financing covenants that would restrict our operations. In addition, sufficient additional funding may not be available on acceptable terms, or at all. If we are not able to secure adequate additional funding, we may be forced to make reductions in spending, extend payment terms with suppliers, liquidate assets where possible and/or suspend or curtail planned programs. Any of these actions could have a material effect on our business, financial condition and results of operations.

**Summary of Statement of Cash Flows**

The following table summarizes our cash flows for the periods indicated (in thousands):

	Year ended December 31,			Change 2020 to 2021	Change 2019 to 2020
	2021	2020	2019		
Net cash provided by (used in):					
Operating activities	\$ (36,715)	\$ (34,778)	\$ (37,321)	\$ (1,937)	\$ 2,543
Investing activities	21,560	44,769	3,255	(23,209)	41,514
Financing activities	62,158	1,310	24	60,848	1,286
Net increase in cash and cash equivalents	<u>\$ 47,003</u>	<u>\$ 11,301</u>	<u>\$ (34,042)</u>	<u>\$ 35,702</u>	<u>\$ 45,343</u>

*Cash Flows from Operating Activities*

Cash used in operating activities during the year ended December 31, 2021 was \$36.7 million, which primarily consisted of a net loss of \$43.2 million, adjusted by non-cash charges of \$9.8 million, primarily consisting of \$4.2 million of stock compensation expense and \$4.8 million in loss from equity method investment, and an increase of \$0.2 million in other assets, partially offset by a decrease of \$2.4 million in accounts payable and accrued and other liabilities, an increase of \$0.5 million in accounts receivable – related party, an increase of \$0.3 million in prepaid and other current assets and an increase of \$0.2 million in operating lease right-of-use asset, net of operating lease liability.

Cash used in operating activities during the year ended December 31, 2020 was \$34.8 million, which primarily consisted of a net loss of \$6.0 million, adjusted by non-cash charges of \$6.8 million, primarily consisting of \$5.7 million of stock compensation expense, a non-cash gain on deconsolidation of Angel Pharmaceuticals of \$37.5 million, an increase of \$1.7 million in accounts payable and accrued and other liabilities and a decrease of \$0.4 million in prepaid and other current and non-current assets, partially offset by a decrease of \$0.2 million in operating lease liability, net of operating lease right-of-use asset amortization.

Cash used in operating activities during the year ended December 31, 2019 was \$37.3 million, which primarily consisted of a net loss of \$46.7 million, adjusted by non-cash charges of \$7.4 million, primarily consisting of \$7.3 million of stock compensation expense, an increase of \$2.5 million in accounts payable and accrued and other liabilities and an increase of \$0.4 million in prepaid and other current assets, primarily associated with the timing of payments to vendors.

*Cash Flows from Investing Activities*

Cash provided by investing activities during the year ended December 31, 2021 was \$21.6 million, which consisted of proceeds from maturities of marketable securities of \$30.9 million, which were partially offset by purchases of marketable securities of \$9.4 million

Cash provided by investing activities during the year ended December 31, 2020 was \$44.8 million, which consisted of proceeds from maturities of marketable securities of \$86.4 million and proceeds from sales of marketable securities of \$1.0 million, partially offset by purchases of marketable securities of \$42.5 million and purchases of property and equipment of \$0.1 million.

Cash provided by investing activities during the year ended December 31, 2019 was \$3.3 million, which consisted of proceeds from maturities of marketable securities of \$141.9 million, which were partially offset by purchases of marketable securities of \$138.6 million.

### *Cash Flows from Financing Activities*

Cash provided by financing activities during the year ended December 31, 2021 was \$62.2 million, which consisted of \$32.0 million in net proceeds from our February 2021 follow-on public offering, \$29.0 million in net proceeds from the issuance of common stock through our at-the-market offering program, and \$1.2 million in proceeds from the exercise of stock options.

Cash provided by financing activities during the year ended December 31, 2020 was \$1.3 million, which consisted of \$1.2 million in net proceeds from the issuance of common stock through our at-the-market offering program and \$0.1 million of proceeds from the exercise of stock options.

Cash provided by financing activities during the year ended December 31, 2019 was negligible.

### **Off-Balance Sheet Arrangements**

We have not entered into any off-balance sheet arrangements and do not have any holdings in variable interest entities.

### **Contractual Obligations**

Our principal commitments consist of obligations under our non-cancelable operating lease for our facilities that expires in 2025 and non-cancellable purchase commitments of \$9.3 million for the purchase of drug substance in 2022.

### **Critical Accounting Estimates**

Our management's discussion and analysis of our financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with United States generally accepted accounting principles ("U.S. GAAP"). The preparation of these consolidated financial statements requires our management to make judgments and estimates 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 revenue generated and expenses incurred during the reporting periods. On an ongoing basis, our management evaluates its estimates including, but not limited to: those related to the accrual for certain liabilities, including accrued clinical trial liabilities; valuations of equity awards used to determine stock-based compensation; valuation of intangible assets and long-lived assets; going concern assessment; and the amounts of deferred tax assets and liabilities, including the related allowance. We base our estimates on our 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. Actual results may differ from these judgments and estimates under different assumptions or conditions and any such differences may be material. We believe our critical accounting policies relating to clinical trial accruals and stock-based compensation reflect the more significant estimates and assumptions used in the preparation of our consolidated financial statements. Our significant accounting policies are more fully described in Note 2 of Notes to Consolidated Financial Statements in Part II, Item 8 of this Annual Report on Form 10 K.

### ***Cash, Cash Equivalents and Marketable Securities***

We consider all highly liquid investment securities with remaining maturities at the date of purchase of three months or less to be cash equivalents.

Investments with remaining maturities, at the date of purchase, greater than three months, but less than one year are considered short-term. We determined the appropriate classification of marketable securities at the time of purchase and evaluates such designation as of each balance sheet date. To date, all marketable securities have been classified as available-for-sale and are carried at fair value with unrealized gains and losses, if any, included as a component of

accumulated other comprehensive income (loss) in stockholders' equity (deficit). Interest and realized gains and losses are included in interest income. Realized gains and losses are recognized based on the specific identification method.

### ***Research and Development Expenses***

We record research and development expenses as incurred. We account for nonrefundable advance payments for goods and services that will be used in future research and development activities as expenses when the goods have been received or when the service has been performed rather than when the payment is made. Research and development expenses consist of costs incurred by us for the discovery and development of our product candidates and include:

- employee-related expenses, including salaries, benefits, travel and non-cash stock-based compensation expense;
- external research and development expenses incurred under arrangements with third parties, such as contract research organizations, contract manufacturing organizations, academic and non-profit institutions and consultants;
- costs to acquire technologies to be used in research and development that have not reached technological feasibility and have no alternative future use;
- license fees; and
- other expenses, which include direct and allocated expenses for laboratory, facilities and other costs.

### ***Clinical Trial Accruals***

Costs for preclinical studies and clinical trial activities are recognized based on an evaluation of the vendors' progress towards completion of specific tasks. We apply significant judgment in developing estimates for clinical trial accruals based on assumptions related to vendors' progress towards completion. In developing these estimates, we estimate vendors' progress towards completion using data such as clinical site activations, patient enrollment or information provided to us by our vendors regarding their actual costs incurred. Payments for these activities are based on the terms of individual contracts and payment timing may differ significantly from the period in which the services are performed. We determine accrual estimates through reports from and discussions with applicable personnel and outside service providers as to the progress or state of completion, or the services completed. Our estimates of accrued expenses as of each balance sheet date are based on the facts and circumstances known at the time.

### ***Recent Accounting Pronouncements***

See Note 2 in Item 8 "Financial Statements and Supplementary Data."

### ***Segment Information***

We have one primary business activity and operate as one reportable segment.

### ***Item 7A. Quantitative and Qualitative Disclosures about Market Risk***

We are exposed to market risk related to changes in interest rates. We had cash, cash equivalents and marketable securities of \$69.5 million as of December 31, 2021, which consisted of U.S. Treasury securities and U.S. government agency securities. Such interest-earning instruments carry a degree of interest rate risk; however, historical fluctuations of interest income have not been significant. Due to the short-term duration of our investment portfolio and the low risk profile of our investments, an immediate 10% increase in interest rates would not have a material effect on the fair market value of our portfolio.

We do not have any foreign currency or other derivative financial instruments.

**Item 8. Financial Statements and Supplementary Data**

**CORVUS PHARMACEUTICALS, INC.**

**ANNUAL REPORT ON FORM 10-K**

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## Report of Independent Registered Public Accounting Firm

To the Board of Directors and Stockholders of Corvus Pharmaceuticals, Inc.

### ***Opinion on the Financial Statements***

We have audited the accompanying consolidated balance sheets of Corvus Pharmaceuticals, Inc. and its subsidiaries (the “Company”) as of December 31, 2021 and 2020, and the related consolidated statements of operations and comprehensive loss, of changes in stockholders’ equity and of cash flows for each of the three years in the period ended December 31, 2021, including 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 as of December 31, 2021 and 2020, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2021 in conformity with accounting principles generally accepted in the United States of America.

### ***Basis for Opinion***

These consolidated financial statements are the responsibility of the Company’s management. Our responsibility is to express an opinion on the Company’s consolidated 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 of these consolidated financial statements 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 consolidated 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 consolidated 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 consolidated 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 consolidated financial statements. We believe that our audits provide a reasonable basis for our opinion.

### ***Emphasis of Matter***

As discussed in Note 1 to the consolidated financial statements, the Company will require additional financing to fund future operations. Management’s plans in regard to this matter are described in Note 1.

### ***Critical Audit Matters***

The critical audit matter communicated below is a matter arising from the current period audit of the consolidated financial statements that was communicated or required to be communicated to the audit committee and that (i) relates to accounts or disclosures that are material to the consolidated financial statements and (ii) involved our especially challenging, subjective, or complex judgments. The communication of critical audit matters does not alter in any way our opinion on the consolidated financial

statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing a separate opinion on the critical audit matter or on the accounts or disclosures to which it relates.

*Clinical Trial Accruals*

As described in Notes 2 and 7 to the consolidated financial statements, the Company recorded \$4.0 million in clinical trial accruals as of December 31, 2021. Management applies significant judgment in developing estimates for clinical trial accruals based on assumptions related to the vendors' progress towards completion. Management estimates the vendors' progress towards completion using data such as clinical site activations, patient enrollment or information provided to the Company by its vendors regarding actual costs incurred. Management determines accrual estimates through reports from and discussions with applicable personnel and outside service providers as to the progress or stage of completion, or the services completed.

The principal considerations for our determination that performing procedures relating to clinical trial accruals is a critical audit matter are (i) the significant judgment by management in estimating the clinical trial accruals and (ii) a high degree of auditor judgment, subjectivity, and effort in performing procedures and evaluating management's significant assumption related to the vendors' progress towards completion of clinical trials.

Addressing the matter involved performing procedures and evaluating audit evidence in connection with forming our overall opinion on the consolidated financial statements. These procedures included, among others (i) testing management's process for estimating the clinical trial accruals; (ii) evaluating the appropriateness of the method used by management to develop the estimate; (iii) testing the completeness and accuracy of data used to develop the estimate; and (iv) evaluating the reasonableness of the significant assumption related to the vendors' progress towards completion of clinical trials. Evaluating management's assumption related to the vendors' progress towards completion of clinical trials involved (i) confirming patient visits on a test basis; (ii) obtaining and examining contract terms on a test basis to evaluate the completeness and consistency of the costs in the contract with the costs used in developing the estimate; and (iii) considering whether this assumption was consistent with evidence obtained in other areas of the audit.

/s/ PricewaterhouseCoopers LLP

San Jose, California  
March 10, 2022

We have served as the Company's auditor since 2015

**CORVUS PHARMACEUTICALS, INC.**

**CONSOLIDATED BALANCE SHEETS**

(in thousands, except share data)

	December 31, 2021	December 31, 2020
<b>Assets</b>		
Current assets:		
Cash and cash equivalents	\$ 63,458	\$ 16,455
Marketable securities	5,993	27,804
Accounts receivable - related party	507	—
Prepaid and other current assets	1,354	1,077
<b>Total current assets</b>	<b>71,312</b>	<b>45,336</b>
Property and equipment, net	451	906
Operating lease right-of-use asset	3,190	1,648
Investment in Angel Pharmaceuticals	34,266	37,225
Other assets	236	414
<b>Total assets</b>	<b>\$ 109,455</b>	<b>\$ 85,529</b>
<b>Liabilities and Stockholders' Equity</b>		
Current liabilities:		
Accounts payable	\$ 1,565	\$ 3,467
Operating lease liability	1,046	1,078
Accrued and other liabilities	7,081	7,604
<b>Total current liabilities</b>	<b>9,692</b>	<b>12,149</b>
Operating lease liability	2,601	1,232
<b>Total liabilities</b>	<b>12,293</b>	<b>13,381</b>
Commitments and contingencies ( <i>Note 13</i> )		
Stockholders' equity:		
Preferred stock: \$0.0001 par value; 10,000,000 shares authorized at December 31, 2021 and December 31, 2020; 0 shares issued and outstanding at December 31, 2021 and December 31, 2020	—	—
Common stock: \$0.0001 par value; 290,000,000 shares authorized at December 31, 2021 and December 31, 2020; 46,553,511 and 28,372,634 shares issued and outstanding at December 31, 2021 and December 31, 2020, respectively	5	3
Additional paid-in capital	361,669	295,281
Accumulated other comprehensive (loss) income	1,869	4
Accumulated deficit	(266,381)	(223,140)
<b>Total stockholders' equity</b>	<b>97,162</b>	<b>72,148</b>
<b>Total liabilities and stockholders' equity</b>	<b>\$ 109,455</b>	<b>\$ 85,529</b>

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

**CORVUS PHARMACEUTICALS, INC.****CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS****(in thousands, except share and per share data)**

	Year Ended December 31,		
	2021	2020	2019
Operating expenses:			
Research and development	\$ 29,115	\$ 31,830	\$ 37,975
General and administrative	9,515	11,930	10,879
Total operating expenses	<u>38,630</u>	<u>43,760</u>	<u>48,854</u>
Loss from operations	(38,630)	(43,760)	(48,854)
Interest income and other expense, net	(15)	540	2,182
Gain on deconsolidation of Angel Pharmaceuticals	—	37,459	—
Sublease income - related party	235	—	—
Loss from equity method investment	(4,831)	(234)	—
Net loss	<u>\$ (43,241)</u>	<u>\$ (5,995)</u>	<u>\$ (46,672)</u>
Net loss per share, basic and diluted	<u>\$ (1.03)</u>	<u>\$ (0.20)</u>	<u>\$ (1.59)</u>
Shares used to compute net loss per share, basic and diluted	<u>41,854,110</u>	<u>29,478,878</u>	<u>29,349,810</u>
Other comprehensive loss:			
Unrealized gain (loss) on marketable securities	(7)	(25)	63
Cumulative foreign currency translation adjustment	1,872	—	—
Comprehensive loss	<u>\$ (41,376)</u>	<u>\$ (6,020)</u>	<u>\$ (46,609)</u>

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

**CORVUS PHARMACEUTICALS, INC.**

**CONSOLIDATED STATEMENTS OF CHANGES IN STOCKHOLDERS' EQUITY**

(in thousands, except share and per share data)

	Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount				
<b>Balance at December 31, 2018</b>	29,323,930	\$ 3	\$ 280,840	\$ (34)	\$ (170,473)	\$ 110,336
Retirement of common stock in exchange for common stock warrant	(1,458,000)	—	(5,030)	—	—	(5,030)
Issuance of common stock warrant in exchange for retirement of common stock	—	—	5,030	—	—	5,030
Common stock issued on exercise of stock options	87,303	—	24	—	—	24
Vesting of restricted stock issued upon early exercise of stock options	—	—	12	—	—	12
Stock-based compensation expense	—	—	7,348	—	—	7,348
Unrealized gain on marketable securities	—	—	—	63	—	63
Net loss	—	—	—	—	(46,672)	(46,672)
<b>Balance at December 31, 2019</b>	27,953,233	\$ 3	\$ 288,224	\$ 29	\$ (217,145)	\$ 71,111
Issuance of common stock in connection with at-the-market offering, net	310,734	—	1,222	—	—	1,222
Common stock issued on exercise of stock options	108,667	—	88	—	—	88
Stock-based compensation expense	—	—	5,747	—	—	5,747
Unrealized loss on marketable securities	—	—	—	(25)	—	(25)
Net loss	—	—	—	—	(5,995)	(5,995)
<b>Balance at December 31, 2020</b>	28,372,634	\$ 3	\$ 295,281	\$ 4	\$ (223,140)	\$ 72,148
Issuance of common stock upon exercise of Exchange Warrants	1,457,947	—	—	—	—	—
Issuance of common stock upon follow-on public offering, net	9,783,660	1	31,988	—	—	31,989
Issuance of common stock in connection with at-the-market offering, net	6,609,605	1	28,953	—	—	28,954
Common stock issued on exercise of stock options	329,665	—	1,215	—	—	1,215
Stock-based compensation expense	—	—	4,232	—	—	4,232
Unrealized loss on marketable securities	—	—	—	(7)	—	(7)
Foreign currency translation adjustment	—	—	—	1,872	—	1,872
Net loss	—	—	—	—	(43,241)	(43,241)
<b>Balance at December 31, 2021</b>	46,553,511	\$ 5	\$ 361,669	\$ 1,869	\$ (266,381)	\$ 97,162

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

**CORVUS PHARMACEUTICALS, INC.**  
**CONSOLIDATED STATEMENTS OF CASH FLOWS**

(in thousands)

	Year Ended December 31,		
	2021	2020	2019
<b>Cash flows from operating activities</b>			
Net loss	\$ (43,241)	\$ (5,995)	\$ (46,672)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	460	632	743
Accretion related to marketable securities	239	154	(644)
Stock-based compensation	4,232	5,747	7,348
Gain on deconsolidation of Angel Pharmaceuticals	—	(37,459)	—
Loss from equity method investment	4,831	234	—
Changes in operating assets and liabilities:			
Accounts receivable - related party	(507)	—	—
Prepaid and other current assets	(277)	285	(370)
Operating lease right-of-use asset	(1,542)	679	599
Other assets	178	99	(50)
Accounts payable	(1,902)	1,019	450
Accrued and other liabilities	(523)	705	2,042
Operating lease liability	1,337	(878)	(767)
Net cash used in operating activities	<u>(36,715)</u>	<u>(34,778)</u>	<u>(37,321)</u>
<b>Cash flows from investing activities</b>			
Purchases of marketable securities	(9,357)	(42,540)	(138,586)
Sales of marketable securities	—	1,009	—
Maturities of marketable securities	30,922	86,376	141,866
Purchases of property and equipment	(5)	(76)	(25)
Net cash provided by investing activities	<u>21,560</u>	<u>44,769</u>	<u>3,255</u>
<b>Cash flows from financing activities</b>			
Proceeds from issuance of common stock, net (includes \$4,850 in aggregate gross proceeds from related parties for the year ended December 31, 2021)	31,989	—	—
Proceeds from issuance of common stock in connection with at-the-market offering, net	28,954	1,222	—
Proceeds from exercise of common stock options	1,215	88	24
Net cash provided by financing activities	<u>62,158</u>	<u>1,310</u>	<u>24</u>
Net increase (decrease) in cash and cash equivalents	47,003	11,301	(34,042)
Cash and cash equivalents at beginning of the period	16,455	5,154	39,196
Cash and cash equivalents at end of the period	<u>\$ 63,458</u>	<u>\$ 16,455</u>	<u>\$ 5,154</u>
<b>Supplemental disclosures of cash flow information</b>			
Purchases of property and equipment incurred but not paid	\$ 5	\$ —	\$ —

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

## CORVUS PHARMACEUTICALS, INC.

### NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

#### 1. Organization

Corvus Pharmaceuticals, Inc. (“Corvus” or the “Company”) was incorporated in Delaware on January 27, 2014 and commenced operations in November 2014. Corvus is a clinical-stage biopharmaceutical company. The Company’s operations are located in Burlingame, California.

#### *Presentation*

The consolidated financial statements include the accounts of the Company and its wholly-owned subsidiaries, Corvus Biopharmaceuticals, Ltd. and Corvus Hong Kong Limited. All significant intercompany accounts and transactions have been eliminated from the consolidated financial statements.

#### *Initial Public Offering*

On March 22, 2016, the Company’s registration statement on Form S-1 (File No. 333-208850) relating to its initial public offering (“IPO”) of its common stock was declared effective by the Securities and Exchange Commission (“SEC”) and the shares of its common stock began trading on the Nasdaq Global Market on March 23, 2016. The public offering price of the shares sold in the IPO was \$15.00 per share. The IPO closed on March 29, 2016, pursuant to which the Company sold 4,700,000 shares of its common stock. On April 26, 2016, the Company sold an additional 502,618 shares of its common stock to the underwriters upon partial exercise of their over-allotment option, at the initial offering price of \$15.00 per share. The Company received aggregate net proceeds of approximately \$70.6 million, after underwriting discounts, commissions and offering expenses. Immediately prior to the consummation of the IPO, all outstanding shares of convertible preferred stock were converted into common stock.

#### *Follow-on Public Offering*

In March 2018, the Company completed a follow-on public offering in which the Company sold 8,117,647 shares of common stock at a price of \$8.50 per share, which included 1,058,823 shares issued pursuant to the underwriters’ exercise of their option to purchase additional shares of common stock. The aggregate net proceeds received by the Company from the offering were approximately \$64.9 million, net of underwriting discounts and commissions and offering expenses payable by the Company.

In February 2021, the Company completed a follow-on public offering in which the Company sold 9,783,660 shares of common stock at a price of \$3.50 per share, which included 1,212,231 shares issued pursuant to the underwriters’ exercise of their option to purchase additional shares of common stock. The aggregate net proceeds received by the Company from the offering were approximately \$32.0 million, net of underwriting discounts and commissions and offering expenses.

#### *Liquidity*

The Company is subject to risks and uncertainties common to early-stage companies in the biotechnology industry, including, but not limited to, development by competitors of new technological innovations, protection of proprietary technology, dependence on key personnel, contract manufacturer and contract research organizations, compliance with government regulations and the need to obtain additional financing to fund operations. Since commencing operations in 2014, the majority of the Company’s efforts have been focused on the research and development of mupadolimab (formerly CPI-006), CPI-818 and ciforadenant. The Company believes that it will continue to expend substantial resources for the foreseeable future as it continues clinical development of, seek regulatory approval for and, if approved, prepare for the commercialization of mupadolimab, CPI-818 and ciforadenant, as well as product candidates under the Company’s other development programs. These expenditures will include costs associated with research and development, conducting preclinical studies and clinical trials, obtaining regulatory

approvals, manufacturing and supply, sales and marketing and general operations. In addition, other unanticipated costs may arise. Because the outcome of any clinical trial and/or regulatory approval process is highly uncertain, the Company may not be able to accurately estimate the actual amounts necessary to successfully complete the development, regulatory approval process and commercialization of mupadolimab, CPI-818, and ciforadenant or any other product candidates. The Company does not expect its existing capital resources to be sufficient to enable it to fund the completion of its clinical trials and remaining development program of mupadolimab, CPI-818 and ciforadenant through commercialization. In addition, its operating plan may change as a result of many factors.

The Company has incurred significant losses and negative cash flows from operations in all periods since inception and had an accumulated deficit of \$266.4 million as of December 31, 2021. The Company has historically financed its operations primarily through the sale of redeemable convertible preferred stock and common stock. While the Company has been able to raise multiple rounds of financing, there can be no assurance that in the event the Company requires additional financing, such financing will be available on terms which are favorable or at all. Failure to generate sufficient cash flows from operations, raise additional capital or reduce certain discretionary spending would have a material adverse effect on the Company's ability to achieve its intended business objectives.

As of December 31, 2021, the Company had cash, cash equivalents and short-term marketable securities of \$69.5 million. Management believes that the Company's current cash, cash equivalents and short-term marketable securities will be sufficient to fund its planned operations for at least 12 months from the date of the issuance of these financial statements.

The current COVID-19 (coronavirus) pandemic, which is impacting worldwide economic activity, poses risks that the Company or its employees, contractors, suppliers, and other partners may be prevented from conducting business activities for an indefinite period of time, including due to shutdowns that may be requested or mandated by governmental authorities. The extent to which COVID-19 impacts the Company's business, including its clinical trials and financial condition, will depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the impact of variants of the COVID-19 virus, the duration of the pandemic, 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. As COVID-19 continues to spread around the globe, including the spread of more contagious and virulent variants, we will likely experience disruptions, including delays or difficulties in enrolling patients in our clinical trials, delays or difficulties in clinical site initiation, interruption of key clinical trial activities, delays in clinical sites receiving the supplies and materials needed to conduct our clinical trials and delays in necessary interactions with local regulatory authorities. COVID-19 may also impact the Company's ability to raise additional capital on a timely basis or at all, which could negatively impact short-term and long-term liquidity.

### ***Exchange Warrants***

On November 8, 2019, the Company entered into an exchange agreement (the "Exchange Agreement") with an investor and its affiliates (the "Exchanging Stockholders"), pursuant to which the Company exchanged an aggregate of 1,458,000 shares of the Company's common stock, par value \$0.0001 per share, owned by the Exchanging Stockholders for pre-funded warrants (the "Exchange Warrants") to purchase an aggregate of 1,458,000 shares of common stock (subject to adjustment in the event of any stock dividends and splits, reverse stock split, recapitalization, reorganization or similar transaction, as described in the Exchange Warrants), with an exercise price of \$0.0001 per share. The Exchange Warrants were exercisable at any time prior to expiration except that the Exchange Warrants could not be exercised by the Exchanging Stockholders if, after giving effect thereto, the Exchanging Stockholders would have beneficially owned more than 9.99% of the Company's common stock, subject to certain exceptions. In accordance with Accounting Standards Codification Topic 505, Equity, and Accounting Research Bulletin 43, the Company recorded the retirement of the common stock exchanged as a reduction of common shares outstanding and elected to record the excess over par value as a debit to additional paid-in-capital at the fair value of the Exchange Warrants on the issuance date. The Exchange Warrants were classified as equity in accordance with Accounting Standards Codification Topic 480, Distinguishing Liabilities from Equity, and Accounting Standards Codification Topic 815, Derivatives and Hedging, and the fair value of the Exchange Warrants was recorded as a credit to additional paid-in capital and is not subject to remeasurement. The Company determined that the fair value of the Exchange Warrants was substantially

similar to the fair value of the retired shares on the issuance date due to the negligible exercise price for the Exchange Warrants.

During the year ended December 31, 2021, the Exchange Warrants were fully exercised, resulting in the issuance of 1,457,947 shares of common stock on a net exercise basis.

## **2. Summary of Significant Accounting Policies**

### ***Basis of Presentation***

The accompanying consolidated financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America (“U.S. GAAP”). The Company’s functional and reporting currency is the U.S. dollar, except for its investment in its equity method investee which is the Chinese renminbi (RMB). The accompanying consolidated financial statements have been prepared on a going-concern basis, which contemplates the realization of assets and discharge of liabilities in the normal course of business. Since its inception, the Company has incurred significant losses and negative cash flows from operations. As of December 31, 2021, the Company had an accumulated deficit of \$266.4 million and cash, cash equivalents and marketable securities of \$69.5 million. The Company has financed its operations primarily with the proceeds from the sale of stock. The Company will need to raise additional capital to meet its business objectives. The Company believes that its current cash, cash equivalents and marketable securities will be sufficient to fund its planned expenditures and meet its obligations through at least the next twelve months from the issuance of these financial statements.

### ***Use of Estimates***

The preparation of the Company’s consolidated financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the amounts reported in the consolidated financial statements and accompanying notes. Actual results could differ from such estimates.

### ***Foreign Currency Translation***

Angel Pharmaceuticals Co., Ltd.’s (“Angel Pharmaceuticals”) functional currency is the Chinese renminbi (RMB). Angel Pharmaceuticals’ consolidated financial statements are reported in RMB. Financial information is translated from RMB to the U.S. dollar (the reporting currency) for inclusion in our consolidated financial statements. Income, expenses and cash flows are translated at average exchange rates prevailing during the fiscal period, assets and liabilities are translated at fiscal period-end exchange rates, and stockholders’ equity is held at historical rates. Resulting translation adjustments are included as a component of accumulated other comprehensive income in stockholders’ equity.

### ***Out of Period Adjustment***

In the three months ended June 30, 2021, the Company recorded a cumulative translation adjustment that affected the Company’s balance sheet at June 30, 2021 by increasing its investment in Angel Pharmaceuticals and accumulated other comprehensive income in the equity section of the balance sheet by \$1.4 million. \$0.9 million of this amount was an out of period adjustment related to the year ended December 31, 2020. The impact of the out of period adjustment in the quarter ended March 31, 2021 was to reduce the Company’s investment in Angel Pharmaceuticals and other comprehensive income by \$83,000. The Company has concluded that the out of period adjustment is not material to the consolidated financial statements for the fiscal year ended December 31, 2020 or the interim financial statements for the quarter ended March 31, 2021.

### ***Concentrations of Credit Risk and Other Risks and Uncertainties***

Substantially all of the Company’s cash and cash equivalents are deposited in accounts with two financial institutions that management believes are of high credit quality. Such deposits may, at times, exceed federally insured limits. The Company maintains its cash with an accredited financial institution and accordingly, such funds are subject to minimal credit risk. The Company’s marketable securities consist of investments in U.S. Treasury securities and U.S.

government agency securities, which can be subject to certain credit risks. However, the Company mitigates the risks by investing in high-grade instruments, limiting its exposure to any one issuer, and monitoring the ongoing creditworthiness of the financial institutions and issuers. The Company has not experienced any losses on its deposits of cash, cash equivalents or marketable securities.

The Company is subject to a number of risks similar to other early stage biopharmaceutical companies, including, but not limited to, the need to obtain adequate additional funding, possible failure of preclinical testing or clinical trials, its reliance on third parties to conduct its clinical trials, the need to obtain marketing approval for its product candidates, competitors developing new technological innovations, the need to successfully commercialize and gain market acceptance of the Company's product candidates, its right to develop and commercialize its product candidates pursuant to the terms and conditions of the licenses granted to the Company, and protection of proprietary technology. If the Company does not successfully commercialize or partner any of its product candidates, it will be unable to generate product revenue or achieve profitability.

### ***Segments***

Operating segments are identified as components of an enterprise about which separate discrete financial information is available for evaluation by the chief operating decision-maker in making decisions regarding resource allocation and assessing performance. The Company views its operations and manages its business in one operating segment, that of the development of and commercialization of precisely targeted oncology therapies.

### ***Cash, Cash Equivalents and Marketable Securities***

The Company considers all highly liquid investment securities with remaining maturities at the date of purchase of three months or less to be cash equivalents.

Investments with remaining maturities, at the date of purchase, greater than three months are classified as "available-for-sale" and are carried at fair value with unrealized gains and losses, if any, included as a component of accumulated other comprehensive income (loss) in stockholders' equity. Interest and realized gains and losses are included in interest income. Realized gains and losses are recognized based on the specific identification model.

### ***Fair Value Measurements***

Fair value accounting is applied for all financial assets and liabilities and non-financial assets and liabilities that are recognized or disclosed at fair value in the consolidated financial statements on a recurring basis (at least annually). The carrying amount of the Company's financial instruments, including cash equivalents, accounts payable and accrued liabilities, approximate fair value due to their short-term maturities.

### ***Investments in Equity Securities***

Investments in equity securities over which the Company is able to exercise significant influence over the investee, but does not control the investee, and is not the primary beneficiary of the investee's activities that are considered Variable Interest Entities ("VIEs") are accounted for using the equity method. Adjustments are made to investments accounted for using the equity method for any earnings or losses incurred and are recorded in loss from operations. Investments in equity securities which do not have readily determinable fair values and for which the Company is not able to exercise significant influence over the investee are accounted for under the measurement alternative which is the cost minus impairment, if any, plus or minus changes resulting from observable price changes in orderly transactions for the identical or similar securities of the same investee and adjustments related to the basis differences, if any.

### ***Property and Equipment, Net***

Property and equipment are stated at cost and depreciated using the straight-line method over the estimated useful lives of the respective assets:

Laboratory equipment	5 years
Computer equipment and purchased software	3 years
Leasehold improvements	Shorter of asset's useful life or remaining term of lease

Maintenance and repairs that do not extend the life or improve the asset are expensed when incurred. When assets are retired or otherwise disposed of, the cost and accumulated depreciation or amortization are removed from the balance sheet and any resulting gain or loss is reflected in operations.

### ***Impairment of Long-Lived Assets***

The Company regularly reviews the carrying value and estimated lives of all of its long-lived assets, including property and equipment, to determine whether indicators of impairment may exist which warrant adjustments to carrying values or estimated useful lives. The determinants used for this evaluation include management's estimate of the asset's ability to generate positive income from operations and positive cash flow in future periods as well as the strategic significance of the assets to the Company's business objectives. Should impairment exist, the impairment loss to be recognized is measured by the amount by which the carrying amount of the asset exceeds the projected discounted future net cash flows arising from the asset. All long-lived assets are maintained in the United States of America.

### ***Research and Development Expenses***

The Company records research and development expenses as incurred. The Company accounts for nonrefundable advance payments for goods and services that will be used in future research and development activities as expenses when the goods have been received or when the service has been performed rather than when the payment is made. Research and development expenses consist of costs incurred by the Company for the discovery and development of the Company's product candidates and include:

- employee-related expenses, including salaries, benefits, travel and non-cash stock-based compensation expense;
- external research and development expenses incurred under arrangements with third parties, such as contract research organizations, contract manufacturing organizations, academic and non-profit institutions and consultants;
- costs to acquire technologies to be used in research and development that have not reached technological feasibility and have no alternative future use;

- license fees; and
- other expenses, which include direct and allocated expenses for laboratory, facilities and other costs.

### ***Clinical Trial Accruals***

Costs for preclinical studies and clinical trial activities are recognized based on an evaluation of the vendors' progress towards completion of specific tasks. The Company applies significant judgment in developing estimates for clinical trial accruals based on assumptions related to vendors' progress towards completion. In developing these estimates, management estimates vendors' progress towards completion using data such as clinical site activations, patient enrollment or information provided to the Company by its vendors regarding their actual costs incurred. Payments for these activities are based on the terms of individual contracts and payment timing may differ significantly from the period in which the services are performed. The Company determines accrual estimates through reports from and discussions with applicable personnel and outside service providers as to the progress or state of completion, or the services completed. The Company's estimates of accrued expenses as of each balance sheet date are based on the facts and circumstances known at the time.

### ***Stock-Based Compensation***

The Company maintains incentive plans under which incentive stock options and nonqualified stock options may be granted to employees and non-employee service providers.

The Company accounts for stock-based employee compensation arrangements in accordance with the provisions of ASC 718, "Compensation—Stock Compensation." For stock options granted to employees, the Company recognizes compensation expense for all stock-based awards based on the grant-date estimated fair values. The value of the award is recognized as an expense ratably over the requisite service period. The fair value of stock options is determined using the Black-Scholes option pricing model. Forfeitures are accounted for when they occur.

Stock-based compensation expense related to stock options granted to non-employees is recognized based on the fair value of the stock options, determined using the Black-Scholes option pricing model. The awards generally vest over the time period the Company expects to receive service from the non-employee.

### ***Income Taxes***

The Company accounts for income taxes under the asset and liability method. The Company estimates actual current tax exposure together with assessing temporary differences resulting from differences in accounting for reporting purposes and tax purposes for certain items, such as accruals and allowances not currently deductible for tax purposes. These temporary differences result in deferred tax assets and liabilities, which are included in the Company's balance sheets. In general, deferred tax assets represent future tax benefits to be received when certain expenses previously recognized in the Company's statements of operations and comprehensive loss become deductible expenses, under applicable income tax laws or when net operating loss or credit carryforwards are utilized. Accordingly, realization of the Company's deferred tax assets is dependent on future taxable income against which these deductions, losses and credits can be utilized.

The Company must assess the likelihood that the Company's deferred tax assets will be recovered from future taxable income and a valuation allowance is recorded when it is more likely than not that the deferred tax asset will not be recovered. The Company applies judgment in the determination of the financial statement recognition and measurement of a tax position taken or expected to be taken in a tax return. Based on the available evidence, the Company is unable, at this time, to support the determination that it is more likely than not that its deferred tax assets will be utilized in the future. Accordingly, the Company recorded a full valuation allowance for all periods presented. The Company intends to maintain a valuation allowance until sufficient evidence exists to support its reversal.

The Company recognizes benefits of uncertain tax positions if it is more likely than not such positions will be sustained upon examination based solely on their technical merits as the largest amount of benefit that is more likely

than not to be realized upon the ultimate settlement. The Company recognizes any material interest and penalties related to unrecognized tax benefits in income tax expense. The Company is required to file income tax returns in the U.S. federal jurisdiction. The Company currently is not under examination by the Internal Revenue Service or other jurisdictions for any tax years.

### **Comprehensive Loss**

Comprehensive loss includes net loss as well as other changes in stockholders' equity that result from transactions and economic events other than those with stockholders. The Company's only element of other comprehensive loss in any period presented was unrealized gains and losses on available-for-sale marketable securities.

### **Net Loss per Share**

Basic net loss per share is calculated by dividing the net loss by the weighted average number of common shares outstanding and Exchange Warrants outstanding during the period, without consideration of potentially dilutive securities. In accordance with Accounting Standards Codification Topic 260, *Earnings Per Share*, the Exchange Warrants are included in the computation of basic net loss per share because the exercise price is negligible and they are fully vested and exercisable at any time after the original issuance date. Diluted net loss per share is computed by dividing the net loss by the weighted average number of common shares, Exchange Warrants, and potentially dilutive securities outstanding for the period. Diluted net loss per share is the same as basic net loss per share for all periods presented since the effect of potentially dilutive securities is anti-dilutive given the net loss of the Company.

### **Recent Accounting Pronouncements**

In December 2019, the FASB issued ASU No. 2019-12, "Income Taxes (Topic 740): Simplifying the Accounting for Income Taxes", which is intended to improve consistency and simplify several areas of existing guidance. ASU 2019-12 removes certain exceptions to the general principles related to the approach for intraperiod tax allocation, the methodology for calculating income taxes in an interim period and the recognition of deferred tax liabilities for outside basis differences. This new standard became effective for the Company for fiscal years beginning after December 15, 2020, including interim periods within those fiscal years. Early adoption is permitted. The Company adopted this standard effective January 1, 2021. Adoption of this standard in the first quarter of fiscal year 2021 did not have a material impact on the Company's consolidated financial statements.

### **3. Net Loss per Share**

The following table shows the calculation of net loss per share (in thousands, except share and per share data):

	Year Ended December 31,		
	2021	2020	2019
Numerator:			
Net loss - basic and diluted	\$ (43,241)	\$ (5,995)	\$ (46,672)
Denominator:			
Weighted average common shares outstanding	41,854,110	29,478,878	29,364,535
Less: weighted average common shares subject to repurchase	—	—	(14,725)
Weighted average common shares outstanding used to compute basic and diluted net loss per share	41,854,110	29,478,878	29,349,810
Net loss per share, basic and diluted	\$ (1.03)	\$ (0.20)	\$ (1.59)

The amounts in the table below were excluded from the calculation of diluted net loss per share, due to their anti-dilutive effect:

	Year Ended December 31,		
	2021	2020	2019
Outstanding options	6,354,308	6,664,173	5,643,410

#### 4. Fair Value Measurements

Financial assets and liabilities are measured and recorded at fair value. The Company is required to disclose information on all assets and liabilities reported at fair value that enables an assessment of the inputs used in determining the reported fair values. The fair value hierarchy prioritizes valuation inputs based on the observable nature of those inputs. The fair value hierarchy applies only to the valuation inputs used in determining the reported fair value of the investments and is not a measure of the investment credit quality. The hierarchy defines three levels of valuation inputs:

- Level 1—Quoted prices in active markets for identical assets or liabilities
- Level 2—Inputs other than quoted prices included within Level 1 that are observable for the asset or liability, either directly or indirectly
- Level 3—Unobservable inputs that reflect the Company’s own assumptions about the assumptions market participants would use in pricing the asset or liability

There have been no transfers of assets and liabilities between levels of hierarchy.

The Company’s Level 2 investments are valued using third-party pricing sources. The pricing services utilize industry standard valuation models, including both income and market-based approaches, for which all significant inputs are observable, either directly or indirectly, to estimate fair value. These inputs include reported trades of and broker/dealer quotes on the same or similar investments, issuer credit spreads, benchmark investments, prepayment/default projections based on historical data and other observable inputs.

The following tables present information as of December 31, 2021 and 2020 about the Company’s assets that are measured at fair value on a recurring basis and indicate the level of the fair value hierarchy the Company utilized to determine such fair values (in thousands):

	December 31, 2021			
	Fair Value Measured Using			Total Balance
	(Level 1)	(Level 2)	(Level 3)	
<b>Assets</b>				
Cash equivalents	\$ 61,992	\$ —	\$ —	\$ 61,992
Marketable securities	1,011	4,982	—	5,993
	<u>\$ 63,003</u>	<u>\$ 4,982</u>	<u>\$ —</u>	<u>\$ 67,985</u>
	December 31, 2020			
	Fair Value Measured Using			Total Balance
	(Level 1)	(Level 2)	(Level 3)	
<b>Assets</b>				
Cash equivalents	\$ 15,974	\$ —	\$ —	\$ 15,974
Marketable securities	6,074	21,730	—	27,804
	<u>\$ 22,048</u>	<u>\$ 21,730</u>	<u>\$ —</u>	<u>\$ 43,778</u>

As of December 31, 2021, marketable securities had a maximum remaining maturity of eleven months.

As of December 31, 2021 and 2020, the fair value of available for sale marketable securities by type of security were as follows (in thousands):

	December 31, 2021			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
U.S. Treasury securities	\$ 1,012	\$ —	\$ (2)	\$ 1,010
U.S. Government agency securities	4,984	—	(1)	4,983
	<u>\$ 5,996</u>	<u>\$ —</u>	<u>\$ (3)</u>	<u>\$ 5,993</u>

  

	December 31, 2020			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
U.S. Treasury securities	\$ 6,074	\$ —	\$ —	\$ 6,074
U.S. Government agency securities	21,726	5	(1)	21,730
	<u>\$ 27,800</u>	<u>\$ 5</u>	<u>\$ (1)</u>	<u>\$ 27,804</u>

## 5. Equity Method Investment

In August 2020, the Company established Angel Pharmaceuticals Co. Ltd. (“Angel”), a wholly-owned corporate venture in the People’s Republic of China (“China”) designed to develop, manufacture, and commercialize CPI-006, CPI-444, and CPI-818 compounds for distribution within the countries of China, Taiwan, Macao, and Hong Kong (collectively, the “Territories”) based on intellectual property licenses to be contributed to Angel by the Company.

In October 2020, Angel raised financing from third-party investors, the licenses were entered into and the Company’s ownership interest was reduced to 53.2%. Under the license agreements, the Company is required to provide manufacturing supply services for future supply of drug products for use in clinical trials, research and development, operational support, and participate in the joint steering committee which oversees the development and commercialization of the compounds. Angel is not required to make any payments to the Company regarding the licensed compounds or the additional services outlined in the agreement. After a 7 year Exclusive Grant Back Period, Angel license grants to the company for sole or jointly owned IP will be non-exclusive, fully paid and sublicensable. During the Exclusive Grant Back Period, Angel license grants to the company for sole and joint IP are exclusive, fully paid and sublicensable.

As a result of the financing, the Company reassessed its interest in Angel and determined that while Angel is a VIE, the Company is not considered the primary beneficiary of such VIE since Corvus does not have the power, through voting or similar rights and the license agreements, to direct the activities of Angel that most significantly impact Angel’s economic performance. Further, the Company determined that as it has a significant influence over Angel, and, therefore, it shall account for its investment in Angel using the equity method starting in October 2020, the date it lost control over Angel. At the date of loss of control, the Company derecognized all of Angel’s assets and liabilities from its balance sheet, recognized the retained equity interest at its fair value of \$37.5 million, and recognized a gain of \$37.5 million, which is included in gain on deconsolidation of Angel Pharmaceuticals on the consolidated statement of operations for the year ended December 31, 2020.

As of December 31, 2021, the Company’s ownership interest in Angel was approximately 49.7%, excluding 7% of Angel’s equity reserved for issuance under the Angel ESOP. The Company recognized its share of losses in Angel for the total amount of \$4.8 million and \$0.2 million as loss from equity method investment on the consolidated statement of operations for the years ended December 31, 2021 and 2020, respectively.

## Summary Financial Information

Summary financial information for Angel Pharmaceuticals is as follows:

Balance Sheet Data (unaudited)	As of	
	December 31, 2021	December 31, 2020
	(In thousands)	
Current assets	\$ 38,407	\$ 38,883
Non-current assets	1,710	—
Current liabilities	1,741	97
Non-current liabilities	276	—
Stockholders' equity	38,100	38,786

Statement of Operations Data (unaudited)	Year Ended	
	December 31, 2021	December 31, 2020 (1)
	(In thousands)	
Net loss	\$ (5,697)	\$ (274)
Share of loss from investments accounted for using the equity method	(4,831)	(234)

(1) The Company's share of loss is based on net loss beginning October 2020 upon the deconsolidation of Angel Pharmaceuticals.

## 6. License and Collaboration Agreements

### *Scripps Licensing Agreement*

In December 2014, the Company entered into a license agreement with The Scripps Research Institute ("Scripps"), pursuant to which it was granted a non-exclusive, world-wide license for all fields of use under Scripps' rights in certain know-how and technology related to a mouse hybridoma clone expressing an anti-human CD73 antibody, and to progeny, mutants or unmodified derivatives of such hybridoma and any antibodies expressed by such hybridoma, from which we developed CPI-006. Scripps also granted the Company the right to grant sublicenses in conjunction with other proprietary rights the Company holds, or to others collaborating with or performing services for the Company. Under this license agreement, Scripps has agreed not to grant any additional commercial licenses with respect to such materials, other than march-in rights granted to the U.S. government.

Upon execution of the agreement, the Company made a one-time cash payment to Scripps of \$10,000 in 2015 and is also obligated to pay a minimum annual fee to Scripps of \$25,000. The one-time cash payment was recorded as research and development expense as technological feasibility of the asset had not been established and there was no alternative future use. A minimum annual fee payment is due on each anniversary of the effective date of the agreement for the term of the agreement. The Company is also required to make performance-based cash payments upon successful completion of clinical and sales milestones. The aggregate potential milestone payments are \$2.5 million. The Company is also required to pay royalties on net sales of licensed products (including CPI-006) sold by it, its affiliates and its sublicensees at a rate in the low-single digits. In addition, should the Company sublicense the rights licensed under the agreement, it has agreed to pay a percentage of sublicense revenue received at specified rates that start at double digit percentages and decrease to single digit percentages based on the elapsed time from the effective date of the agreement and the time of entry into such sublicense. To date, no milestone payments have been made.

The Company's license agreement with Scripps will terminate upon expiration of its obligation to pay royalties to Scripps under the license agreement. The Company's license agreement with Scripps is terminable by the consent of the parties, at will by the Company upon providing 90 days written notice to Scripps, or by Scripps for certain material

breaches, or if the Company undergoes a bankruptcy event. In addition, Scripps may terminate the license on a product-by-product basis, or the entire agreement, if the Company fails to meet specified diligence obligations related to the development and commercialization of licensed products. Scripps may also terminate the agreement after the third anniversary of the effective date of the agreement if it reasonably believes, based on reports the Company provides to Scripps, that the Company has not used commercially reasonable efforts as required under the agreement, subject to a specified notice and cure period.

#### ***Vernalis Licensing Agreement***

In February 2015, the Company entered into a license agreement with Vernalis (R&D) Limited (“Vernalis”), which was subsequently amended as of November 5, 2015, and, pursuant to which the Company was granted an exclusive, worldwide license under certain patent rights and know-how, including a limited right to grant sublicenses, for all fields of use to develop, manufacture and commercialize products containing certain adenosine receptor antagonists, including ciforadenant. Pursuant to this agreement, the Company made a one-time cash payment to Vernalis in the amount of \$1.0 million, which was recorded as research and development expense as technological feasibility of the asset had not been established and there was no alternative future use. The Company is also required to make cash milestone payments to Vernalis upon the successful completion of clinical and regulatory milestones for licensed products depending on the indications for which such licensed products are developed and upon achievement of certain sales milestones. In February 2017, the Company made a milestone payment of \$3.0 million to Vernalis following the expansion of a cohort of patients with renal cell cancer treated with single agent ciforadenant in the Company’s Phase 1/1b clinical trial. The aggregate potential milestone payments are approximately \$220 million for all The Company has also agreed to pay Vernalis tiered incremental royalties based on the annual net sales of licensed products containing ciforadenant on a product-by-product and country-by-country basis, subject to certain offsets and reductions. The tiered royalty rates for products containing ciforadenant range from the mid-single digits up to the low-double digits on a country-by-country net sales basis. The royalties on other licensed products that do not include ciforadenant also increase with the amount of net sales on a product-by-product and country-by-country basis and range from the low-single digits up to the mid-single digits on a country-by-country net sales basis. The Company is also obligated to pay to Vernalis certain sales milestones as indicated above when worldwide net sales reach specified levels over an agreed upon time period.

The agreement will expire on a product-by-product and country-by-country basis upon the expiration of the Company’s payment obligations to Vernalis in respect of a particular product and country. Both parties have the right to terminate the agreement for an unsecured material breach by the other party. The Company may also terminate the agreement at its convenience by providing 90 days written notice, provided that the Company has not received notice of its own default under the agreement at the time the Company exercises such termination right. Vernalis may also terminate the agreement if the Company challenges a licensed patent or undergoes a bankruptcy event.

#### ***Genentech Collaboration Agreement***

In October 2015, the Company entered into a clinical trial collaboration agreement with Genentech to evaluate the safety, tolerability and preliminary efficacy of ciforadenant combined with Genentech’s investigational cancer immunotherapy, Tecentriq, a fully humanized monoclonal antibody targeting PD-L1, in a variety of solid tumors in our Phase 1/1b clinical trial. Pursuant to this agreement, the Company will be responsible for the conduct and cost of the relevant studies, under the supervision of a joint development committee made up of the Company’s representatives and representatives of Genentech. Genentech will supply Tecentriq. At this time, no further patients are being enrolled in this trial. As part of the agreement, the Company granted Genentech certain rights of first negotiation to participate in future clinical trials that the Company may conduct evaluating the administration of ciforadenant in combination with an anti-PD-1 or anti-PD-L1 antibody. If both parties do not reach agreement on the terms of any such participation by Genentech within a specified time period, the Company retains the right to collaborate with third parties in such activities. The Company also granted Genentech certain rights of first negotiation should the Company decide to license development and commercialization rights to ciforadenant. Should both parties not reach agreement on the terms of such a license within a specified time of period, the Company retains the right to enter into a license with another third party. This agreement will expire after a set period of time following the provision by the Company of the final clinical study report to Genentech, which has not yet been finalized.

In May 2017, the Company entered into a second clinical trial collaboration agreement with Genentech. Under the new agreement, ciforadenant administered in combination with Tecentriq will be evaluated in a Phase 1b/2 randomized, controlled clinical study as second-line therapy in patients with NSCLC who are resistant and/or refractory to prior therapy with an anti-PD-(L)1 antibody. This study has completed patient enrollment of 16 patients. Genentech was responsible for the conduct of the study and the Company will share the cost of the Phase 1b/2 trial, which began enrolling patients in the fourth quarter of 2017. The Company is responsible for supplying ciforadenant and retains global development and commercialization rights to ciforadenant. This agreement will expire after a set period of time following the provision by Genentech of a final study report to the Company.

#### ***Monash License Agreement***

In April 2017, the Company entered into a license agreement with Monash University (“Monash”), pursuant to which the Company was granted an exclusive, sublicensable worldwide license under certain know-how, patent rights and other intellectual property rights controlled by Monash to research, develop, and commercialize certain antibodies directed to CXCR2 for the treatment of human diseases.

Upon execution of the agreement, the Company made a one-time cash payment to Monash of \$275,000 and reimbursed Monash for certain patent prosecution costs incurred prior to execution of the agreement. The Company is also obligated to pay an annual license maintenance fee to Monash of \$25,000 until a certain development milestone is met with respect to the licensed product, after which no further maintenance fee will be due. The Company is also required to make development and sales milestone payments to Monash with respect to the licensed products in the aggregate of up to \$45.1 million. The Company is also required to pay to Monash tiered royalties on net sales of licensed products sold by it, its affiliates and its sublicensees at a rate ranging in the low-single digits. In addition, should the Company sublicense its rights under the agreement, the Company has agreed to pay a percentage of sublicense revenue received at specified rates that are currently at low double digit percentages and decrease to single digit percentages based on the achievement of development milestones.

The term of the Company’s agreement with Monash continues until the expiration of its obligation to pay royalties to Monash thereunder. The license agreement is terminable at will by the Company upon providing 30 days written notice to Monash, or by either party for material breaches by the other party. In addition, Monash may terminate the entire agreement or convert the license to a non-exclusive license if the Company has materially breached our obligation to use commercially reasonable efforts to develop and commercialize a licensed product, subject to a specified notice and cure mechanism.

**7. Balance Sheet Components (in thousands):**

	December 31, 2021	December 31, 2020
<b><i>Prepaid and Other Current Assets</i></b>		
Interest receivable	\$ 32	\$ 86
Prepaid research and development manufacturing expenses	740	181
Prepaid facility expenses	174	160
Prepaid insurance	280	244
Other	128	406
	<u>\$ 1,354</u>	<u>\$ 1,077</u>
<b><i>Property and Equipment</i></b>		
Laboratory equipment	\$ 2,477	\$ 2,472
Computer equipment and purchased software	142	142
Leasehold improvements	2,084	2,084
	<u>4,703</u>	<u>4,698</u>
Less: accumulated depreciation and amortization	<u>(4,252)</u>	<u>(3,792)</u>
	<u>\$ 451</u>	<u>\$ 906</u>
<b><i>Accrued and Other Liabilities</i></b>		
Accrued clinical trial expense	\$ 4,010	\$ 4,681
Accrued manufacturing expense	839	321
Personnel related	1,846	2,225
Accrued legal and accounting	265	197
Other	121	180
	<u>\$ 7,081</u>	<u>\$ 7,604</u>

**8. Common Stock**

As of December 31, 2021, the amended and restated certificate of incorporation authorizes the Company to issue 290 million shares of common stock and 10 million shares of preferred stock.

Each share of common stock is entitled to one vote. Common stockholders are entitled to dividends if and when declared by the board of directors. As of December 31, 2021, no dividends on common stock had been declared.

In March 2020, the Company entered into an open market sale agreement (the "2020 Sales Agreement") with Jefferies LLC ("Jefferies") to sell shares of the Company's common stock, from time-to-time, with aggregate gross sales proceeds of up to \$50,000,000, through an at-the-market equity offering program under which Jefferies will act as its sales agent. In November 2021, the Company entered into another Sale Agreement ("2021 Sales Agreement") with Jefferies to sell shares of our common stock from time-to-time, with aggregate gross sales proceeds of up to \$40,000,000. The issuance and sale of shares of common stock by the Company pursuant to the Sales Agreements are deemed an "at-the-market" offering under the Securities Act of 1933, as amended. Jefferies is entitled to compensation for its services equal to up to 3.0% of the gross proceeds of any shares of common stock sold through Jefferies under the Sales Agreements.

During the year ended December 31, 2021, the Company sold 6,609,605 shares under its at-the-market offering program resulting in net proceeds of \$29.0 million. As of December 31, 2021, \$18.9 million remained for sale under the 2020 Sales Agreement and \$40.0 million remained for sale under the 2021 Sales Agreement.

The Company has reserved shares of common stock, for issuance as follows:

	<b>December 31,</b>		
	<b>2021</b>	<b>2020</b>	<b>2019</b>
Exchange warrants	—	1,458,000	1,458,000
Shares available for future option grants	2,806,953	1,692,753	1,704,183
Outstanding options	6,354,308	6,664,173	5,643,410
Shares reserved for employee stock purchase plan	400,000	400,000	400,000
<b>Total</b>	<b><u>9,561,261</u></b>	<b><u>10,214,926</u></b>	<b><u>9,205,593</u></b>

## 9. Stock Option Plans

In February 2014, the Company adopted the 2014 Equity Incentive Plan (the “2014 Plan”), which was subsequently amended in November 2014, July 2015 and September 2015, under which it granted incentive stock options (“ISOs”) or non-qualified stock options (“NSOs”). Terms of stock agreements, including vesting requirements, are determined by the board of directors or a committee authorized by the board of directors, subject to the provisions of the 2014 Plan. In general, awards granted by the Company vest over four years and have maximum exercise term of 10 years. The 2014 Plan provides that grants must be at an exercise price of 100% of fair market value of the Company’s common stock as determined by the board of directors on the date of the grant.

In connection with the consummation of the IPO in March 2016, the 2016 Equity Incentive Award Plan (the “2016 Plan”), became effective. Under the 2016 Plan, incentive stock options, non-statutory stock options, stock purchase rights and other stock-based awards may be granted. Terms of stock agreements, including vesting requirements, are determined by the board of directors or a committee authorized by the board of directors, subject to the provisions of the 2016 Plan. In general, awards granted by the Company vest over four years and have a maximum exercise term of 10 years. The 2016 Plan provides that grants must be at an exercise price of 100% of fair market value of the Company’s common stock as determined by the board of directors on the date of the grant. In conjunction with adopting the 2016 Plan, the 2014 Plan was terminated and no further awards will be granted under the 2014 Plan. Options outstanding under the 2014 Plan as of the effective date of the 2016 Plan that are forfeited or lapse unexercised may be re-issued under the 2016 Plan, up to a maximum of 1,136,229 shares.

Activity under the Company’s stock option plans is set forth below:

	<b>Shares Available for Grant</b>	<b>Options Outstanding</b>	
		<b>Number of Options</b>	<b>Weighted - Average Exercise Price</b>
Balance at December 31, 2020	1,692,753	6,664,173	\$ 7.26
Additional shares authorized	1,134,000	—	—
Options granted	(1,645,000)	1,645,000	2.68
Options exercised	—	(329,665)	3.69
Options forfeited	1,625,200	(1,625,200)	5.14
<b>Balance at December 31, 2021</b>	<b><u>2,806,953</u></b>	<b><u>6,354,308</u></b>	<b>\$ 6.80</b>

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The following tables summarize information about stock options outstanding at December 31, 2021 and 2020:

		Options Outstanding at December 31, 2021		Options Vested at December 31, 2021	
Exercise Price	Number	Weighted Average Remaining Contractual Life (in Years)	Weighted Average Exercise Price	Number	Weighted Average Exercise Price
\$0.28 - \$2.00	110,000	6.65	\$ 1.45	110,000	\$ 1.45
\$2.56 - \$3.84	2,483,169	8.47	\$ 3.06	785,426	\$ 3.44
\$3.88 - \$5.82	999,064	8.64	\$ 4.02	288,670	\$ 4.03
\$5.94 - \$8.91	765,439	5.31	\$ 5.98	619,649	\$ 5.98
\$9.52 - \$14.28	846,636	3.83	\$ 10.74	829,640	\$ 10.72
\$14.43 - \$21.64	1,150,000	3.94	\$ 15.45	1,150,000	\$ 15.45
	<u>6,354,308</u>	6.65	\$ 6.80	<u>3,783,385</u>	\$ 9.09

		Options Outstanding at December 31, 2020		Options Vested at December 31, 2020	
Exercise Price	Number	Weighted Average Remaining Contractual Life (in Years)	Weighted Average Exercise Price	Number	Weighted Average Exercise Price
\$0.28 - \$2.00	190,500	5.56	\$ 1.09	100,500	\$ 0.28
\$2.56 - \$3.84	1,628,459	8.85	\$ 3.53	468,939	\$ 3.56
\$3.88 - \$5.82	1,707,500	9.65	\$ 4.00	130,106	\$ 3.99
\$5.94 - \$8.91	899,959	7.42	\$ 5.98	482,065	\$ 5.98
\$9.52 - \$14.28	955,947	6.47	\$ 10.77	762,488	\$ 10.76
\$14.43 - \$21.64	1,281,808	5.17	\$ 15.44	1,265,434	\$ 15.42
	<u>6,664,173</u>	7.72	\$ 7.26	<u>3,209,532</u>	\$ 10.23

The weighted average grant date fair value of options granted for the years ended December 31, 2021, 2020 and 2019, was \$1.93, \$2.66 and \$2.53, respectively.

Options outstanding and exercisable that had vested or were expected to vest at December 31, 2021 were as follows:

	Number of shares	Weighted Average Exercise Price	Weighted Average Remaining Contractual Life (years)	Aggregate Intrinsic Value (in thousands)
Vested	3,783,385	\$ 9.09	5.03	\$ 105
Expected to vest	2,570,923	\$ 3.43	9.03	\$ —

In the table above, aggregate intrinsic value represents the difference between the exercise price of the options to purchase common stock and the fair value of the Company's common stock of \$2.41 per share as of December 31, 2021.

The aggregate intrinsic value of stock options exercised in the years ended December 31, 2021, 2020 and 2019, was \$1.0 million, \$0.3 million and \$0.4 million, respectively.

The total fair value of options that vested in the year ended December 31, 2021, 2020 and 2019, was \$4.5 million, \$6.0 million, and \$7.8 million, respectively.

## 10. Stock-Based Compensation

The Company's results of operations include expenses relating to stock-based awards as follows (in thousands):

	Year Ended December 31,		
	2021	2020	2019
Research and development	\$ 2,161	\$ 2,791	\$ 3,103
General and administrative	2,071	2,956	4,245
Total	<u>\$ 4,232</u>	<u>\$ 5,747</u>	<u>\$ 7,348</u>

### Valuation Assumptions

The Company estimated the fair value of employee stock options using the Black-Scholes valuation model. The fair value of employee stock options is being amortized on a straight-line basis over the requisite service period of the awards. The fair value of employee stock options were estimated using the following assumptions for the years ended December 31, 2021, 2020 and 2019:

	Year Ended December 31,		
	2021	2020	2019
Risk-free interest rate	0.9 %	0.5 %	1.9 %
Expected volatility	86.7 %	82.7 %	82.1 %
Expected term (in years)	6.0	6.0	6.0
Expected dividend yield	0 %	0 %	0 %

**Risk-free Interest Rate:** The Company based the risk-free interest rate over the expected term of the options based on the constant maturity rate of U.S. Treasury securities with similar maturities as of the date of the grant.

**Volatility:** The Company uses an average historical stock price volatility of a peer group of publicly traded companies to be representative of its expected future stock price volatility, as the Company does not have sufficient trading history for its common stock. For purposes of identifying these peer companies, the Company considers the industry, stage of development, size and financial leverage of potential comparable companies. For each grant, the Company measures historical volatility over a period equivalent to the expected term. The Company will continue to apply this process until a sufficient amount of historical information regarding the volatility of its own stock price becomes available.

**Expected Term:** The Company uses the simplified method prescribed in the ASC 718, Compensation—Stock Compensation, to calculate the expected term of options granted to employees and directors.

**Expected Dividends:** The Company has not paid and does not anticipate paying any dividends in the near future.

At December 31, 2021, 2020 and 2019, the unrecognized compensation expense associated with respect to options granted to employees was \$5.9 million, \$10.4 million and \$13.4 million, respectively, and is expected to be recognized on a straight-line basis over 2.69, 2.78, and 2.71 years, respectively.

## 11. Income Taxes

The components of loss before income tax is as follows (in thousands):

	December 31,		
	2021	2020	2019
Domestic	\$ (43,241)	\$ (5,995)	\$ (46,672)
Foreign	—	—	—
	<u>\$ (43,241)</u>	<u>\$ (5,995)</u>	<u>\$ (46,672)</u>

During the years ended December 31, 2021, 2020 and 2019, the Company recorded no income tax benefits for the net operating losses (NOLs) incurred due to the uncertainty of realizing a benefit from those items.

A reconciliation of the Company's effective tax rate to the U.S. Federal statutory rate is as follows:

	December 31,		
	2021	2020	2019
Federal tax benefit at statutory rate	21 %	21 %	21 %
State tax, net of Federal benefit	9 %	14 %	6 %
Change in valuation allowance	(26)%	(24)%	(28)%
Research and development tax credits	3 %	19 %	4 %
Share based Compensation	(1)%	(10)%	(1)%
162(m) covered employees compensation limitation	— %	(6)%	—
FIN48 Reserve	(1)%	(161)%	(1)%
Deconsolidation gain	(3)%	174 %	—
Gain on transfer of intellectual property	—	(20)%	—
Prior year federal true-up	(1)%	(7)%	— %
Other	(1)%	—	(1)
Effective income tax rate	<u>0 %</u>	<u>0 %</u>	<u>0 %</u>

The effective tax rate is different from the federal statutory tax rate primarily due to a foreign rate differential and a valuation allowance against deferred tax assets as a result of the Company's history of losses.

The significant components of the Company's net deferred tax assets are as follows (in thousands)

	December 31,		
	2021	2020	2019
<b>Deferred tax assets</b>			
Net operating loss carryforwards	\$ 52,539	\$ 42,344	\$ 42,486
Tax credit carryforwards	9,181	7,894	6,990
Capitalized tax assets	125	63	(3)
Accruals	137	207	152
Stock compensation	5,006	4,942	4,317
Operating lease liability	1,021	646	892
Other	12	47	40
Total deferred tax assets	<u>\$ 68,021</u>	<u>\$ 56,143</u>	<u>\$ 54,874</u>
<b>Deferred tax liabilities</b>			
Operating lease right-of-use asset	<u>\$ (893)</u>	<u>\$ (461)</u>	<u>\$ (651)</u>
Valuation allowance	<u>(67,128)</u>	<u>(55,682)</u>	<u>(54,223)</u>
Net deferred tax assets	<u>\$ —</u>	<u>\$ —</u>	<u>\$ —</u>

The Company recorded a valuation allowance against its deferred tax assets at December 31, 2021 and 2020 because Company management believed that it was more likely than not that these assets would not be fully realized in the future. The valuation allowance increased by approximately \$11.4 million and \$1.5 million for the years ended

December 31, 2021 and 2020, respectively. Changes in the valuation allowance for deferred tax assets relate primarily to the increase in the Company's net operating loss carryforward.

As of December 31, 2021, the Company had federal NOL carryforwards of approximately \$212.6 million and state NOL carryforwards of approximately \$246.3 million which are available to reduce future taxable income. The NOLs will begin to expire in 2034, if not utilized. Utilization of the net operating loss carryforwards are subject to various limitations due to the ownership change limitations provided by Internal Revenue Code (IRC) Section 382 and similar state provisions.

On March 27, 2020, the President signed into law the Coronavirus Aid, Relief, and Economic Security Act, or the CARES Act, an economic stimulus package in response to the COVID-19 global pandemic and the Families First Coronavirus Response Act, or FFCR Act, which permits employees of certain organizations paid sick time stemming from COVID-19-related issues. The CARES Act contains several corporate income tax provisions, including making remaining alternative minimum tax credits immediately refundable; providing a 5-year carryback of NOLs generated in tax years 2018, 2019, and 2020, and removing the 80% taxable income limitation on utilization of those NOLs if carried back to prior tax years or utilized in tax years beginning before 2021; temporarily liberalizing the interest deductibility rules under Section 163(j) of the CARES Act, by raising the adjusted taxable income limitation from 30% to 50% for tax years 2019 and 2020 and giving taxpayers the election of using 2019 adjusted taxable income for purposes of computing 2020 interest deductibility. The CARES Act did not have a material impact on the Company's tax provision for the years ended December 31, 2020 or 2021.

The Consolidated Appropriations Act, 2021, which was enacted on December 27, 2020, has expanded, extended, and clarified selected CARES Act provisions, specifically on Paycheck Protection Program loans and Employee Retention Tax Credits, 100% deductibility of business meals as well as other tax extenders. The Consolidated Appropriations Act did not have a material impact on the Company's tax provision for the years ended December 31, 2020 or 2021.

On June 29, 2020, Assembly Bill 85 ("A.B. 85") was signed into California law. A.B. 85 provides for a three-year suspension of the use of net operating losses for medium and large businesses and a three-year cap on the use of business incentive tax credits to offset no more than \$5.0 million of tax per year. A.B. 85 suspends the use of net operating losses for taxable years 2020, 2021 and 2022 for certain taxpayers with taxable income of \$1.0 million or more. The carryover period for any net operating losses that are suspended under this provision will be extended. A.B. 85 also requires that business incentive tax credits including carryovers may not reduce the applicable tax by more than \$5.0 million for taxable years 2020, 2021 and 2022. The Company does not expect the impact of this standard on its consolidated financial statements to be material.

California Senate Bill 113 (SB 113), was signed into law by Governor Newsom on February 9, 2022. The legislation contains important California tax law changes, including reinstatement of business tax credits and net NOL deductions limited by AB 85 mentioned above. The new tax law should be accounted for under ASC 740 in the period of enactment (2022) but is not expected to have a material impact on the Company's tax provision due to its taxable loss position.

As of December 31, 2021, the Company also had \$7.9 million of federal and \$4.5 million of state research and development tax credit carryforwards available to reduce future income taxes. The federal research and development tax credits will begin to expire 2035, if not utilized. The state research and development tax credits have no expiration date.

U.S. income and foreign withholding taxes have not been recognized on the excess of the amount for financial reporting over the tax basis of investments in foreign subsidiaries that are essentially permanent in duration. This excess totaled approximately \$35.0 million as of December 31, 2021, which will be indefinitely reinvested; deferred income taxes have not been provided on such foreign earnings.

As of December 31, 2021, the Company had unrecognized tax benefits (“UTBs”) of approximately \$12.5 million. All of the deferred tax assets associated with these UTBs are fully offset by a valuation allowance. The following table summarizes the activity related to UTBs:

	December 31,		
	2021	2020	2019
Unrecognized tax benefits beginning of the period	\$ 12,157	\$ 1,885	\$ 1,804
Decrease related to the prior year	—	—	(365)
Increased related to the current year	347	10,272	446
Unrecognized tax benefits, end of the period	<u>\$ 12,504</u>	<u>\$ 12,157</u>	<u>\$ 1,885</u>

The Company follows the provisions of ASC 740, Accounting for Income Taxes, and the accounting guidance related to accounting for uncertainty in income taxes. The Company determines its uncertain tax positions based on a determination of whether and how much of a tax benefit taken by the Company in its tax filings or positions is more likely than not to be sustained upon examination by the relevant income tax authorities. None of the Company’s unrecognized tax benefits that, if recognized, would affect its effective tax rate. The Company does not anticipate the total amounts of unrecognized tax benefits will significantly increase or decrease in the next 12 months. The Company will recognize both accrued interest and penalties related to unrecognized benefits in income tax expense. Management determined that no accrual for interest or penalties was required as of December 31, 2021, 2020 and 2019.

The Company currently has no federal or state tax examinations in progress nor has it had any federal or state examinations since inception. As a result of the Company’s net operating loss carryforwards, all of its tax years are subject to federal, state and foreign tax examinations.

## 12. Facility Lease

In January 2015, the Company signed an initial operating lease, effective February 1, 2015 for 8,138 square feet of office and laboratory space with a one year term. Between January 2015 and September 2021, the Company entered into a series of lease amendments to increase the amount of leased space to 27,280 square feet and extend the expiration of the lease to February 2025. The lease agreement includes annual rent escalations. Under the lease and subsequent amendments, the landlord provided approximately \$1.9 million in free rent and lease incentives. The Company records rent expense on a straight-line basis over the effective term of the lease, including any free rent periods and incentives. As the interest rate implicit in lease arrangements is typically not readily available, in calculating the present value of the lease payments, the Company has utilized its incremental borrowing rate, which is determined based on the prevailing market rates for collateralized debt with maturity dates commensurate with the term of its lease. The Company’s facility lease is a net lease, as the non-lease components (i.e. common area maintenance) are paid separately from rent based on actual costs incurred. Therefore, the non-lease components were not included in the right-of-use asset and liability and are reflected as an expense in the period incurred.

In September 2021, the Company entered into a lease amendment to extend the expiration of its operating lease by two years, from February 2023 to February 2025. As a result of this lease extension, the Company recorded a \$2.4 million increase in the operating lease right-of-use asset and a corresponding increase in the operating lease liability

As of December 31, 2021 and 2020, the right-of-use asset under operating lease was \$3.2 million and \$1.6 million, respectively. The elements of lease expense were as follows (in thousands):

	Statements of operations and comprehensive loss location	Year Ended December 31,		
		2021	2020	2019
<b>Costs of operating lease</b>				
Operating lease costs	Research and development, General and administrative	\$ 1,046	\$ 957	\$ 960
Costs of non-lease components (previously common area maintenance)	Research and development, General and administrative	396	351	324

Total operating lease cost	\$ 1,442	\$ 1,308	\$ 1,284
<b>Other Information</b>			
Operating cash flows used for operating lease	\$ 1,645	\$ 1,506	\$ 1,449
Remaining lease term	3.1 years	2.1 years	3.1 years
Discount rate	8.0%	10.0%	10.0%

As of December 31, 2021, minimum rental commitments under this lease were as follows (in thousands)

<u>Year Ended December 31 (in thousands)</u>	
2022	\$ 1,300
2023	1,391
2024	1,434
Total lease payments	4,125
Less: imputed interest	(478)
Total	<u>\$ 3,647</u>

As of December 31, 2020, minimum rental commitments under this lease were as follows (in thousands)

<u>Year Ended December 31 (in thousands)</u>	
2021	\$ 1,260
2022	1,299
Total lease payments	2,559
Less: imputed interest	(249)
Total	<u>\$ 2,310</u>

In August 2021, the Company entered into an agreement to sublease 7,585 square feet of its office and laboratory space in Burlingame, California to Angel Pharmaceuticals. Pursuant to the sublease, rent is due monthly and is subject to scheduled annual increases and Angel Pharmaceuticals is responsible for certain operating expenses and taxes throughout the life of the sublease. The sublease will expire in February 2023 and Angel Pharmaceuticals has no option to extend the sublease term. Sublease income is recognized on a straight-line basis as other income in our consolidated statements of operations. For the year ended December 31, 2021, the Company recognized \$0.2 million of sublease income.

### 13. Commitments and Contingencies

#### *Commitments*

As of December 31, 2021, the Company had total non-cancellable purchase commitments of \$9.3 million for the purchase of drug substance in 2022.

#### *Contingencies*

In August 2015, the Company entered into an agreement for a line of credit of \$0.1 million for the purpose of issuing its landlord a letter of credit of \$0.1 million as a security deposit under its facility lease. The Company pledged money market funds and marketable securities as collateral for the line of credit. For further discussion of the Company's facility lease agreement, see Note 12.

Pursuant to the Company's license agreements with each of Vernalis and Scripps, it has obligations to make future milestone and royalty payments to these parties, respectively. However, because these amounts are contingent,

they have not been included on the Company's balance sheet. For further discussion of the Vernalis and Scripps licensing agreements, see Note 6.

### **Indemnifications**

In the ordinary course of business, the Company enters into agreements that may include indemnification provisions. Pursuant to such agreements, the Company may indemnify, hold harmless and defend an indemnified party for losses suffered or incurred by the indemnified party. Some of the provisions will limit losses to those arising from third-party actions. In some cases, the indemnification will continue after the termination of the agreement. The maximum potential amount of future payments the Company could be required to make under these provisions is not determinable. The Company has never incurred material costs to defend lawsuits or settle claims related to these indemnification provisions. The Company has also entered into indemnification agreements with its directors and officers that may require the Company to indemnify its directors and officers against liabilities that may arise by reason of their status or service as directors or officers to the fullest extent permitted by Delaware corporate law. There have been no claims to date and the Company has a directors and officers insurance policy that may enable it to recover a portion of any amounts paid for future claims.

### **Legal Proceedings**

The Company is not a party to any material legal proceedings.

## **14. Related Party Transactions**

In February 2021, the Company completed a follow-on public offering in which the Company sold 9,783,660 shares of common stock at a price of \$3.50 per share, which included 1,212,231 shares issued pursuant to the underwriters' exercise of their option to purchase additional shares of common stock. The aggregate net proceeds received by the Company from the offering were approximately \$32.0 million, net of underwriting discounts and commissions and offering expenses.

The following aggregate number of shares of common stock were sold to the Company's owners of more than 5% of our common stock, directors, or executive officers during the February 2021 underwritten public offering:

	<b>Number of Shares of Common Stock</b>	<b>Aggregate Purchase Price</b>
<b>Owners of More Than 5% of Our Common Stock</b>		
OrbiMed Advisors LLC (1)	1,285,714	\$ 4,499,999
<b>Board of Directors</b>		
Richard A. Miller, M.D.	100,000	350,000

(1) Peter Thompson, M.D., a member of our Board of Directors since November 2014, is a Private Equity Partner at OrbiMed Advisors, LLC.

As more fully described in Note 5, the Company holds a 49.7% ownership in Angel Pharmaceuticals and, in connection with intellectual property licensing agreements between the Company and Angel Pharmaceuticals, the Company provides operational support and clinical drug supplies to Angel Pharmaceuticals. Third-party and internal personnel costs incurred by the Company are billed to Angel Pharmaceuticals in the period incurred and recorded as an offset to expenses. During the year ended December 31, 2021, the Company billed Angel for approximately \$0.2 million in internal personnel costs and \$1.6 million in third-party costs. Of the third-party costs, approximately \$0.6 million were associated with clinical drug supply manufactured and expensed in prior years. The remaining \$1.0 million in third-party costs were primarily associated with clinical drug supply passthrough costs incurred during the year ended December 31, 2021 and did not have an impact on the Company's consolidated statements of operations.

In August 2021, the Company entered into an agreement to sublease 7,585 square feet of its office and laboratory space in Burlingame, California to Angel Pharmaceuticals. Pursuant to the sublease, rent is due monthly and is subject to scheduled annual increases and Angel Pharmaceuticals is responsible for certain operating expenses and taxes throughout the life of the sublease. The sublease will expire in February 2023 and Angel Pharmaceuticals has no option to extend the sublease term. Sublease income is recognized on a straight-line basis as other income in our consolidated statements of operations. For the year ended December 31, 2021, the Company recognized \$0.2 million of sublease income.

In July 2021, Linda S. Grais, M.D., J.D., a member of the Company's Board of Directors, was appointed as a non-executive member of the Board of Directors of ICON plc ("ICON"), effective upon completion of ICON's acquisition of PRA Health Sciences, Inc. ICON is a clinical research organization and provides services to support the Company's clinical trials. During the year ended December 31, 2021, the Company recorded approximately \$246,000 in clinical trial expenses under its agreements with ICON.

#### 15. Quarterly Selected Financial Data (unaudited)

	Quarter Ended			
	December 31, 2021	September 30, 2021	June 30, 2021	March 31, 2021
<i>(in thousands, except per share amounts)</i>				
Operating expenses	\$ 6,810	\$ 9,047	\$ 11,290	\$ 11,483
Net loss	(9,236)	(10,673)	(11,752)	(11,580)
Net loss per share, basic and diluted	\$ (0.20)	\$ (0.24)	\$ (0.28)	\$ (0.34)

	Quarter Ended			
	December 31, 2020	September 30, 2020	June 30, 2020	March 31, 2020
<i>(in thousands, except per share amounts)</i>				
Operating expenses	\$ 9,879	\$ 9,845	\$ 10,767	\$ 13,269
Net income (loss)	27,347	(9,796)	(10,611)	(12,935)
Net income (loss) per share, basic and diluted	\$ 0.92	\$ (0.33)	\$ (0.36)	\$ (0.44)

#### 16. Subsequent Event

None

#### 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.

The term "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended (the "Exchange Act") refers to controls and procedures 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 SEC'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, or persons performing similar functions, 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. Due to the inherent limitations of control

systems, not all misstatements may be detected. These inherent limitations include the realities that judgments in decision-making can be faulty and that breakdowns can occur because of a simple error or mistake. Our disclosure controls and procedures are designed to provide reasonable assurance of achieving their control objectives.

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer, has evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2021, the end of the period covered by this Annual Report on Form 10-K. Based upon such evaluation, our Chief Executive Officer and Chief Financial Officer have concluded that our disclosure controls and procedures were effective at the reasonable assurance level as of such date.

### **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 15d-15(f) of the Exchange Act). Internal control over financial reporting is a process designed by, or under the supervision of, our Chief Executive Officer and Chief Financial Officer, and effected by our Board of Directors, management and other personnel, 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 and includes those policies and procedures that:

- Pertain to the maintenance of records that accurately and fairly reflect in reasonable detail the transactions and dispositions of the assets of our company;
- 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
- Provide reasonable assurances regarding prevention or timely detection of unauthorized acquisition, use or disposition of our assets that could have a material effect on our financial statements.

Under the supervision and with the participation of our management, including our Chief Executive Officer and Chief Financial Officer, we conducted an evaluation of the effectiveness of our internal control over financial reporting as of December 31, 2021 based on the criteria established in *Internal Control - Integrated Framework* issued by the Committee of Sponsoring Organizations of the Treadway Commission, or COSO 2013. Based on our evaluation under the criteria set forth in *Internal Control - Integrated Framework* issued by the COSO, our management concluded our internal control over financial reporting was effective as of December 31, 2021.

Internal control over financial reporting has inherent limitations. Internal control over financial reporting is a process that involves human diligence and compliance and is subject to lapses in judgment and breakdowns resulting from human failures. Internal control over financial reporting also can be circumvented by collusion or improper management override. Because of such limitations, there is a risk that material misstatements will not be prevented or detected on a timely basis by internal control over financial reporting. However, these inherent limitations are known features of the financial reporting process. Therefore, it is possible to design into the process safeguards to reduce, though not eliminate, this risk.

### **Changes in Internal Control Over Financial Reporting**

There were no changes in our internal control over financial reporting that occurred during the quarter ended December 31, 2021 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

### **Item 9B. Other Information**

Not applicable.

**Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections**

Not applicable.

**PART III**

**Item 10. Directors, Executive Officers and Corporate Governance**

The information required by this Item will be set forth in the Company's proxy statement to be filed with the SEC within 120 days after the Company's fiscal year end and is incorporated herein by reference.

We have adopted a code of business conduct and ethics that applies to all employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions. The code of business conduct and ethics is available on our website at <http://corvuspharma.com>. Amendments to, and waivers from, the code of business conduct and ethics that apply to any director, executive officer or persons performing similar functions will be disclosed at the website address provided above and, to the extent required by applicable regulations, on a Current Report on Form 8-K filed with the SEC.

**Item 11. Executive Compensation**

The information required by this Item will be set forth in the Company's proxy statement to be filed with the SEC within 120 days after the Company's fiscal year end and is incorporated herein by reference.

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

The information required by this Item will be set forth in the Company's proxy statement to be filed with the SEC within 120 days after the Company's fiscal year end and is incorporated herein by reference.

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

The information required by this Item will be set forth in the Company's proxy statement to be filed with the SEC within 120 days after the Company's fiscal year end and is incorporated herein by reference.

**Item 14. Principal Accountant Fees and Services**

The information required by this Item will be set forth in the Company's proxy statement to be filed with the SEC within 120 days after the Company's fiscal year end and is incorporated herein by reference.

**PART IV**

**Item 15. Exhibits and Financial Statement Schedules**

(1) Financial Statements:

The consolidated financial statements required by Item 15(a) are filed as part of this Annual Report on Form 10-K under Item 8 “Consolidated Financial Statements and Supplementary Data.”

(2) Financial Statement Schedules:

All schedules are omitted because they are not applicable or the required information is shown in the consolidated financial statements or notes thereto.

(3) Exhibits.

**EXHIBIT INDEX**

Exhibit Number	Exhibit Description	Incorporated by Reference			Filed Herewith
		Form	Date	Number	
3.1	<a href="#">Amended and Restated Certificate of Incorporation.</a>	8-K	3/29/2016	3.1	
3.2	<a href="#">Amended and Restated Bylaws.</a>	8-K	3/29/2016	3.2	
4.1	Reference is made to Exhibits 3.1 through 3.2.				
4.2	<a href="#">Form of Common Stock Certificate.</a>	S-1	1/4/2016	4.2	
4.3	<a href="#">Amended and Restated Investors' Rights Agreement, dated September 16, 2015, by and among Corvus Pharmaceuticals, Inc. and the investors listed therein.</a>	S-1/A	2/8/2016	4.3	
4.4	<a href="#">Form of Warrant</a>	8-K	11/12/2019	4.1	
4.5	<a href="#">Description of Registrant's Securities Registered Pursuant to Section 12 of the Securities Exchange Act of 1934</a>	10-K	3/25/2021	4.5	
10.1(a)	<a href="#">Office Lease, dated as of January 27, 2015, by and between Corvus Pharmaceuticals, Inc. and ARE-819/863 Mitten Road, LLC.</a>	S-1	1/4/2016	10.2(a)	
10.1(b)	<a href="#">First Amendment to Office Lease, dated as of March 19, 2015, by and between Corvus Pharmaceuticals, Inc. and ARE-819/863 Mitten Road, LLC.</a>	S-1	1/4/2016	10.2(b)	
10.1(c)	<a href="#">Second Amendment to Office Lease, dated as of August 20, 2015, by and between Corvus Pharmaceuticals, Inc. and ARE-819/863 Mitten Road, LLC</a>	S-1	1/4/2016	10.2(c)	
10.1(d)	<a href="#">Third Amendment to Office Lease, dated as of June 27, 2016, by and between Corvus Pharmaceuticals, Inc. and ARE-819/863 Mitten Road, LLC.</a>	10-Q	8/4/2016	10.1(d)	
10.1(e)	<a href="#">Fourth Amendment to Office Lease, dated as of August 15, 2016, by and between Corvus Pharmaceuticals, Inc. and ARE-819/863 Mitten Road, LLC.</a>	10-Q	11/3/2016	10.1(e)	
10.1(f)	<a href="#">Fifth Amendment to Office Lease, dated as of March 2, 2018, by and between Corvus Pharmaceuticals, Inc. and ARE-819/863 Mitten Road, LLC.</a>	10-Q	5/3/2018	10.3	
10.1(g)	<a href="#">Sixth Amendment to Office Lease, dated as of April 5, 2018, by and between Corvus Pharmaceuticals, Inc. and ARE-819/863 Mitten Road, LLC.</a>	10-Q	8/2/2018	10.2	
10.1(h)	<a href="#">Seventh Amendment to Office Lease, dated as of October 11, 2018, by and between Corvus Pharmaceuticals, Inc. and ARE-819/863 Mitten Road, LLC.</a>	10-K	3/7/2019	10.1(h)	
10.1(i)	<a href="#">Eighth Amendment to Office Lease, dated as of September 13, 2021, by and between Corvus Pharmaceuticals, Inc. and ARE 819/863 Mitten Road, LLC.</a>	10-Q	11/1/2021	10.2	
10.2	<a href="#">Sublease agreement, dated August 1, 2021, by and between Corvus Pharmaceuticals, Inc. and Angel Pharmaceuticals US Inc.</a>	10-Q	11/1/2021	10.1	
10.3(a)#	<a href="#">2014 Equity Incentive Plan.</a>	S-1	1/4/2016	10.4(a)	
10.3(b)#	<a href="#">Amendment to the 2014 Equity Incentive Plan, dated November 26, 2014.</a>	S-1	1/4/2016	10.4(b)	
10.3(c)#	<a href="#">Amendment to the 2014 Equity Incentive Plan, dated July 24, 2015.</a>	S-1	1/4/2016	10.4(c)	
10.3(d)#	<a href="#">Amendment to the 2014 Equity Incentive Plan, dated September 14, 2015.</a>	S-1	1/4/2016	10.4(d)	
10.3(e)#	<a href="#">Form of Stock Option Grant Notice and Stock Option Agreement under the 2014 Equity Incentive Award Plan.</a>	S-1	1/4/2016	10.4(e)	

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Exhibit Number	Exhibit Description	Incorporated by Reference			Filed Herewith
		Form	Date	Number	
10.3(f)#	<a href="#">Form of Restricted Stock Purchase Right Grant Notice and Restricted Stock Purchase Agreement under the 2014 Equity Incentive Plan.</a>	S-1	1/4/2016	10.4(f)	
10.4(a)#	<a href="#">2016 Equity Incentive Award Plan.</a>	S-8	3/29/2016	99.2(a)	
10.4(b)#	<a href="#">Form of Stock Option Grant Notice and Stock Option Agreement under the 2016 Equity Incentive Award Plan.</a>	S-1	1/4/2016	10.5(b)	
10.4(c)#	<a href="#">Form of Restricted Stock Award Agreement and Restricted Stock Award Grant Notice under the 2016 Equity Incentive Award Plan.</a>	S-1	1/4/2016	10.5(c)	
10.4(d)#	<a href="#">Form of Restricted Stock Unit Award Agreement and Restricted Stock Unit Award Grant Notice under the 2016 Equity Incentive Award Plan.</a>	S-1	1/4/2016	10.5(d)	
10.5#	<a href="#">Form of Indemnification Agreement for directors and officers.</a>	S-1	1/4/2016	10.6	
10.6#	<a href="#">Amended and Restated Employment Agreement, dated as of December 22, 2015, by and between Corvus Pharmaceuticals, Inc. and Richard A. Miller.</a>	S-1	1/4/2016	10.7	
10.7#	<a href="#">Amended and Restated Employment Agreement, dated as of December 22, 2015, by and between Corvus Pharmaceuticals, Inc. and Leiv Lea.</a>	S-1	1/4/2016	10.8	
10.8(a)#	<a href="#">Offer Letter, dated as of November 27, 2014, by and between Corvus Pharmaceuticals, Inc. and William B. Jones.</a>	S-1	1/4/2016	10.9(a)	
10.8(b)#	<a href="#">Change in Control and Severance Agreement, dated December 23, 2015, by and between Corvus Pharmaceuticals, Inc. and William B. Jones.</a>	S-1	1/4/2016	10.9(b)	
10.9#	<a href="#">Corvus Pharmaceuticals, Inc. 2016 Employee Stock Purchase Plan.</a>	S-8	3/29/2016	99.3	
10.10#	<a href="#">Non-Employee Director Compensation Program.</a>	S-1	1/4/2016	10.12	
10.11(a)†	<a href="#">License Agreement, dated February 25, 2015, by and between Corvus Pharmaceuticals, Inc. and Vernalis (R&amp;D) Limited.</a>	S-1/A	3/10/2016	10.13(a)	
10.11(b)†	<a href="#">Amendment to License Agreement dated November 5, 2015, by and between Corvus Pharmaceuticals, Inc. and Vernalis (R&amp;D) Limited.</a>	S-1	1/4/2016	10.13(b)	
10.12†	<a href="#">License Agreement, dated December 20, 2014, by and between Corvus Pharmaceuticals, Inc. and The Scripps Research Institute</a>	S-1	1/4/2016	10.14	
10.13(a)†	<a href="#">Phase I/IB Combination Study Agreement, dated October 5, 2015, by and between Corvus Pharmaceuticals, Inc. and Genentech, Inc.</a>	S-1/A	2/8/2016	10.15	
10.13(b)	<a href="#">Amendment No. 1 to the Phase I/IB Combination Study Agreement, dated December 20, 2017, by and between Corvus Pharmaceuticals, Inc. and Genentech, Inc.</a>	10-K	3/9/2020	10.16(b)	
10.13(c) ††	<a href="#">Amendment No. 2 to the Phase I/IB Combination Study Agreement, dated August 1, 2019, by and between Corvus Pharmaceuticals, Inc. and Genentech, Inc.</a>	10-K	3/9/2020	10.16(c)	
10.14(a)	<a href="#">Phase 1b/II Combination Study Agreement dated May 1, 2017, by and between Corvus Pharmaceuticals, Inc. and Genentech, Inc.</a>	10-Q	8/3/2017	10.1	
10.14(b)	<a href="#">Amendment No. 1 to the Phase 1b/II Combination Study Agreement dated December 20, 2017, by and between Corvus Pharmaceuticals, Inc. and Genentech, Inc.</a>	10-K	3/9/2020	10.17(b)	
10.15††	<a href="#">Exclusive License Agreement dated April 21, 2017, by and between Corvus Pharmaceuticals, Inc. and Monash University.</a>	10-K	3/9/2020	10.18	

Exhibit Number	Exhibit Description	Incorporated by Reference			Filed Herewith
		Form	Date	Number	
10.16	<a href="#">Framework Agreement, dated as of October 5, 2020, by and between Corvus Hong Kong Limited, Jiaxing Puissance Angel Equity Investment Partnership (Limited Partnership) and AP BIOTECH DEVELOPMENT CORP.</a>	8-K	10/5/2020	2.1	
10.17	<a href="#">Open Market Sale Agreement, dated March 9, 2020, by and between Corvus Pharmaceuticals, Inc. and Jefferies LLC.</a>	S-3	3/9/2020	1.2	
10.18	<a href="#">Open Market Sale Agreement, dated November 1, 2021, by and between Corvus Pharmaceuticals, Inc. and Jefferies LLC.</a>				X
21.1	<a href="#">List of subsidiaries</a>				X
23.1	<a href="#">Consent of Independent Registered Public Accounting Firm.</a>				X
24.1	<a href="#">Power of Attorney (included on signature page)</a>				X
31.1	<a href="#">Certification by Chief Executive Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.</a>				X
31.2	<a href="#">Certification by Chief Financial Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.</a>				X
32.1**	<a href="#">Certification of Chief Executive Officer and Chief Financial Officer pursuant to 18 USC Section 1350 as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.</a>				X
101.INS	Inline XBRL Instance Document.				X
101.SCH	Inline XBRL Taxonomy Extension Schema Document.				X
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document.				X
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document.				X
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document.				X
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document.				X
104	The cover page of Corvus Pharmaceuticals, Inc.'s Annual Report on Form 10-K for the year ended December 31, 2020, formatted in Inline XBRL (contained in Exhibit 101)				X

† Confidential treatment has been granted for a portion of this exhibit.

†† Portions of this exhibit have been omitted in accordance with Item 601(b)(10) of Regulation S-K.

# Indicates management contract or compensatory plan.

\*\* The certification attached as Exhibit 32.1 that accompanies this Annual Report on Form 10-K is not deemed filed with the Securities and Exchange Commission and is not to be incorporated by reference into any filing of Corvus Pharmaceuticals, Inc. under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, whether made before or after the date of this Annual Report on Form 10-K, irrespective of any general incorporation language contained in such filing.

#### Item 16. Form 10-K Summary

Registrants may voluntarily include a summary of information required by Form 10-K under this Item 16. We have elected not to include such summary.



**OPEN MARKET SALE AGREEMENT**<sup>SM</sup>

November 1, 2021

JEFFERIES LLC  
520 Madison Avenue  
New York, New York 10022

Ladies and Gentlemen:

Corvus Pharmaceuticals, Inc., a Delaware corporation (the “**Company**”), proposes, subject to the terms and conditions stated herein, to issue and sell from time to time through Jefferies LLC, as sales agent and/or principal (the “**Agent**”), shares of the Company’s common stock, par value \$0.0001 per share (the “**Common Shares**”), having an aggregate offering price of up to \$40,000,000 on the terms set forth in this agreement (this “**Agreement**”).

**Section 1. DEFINITIONS**

(a) Certain Definitions. For purposes of this Agreement, capitalized terms used herein and not otherwise defined shall have the following respective meanings:

“**Affiliate**” of a Person means another Person that directly or indirectly, through one or more intermediaries, controls, is controlled by, or is under common control with, such first- mentioned Person. The term “control” (including the terms “controlling,” “controlled by” and “under common control with”) means the possession, direct or indirect, of the power to direct or cause the direction of the management and policies of a Person, whether through the ownership of voting securities, by contract or otherwise.

“**Agency Period**” means the period commencing on the date of this Agreement and expiring on the earliest to occur of (x) the date on which the Agent shall have placed the Maximum Program Amount pursuant to this Agreement and (y) the date this Agreement is terminated pursuant to Section 7.

“**Commission**” means the U.S. Securities and Exchange Commission.

“**Exchange Act**” means the Securities Exchange Act of 1934, as amended, and the rules and regulations of the Commission thereunder.

“**Floor Price**” means the minimum price set by the Company in the Issuance Notice below which the Agent shall not sell Shares during the applicable period set forth in the Issuance Notice, which may be adjusted by the Company at any time during the period set forth in the Issuance Notice by delivering written notice of such change to the Agent and which in no event shall be less than \$1.00 without the prior written consent of the Agent, which may be withheld in the Agent’s sole discretion.

“**Issuance Amount**” means the aggregate Sales Price of the Shares to be sold by the Agent pursuant to any Issuance Notice.

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<sup>SM</sup> “Open Market Sale Agreement” is a service mark of Jefferies LLC

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“**Issuance Notice**” means a written notice delivered to the Agent by the Company in accordance with this Agreement in the form attached hereto as Exhibit A that is executed by its Chief Executive Officer, President or Chief Financial Officer.

“**Issuance Notice Date**” means any Trading Day during the Agency Period that an Issuance Notice is delivered pursuant to Section 3(b)(i).

“**Issuance Price**” means the Sales Price less the Selling Commission.

“**Maximum Program Amount**” means Common Shares with an aggregate Sales Price of the lesser of (a) the number or dollar amount of Common Shares registered under the effective Registration Statement (defined below) pursuant to which the offering is being made, (b) the number of authorized but unissued Common Shares (less Common Shares issuable upon exercise, conversion or exchange of any outstanding securities of the Company or otherwise reserved from the Company’s authorized capital stock), (c) the number or dollar amount of Common Shares permitted to be sold under Form S-3 (including General Instruction I.B.6 thereof, if applicable), or (d) \$40,000,000.

“**Person**” means an individual or a corporation, partnership, limited liability company, trust, incorporated or unincorporated association, joint venture, joint stock company, governmental authority or other entity of any kind.

“**Principal Market**” means the Nasdaq Global Market or such other national securities exchange on which the Common Shares, including any Shares, are then listed.

“**Sales Price**” means the actual sale execution price of each Share placed by the Agent pursuant to this Agreement.

“**Securities Act**” means the Securities Act of 1933, as amended, and the rules and regulations of the Commission thereunder.

“**Securities Laws**” means, collectively, the Sarbanes Oxley Act of 2002 (“Sarbanes-Oxley”), the Securities Act, the Exchange Act, the rules and regulations of the Commission, the auditing principles, rules, standards and practices applicable to the auditors of “issuers” (as defined in Sarbanes-Oxley) promulgated or approved by the Public Company Accounting Oversight Board and the rules of the Nasdaq Stock Market LLC (“Exchange Rules”).

“**Selling Commission**” means three percent (3%) of the gross proceeds of Shares sold pursuant to this Agreement, or as otherwise agreed between the Company and the Agent with respect to any Shares sold pursuant to this Agreement.

“**Settlement Date**” means the second business day following each Trading Day during the period set forth in the Issuance Notice on which Shares are sold pursuant to this Agreement, when the Company shall deliver to the Agent the amount of Shares sold on such Trading Day and the Agent shall deliver to the Company the Issuance Price received on such sales.

“**Shares**” shall mean the Company’s Common Shares issued or issuable pursuant to this Agreement.

“**Trading Day**” means any day on which the Principal Market is open for trading.

## Section 2. REPRESENTATIONS AND WARRANTIES OF THE COMPANY

The Company represents and warrants to, and agrees with, the Agent that as of (1) the date of this Agreement, (2) each Issuance Notice Date, (3) each Settlement Date, (4) each Triggering Event Date with respect to which the Company is obligated to deliver a certificate pursuant to Section 4(o) and (5) as of each Time of Sale (each of the times referenced above is referred to herein as a “**Representation Date**”), except as may be disclosed in the Prospectus (including any documents incorporated by reference therein and any supplements thereto) on or before a Representation Date:

(a) Registration Statement. The Company has prepared and filed with the Commission a shelf registration statement on Form S-3 (File No. 333-237040) that contains a base prospectus (the “**Base Prospectus**”). Such registration statement registers the issuance and sale by the Company of the Shares under the Securities Act. Except where the context otherwise requires, such registration statement(s), including any information deemed to be a part thereof pursuant to Rule 430B under the Securities Act, including all financial statements, exhibits and schedules thereto and all documents incorporated or deemed to be incorporated therein by reference pursuant to Item 12 of Form S-3 under the Securities Act as from time to time amended or supplemented, is herein referred to as the “**Registration Statement**,” and the Base Prospectus constituting a part of such registration statement(s), together with any prospectus supplement filed with the Commission pursuant to Rule 424(b) under the Securities Act relating to a particular issuance of the Shares, including all documents incorporated or deemed to be incorporated therein by reference pursuant to Item 12 of Form S-3 under the Securities Act, in each case, as from time to time amended or supplemented, is referred to herein as the “**Prospectus**,” except that if any revised prospectus is provided to the Agent by the Company for use in connection with the offering of the Shares that is not required to be filed by the Company pursuant to Rule 424(b) under the Securities Act, the term “**Prospectus**” shall refer to such revised prospectus from and after the time it is first provided to the Agent for such use. The Registration Statement at the time it originally became effective is herein called the “**Original Registration Statement**.” As used in this Agreement, the terms “amendment” or “supplement” when applied to the Registration Statement or the Prospectus shall be deemed to include the filing by the Company with the Commission of any document under the Exchange Act after the date hereof that is or is deemed to be incorporated therein by reference.

All references in this Agreement to financial statements and schedules and other information which is “contained,” “included” or “stated” in the Registration Statement or the Prospectus (and all other references of like import) shall be deemed to mean and include all such financial statements and schedules and other information which is or is deemed to be incorporated by reference in or otherwise deemed under the Securities Act to be a part of or included in the Registration Statement or the Prospectus, as the case may be, as of any specified date; and all references in this Agreement to amendments or supplements to the Registration Statement or the Prospectus shall be deemed to mean and include, without limitation, the filing of any document under the Exchange Act which is or is deemed to be incorporated by reference in or otherwise deemed under the Securities Act to be a part of or included in the Registration Statement or the Prospectus, as the case may be, as of any specified date.

At the time the Registration Statement was or will be originally declared effective and at the time the Company’s most recent annual report on Form 10-K was filed with the Commission, if later, the Company met the then-applicable requirements for use of Form S-3 under the Securities Act. During the Agency Period, each time the Company files an annual report on Form 10-K the Company will meet the then-applicable requirements for use of Form S-3 under the Securities Act.

(b) Compliance with Registration Requirements. The Original Registration Statement and any Rule 462(b) Registration Statement have been declared effective by the Commission under the Securities Act. The Company has complied to the Commission’s satisfaction with all requests of the Commission for

additional or supplemental information. No stop order suspending the effectiveness of the Registration Statement or any Rule 462(b) Registration Statement is in effect and no proceedings for such purpose have been instituted or are pending or, to the knowledge of the Company, are contemplated or threatened by the Commission.

The Prospectus when filed complied in all material respects with the Securities Act and, if filed with the Commission through its Electronic Data Gathering, Analysis and Retrieval system (“**EDGAR**”) (except as may be permitted by Regulation S-T under the Securities Act), was identical to the copy thereof delivered to the Agent for use in connection with the issuance and sale of the Shares. Each of the Registration Statement, any Rule 462(b) Registration Statement and any post-effective amendment thereto, at the time it became effective and at all subsequent times, complied and will comply in all material respects with the Securities Act and did not and will not contain any untrue statement of a material fact or omit to state a material fact required to be stated therein or necessary to make the statements therein not misleading. As of the date of this Agreement, the Prospectus and any Free Writing Prospectus (as defined below) considered together (collectively, the “**Time of Sale Information**”) did not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements therein, in the light of the circumstances under which they were made, not misleading. The Prospectus, as amended or supplemented, as of its date, did not, and, at each Settlement Date, will not contain any untrue statement of a material fact or omit to state a material fact necessary in order to make the statements therein, in the light of the circumstances under which they were made, not misleading. The representations and warranties set forth in the three immediately preceding sentences do not apply to statements in or omissions from the Registration Statement, any Rule 462(b) Registration Statement, or any post-effective amendment thereto, or the Prospectus, or any amendments or supplements thereto, made in reliance upon and in conformity with information relating to the Agent furnished to the Company in writing by the Agent expressly for use therein, it being understood and agreed that the only such information furnished by the Agent to the Company consists of the information described in Section 6 below. There are no contracts or other documents required to be described in the Prospectus or to be filed as exhibits to the Registration Statement which have not been described or filed as required. The Registration Statement and the offer and sale of the Shares as contemplated hereby meet the requirements of Rule 415 under the Securities Act and comply in all material respects with said rule.

(c) Ineligible Issuer Status. The Company is not an “ineligible issuer” in connection with the offering of the Shares pursuant to Rules 164, 405 and 433 under the Securities Act. Any Free Writing Prospectus that the Company is required to file pursuant to Rule 433(d) under the Securities Act has been, or will be, filed with the Commission in accordance with the requirements of the Securities Act. Each Free Writing Prospectus that the Company has filed, or is required to file, pursuant to Rule 433(d) under the Securities Act or that was prepared by or on behalf of or used or referred to by the Company complies or will comply in all material respects with the requirements of Rule 433 under the Securities Act including timely filing with the Commission or retention where required and legending, and each such Free Writing Prospectus, as of its issue date and at each Settlement Date does not and will not include any information that conflicted, conflicts with or will conflict with the information contained in the Registration Statement or the Prospectus, including any document incorporated by reference therein. Except for the Free Writing Prospectuses, if any, and electronic road shows, if any, furnished to you before first use, the Company has not prepared, used or referred to, and will not, without your prior consent, prepare, use or refer to, any Free Writing Prospectus.

(d) Incorporated Documents. The documents incorporated or deemed to be incorporated by reference in the Registration Statement and the Prospectus, at the time they were filed with the Commission, complied in all material respects with the requirements of the Exchange Act, as applicable, and, when read together with the other information in the Prospectus, do not contain an untrue statement of a material fact or omit to state a material fact required to be stated therein or necessary to make the statements therein, in

light of the circumstances under which they were made, not misleading. The representation and warranty set forth in the immediately preceding sentence does not apply to statements in or omissions from the Registration Statement, any Rule 462(b) Registration Statement, or any post-effective amendment thereto, or the Prospectus, or any amendments or supplements thereto, made in reliance upon and in conformity with the Agent Information (as defined below) furnished to the Company in writing by the Agent expressly for use therein.

(e) Exchange Act Compliance. The documents incorporated or deemed to be incorporated by reference in the Prospectus, at the time they were or hereafter are filed with the Commission and any Free Writing Prospectus or amendment or supplement thereto complied and will comply in all material respects with the requirements of the Exchange Act.

(f) Good Standing of the Company. The Company has been duly incorporated and is existing and in good standing under the laws of the State of Delaware, with power and authority (corporate and other) to own its properties and conduct its business as described in the Registration Statement and the Prospectus; and the Company is duly qualified to do business as a foreign corporation in good standing in all other jurisdictions in which its ownership or lease of property or the conduct of its business requires such qualification, except where the failure to be so qualified or in good standing in such other jurisdictions would not, individually or in the aggregate, reasonably be expected to result in a material adverse effect on the condition (financial or otherwise), results of operations, business, properties or prospects of the Company and its subsidiaries, taken as a whole (“**Material Adverse Effect**”).

(g) Subsidiaries. Each subsidiary of the Company has been duly incorporated and is existing and in good standing under the laws of the jurisdictions of its incorporation, with power and authority (corporate and other) to own its properties and conduct its business as described in the Registration Statement and the Prospectus; and each subsidiary of the Company is duly qualified to do business as a foreign corporation in good standing in all other jurisdictions in which its ownership or lease of property or the conduct of its business requires such qualification, except where the failure to be so qualified or in good standing in such other jurisdictions would not, individually or in the aggregate, reasonably be expected to result in a Material Adverse Effect; all of the issued and outstanding capital stock of each subsidiary of the Company has been duly authorized and validly issued and is fully paid and nonassessable; and the capital stock of each subsidiary owned by the Company, directly or through subsidiaries, is owned free from liens, encumbrances and defects.

(h) Common Shares. The Common Shares and all other outstanding shares of capital stock of the Company have been duly authorized; the authorized equity capitalization of the Company is as set forth in the Prospectus; all outstanding shares of capital stock of the Company are, and, when the Common Shares have been delivered and paid for in accordance with this Agreement, such Common Shares will have been, validly issued, fully paid and nonassessable, will conform in all material respects to the information in the Prospectus and to the description of such Common Shares contained in the Prospectus; the stockholders of the Company have no preemptive rights with respect to the Common Shares that have not been duly waived or satisfied; and none of the outstanding shares of capital stock of the Company have been issued in violation of any preemptive or similar rights of any security holder.

(i) No Finder’s Fee. Except as disclosed in the Prospectus, there are no contracts, agreements or understandings between the Company and any person that would give rise to a valid claim against the Company or the Agent for a brokerage commission, finder’s fee or other like payment in connection with this offering.

(j) Registration Rights. Except as disclosed in the Registration Statement and the Prospectus, there are no contracts, agreements or understandings between the Company and any person granting such

person the right to require the Company to file a registration statement under the Securities Act with respect to any securities of the Company owned or to be owned by such person or to require the Company to include such securities in the securities registered pursuant to the Registration Statement or in any securities being registered pursuant to any other registration statement filed by the Company under the Securities Act.

(k) Listing. The Shares have been approved for listing on the Nasdaq Global Market, subject to notice of issuance.

(l) Absence of Further Requirements. No consent, approval, authorization, or order of, or filing or registration with, any person (including any governmental agency or body or any court) is required for the consummation of the transactions contemplated by this Agreement in connection with the offering, issuance and sale of the Shares by the Company, except such as have been obtained, or made and such as may be required under state securities laws or the Financial Industry Regulatory Authority (“FINRA”).

(m) Title to Property. Except as disclosed in the Registration Statement and the Prospectus or as would not reasonably be expected to result in a Material Adverse Effect, the Company and its subsidiaries have good and marketable title to all personal property and assets owned by them, in each case free from liens, charges, encumbrances and defects, and the Company and its subsidiaries hold any leased real or personal property under valid and enforceable leases with no terms or provisions that would materially interfere with the use made or to be made thereof by them. Neither the Company nor any of its subsidiaries own any real property.

(n) Absence of Defaults and Conflicts Resulting from Transaction. The execution, delivery and performance of this Agreement, and the issuance and sale of the Shares will not result in a breach or violation of any of the terms and provisions of, or constitute a default or a Debt Repayment Triggering Event (as defined below) under, or result in the imposition of any lien, charge or encumbrance upon any property or assets of the Company or any of its subsidiaries pursuant to, (i) the charter or bylaws of the Company or any of its subsidiaries, (ii) any statute, rule, regulation or order of any governmental agency or body or any court, domestic or foreign, having jurisdiction over the Company, any of its subsidiaries or any of their properties, or (iii) any agreement or instrument to which the Company or any of its subsidiaries is a party or by which the Company or any of its subsidiaries is bound or to which any of the properties of the Company or any of its subsidiaries is subject, except in the case of each of clauses (ii) and (iii), where such breaches, violations, defaults, liens, charges or encumbrances would not, individually or in the aggregate, reasonably be expected to result in a Material Adverse Effect; a “Debt Repayment Triggering Event” means any event or condition that gives, or with the giving of notice or lapse of time would give, the holder of any note, debenture, or other evidence of indebtedness (or any person acting on such holder’s behalf) the right to require the repurchase, redemption or repayment of all or a portion of such indebtedness by the Company or any of its subsidiaries.

(o) Absence of Existing Defaults and Conflicts. Neither the Company nor any of its subsidiaries is in violation of its respective charter or bylaws or in default (or with the giving of notice or lapse of time would be in default) under any existing obligation, agreement, covenant or condition contained in any indenture, loan agreement, mortgage, lease or other agreement or instrument to which any of them is a party or by which any of them is bound or to which any of the properties of any of them is subject, except such defaults that would not, individually or in the aggregate, reasonably be expected to result in a Material Adverse Effect.

(p) Authorization of Agreement. This Agreement has been duly authorized, executed and delivered by the Company.

(q) Possession of Licenses and Permits. Except in such cases that would not reasonably be expected to result in a Material Adverse Effect, the Company and its subsidiaries possess, and are in compliance with the terms of, all adequate certificates, authorizations, franchises, licenses and permits (“**Licenses**”) necessary or material to the conduct of the business now conducted or proposed in the Registration Statement and the Prospectus to be conducted by them, including, without limitation, from the U.S. Food and Drug Administration (“**FDA**”) and neither the Company nor any of its subsidiaries has received any notice of proceedings relating to the revocation or modification of any Licenses that, if determined adversely to the Company and or any of its subsidiaries, would, individually or in the aggregate, reasonably be expected to have a Material Adverse Effect.

(r) Absence of Labor Dispute. No labor dispute with the employees of the Company or any of its subsidiaries exists or, to the knowledge of the Company, is imminent that would reasonably be expected to have a Material Adverse Effect.

(s) Intellectual Property. Except as would not reasonably be expected to have a Material Adverse Effect or as otherwise expressly disclosed in the Registration Statement and the Prospectus, the Company and its subsidiaries own or have obtained valid and enforceable licenses for, or otherwise have the right to use, all patents, patent applications, inventions, copyrights, know how (including trade secrets and other unpatented and/or unpatentable proprietary or confidential information, systems or procedures), trademark registrations and applications for registration, service marks, trade names, domain names, and other similar intellectual property or proprietary rights, whether or not registered (including all goodwill associated with the foregoing, as applicable) (collectively, “**Intellectual Property Rights**”) necessary and material to the conduct of the business now conducted by them. To the Company’s knowledge the conduct of the business of the Company and its subsidiaries has not conflicted with, infringed, misappropriated or otherwise violated any Intellectual Property Rights of any third party. Except as expressly disclosed in the Registration Statement and in the Prospectus and except as would not, if determined adversely to the Company and its subsidiaries, individually or in the aggregate, reasonably be expected to have a Material Adverse Effect, (i) there are no claims asserted in writing by third parties to ownership of any of the Intellectual Property Rights owned by the Company or any of its subsidiaries; (ii) to the Company’s knowledge, all issued patents contained within the Intellectual Property Rights owned or licensed by the Company or any of its subsidiaries are valid and enforceable, solely owned or licensed by the Company or its subsidiaries and, to the extent owned, are owned free and clear of all liens and encumbrances; (iii) to the Company’s knowledge, without any duty to conduct a special search, there is no material infringement, misappropriation, breach, default or other violation by any third party of any of the Intellectual Property Rights owned by or licensed to the Company or any of its subsidiaries; (iv) there is no pending or, to the Company’s knowledge, without any duty to conduct a special search, threatened action, suit, proceeding or claim by others challenging the rights of the Company or any of its subsidiaries in or to the Intellectual Property Rights owned by or licensed to the Company or any of its subsidiaries; (v) there is no pending or, to the Company’s knowledge, without any duty to conduct a special search, threatened action, suit, proceeding or claim by others challenging the validity, enforceability or scope of any such Intellectual Property Rights; (vi) there is no pending or, to the Company’s knowledge, without any duty to conduct a special search, threatened action, suit, proceeding or claim by others that the Company or any of its subsidiaries infringes, misappropriates or otherwise violates any Intellectual Property Rights or other proprietary rights of others and the Company is unaware of any other fact which would form a reasonable basis for any such claim; and (vii) none of the Intellectual Property Rights used by the Company or any of its subsidiaries in their respective businesses has been obtained or is being used by the Company or any of its subsidiaries in violation of any contractual obligation binding on the Company or any of its subsidiaries.

(t) Environmental Laws. Except as disclosed in the Registration Statement and the Prospectus, neither the Company nor any of its subsidiaries is in violation of any statute, any rule, regulation, decision or order of any governmental agency or body or any court, domestic or foreign, relating

to the use, disposal or release of hazardous or toxic substances or relating to the protection or restoration of the environment or human exposure to hazardous or toxic substances (collectively, “**environmental laws**”), the Company and its subsidiaries do not own or operate any real property contaminated with any substance that is subject to any environmental laws, are not liable for any off-site disposal or contamination pursuant to any environmental laws, and are not subject to any claim relating to any environmental laws, which violation, contamination, liability or claim would, individually or in the aggregate, reasonably be expected to have a Material Adverse Effect; and the Company is not aware of any pending investigation which might lead to such a claim.

(u) Absence of Manipulation. The Company has not taken, directly or indirectly, any action that is designed to or that has constituted or that would reasonably be expected to cause or result in the stabilization or manipulation of the price of any security of the Company to facilitate the sale or resale of the Shares; provided, that no representation is made in this subsection with respect to the actions of the Agent.

(v) Statistical and Market-Related Data. Any third-party statistical and market-related data included in the Prospectus or in any oral or written communication with potential investors is based on or derived from sources that the Company believes to be reliable and accurate.

(w) Internal Controls and Compliance with the Sarbanes-Oxley Act. Except as disclosed in the Registration Statement and the Prospectus, the Company, its subsidiaries and the Company’s Board of Directors (the “**Board**”) are in compliance with the applicable provisions of Sarbanes-Oxley and all applicable Exchange Rules. The Company maintains a system of “internal controls over financial reporting” (as defined in Rule 13a-15(f) of the Exchange Act), including, but not limited to, disclosure controls and procedures and internal controls over accounting matters and financial reporting and legal and regulatory compliance controls (collectively, “**Internal Controls**”) comply with the Securities Laws (to the extent applicable) and are sufficient to provide reasonable assurances that (i) transactions are executed in accordance with management’s general or specific authorizations, (ii) transactions are recorded as necessary to permit preparation of financial statements in conformity with U.S. Generally Accepted Accounting Principles (“**GAAP**”) and to maintain accountability for assets, (iii) access to assets is permitted only in accordance with management’s general or specific authorization and (iv) the recorded accountability for assets is compared with the existing assets at reasonable intervals and appropriate action is taken with respect to any differences. The Internal Controls are, or upon consummation of the offering of the Shares will be, overseen by the Audit Committee (the “**Audit Committee**”) of the Board in accordance with Exchange Rules. Except as disclosed to the Agent, the Company has not publicly disclosed or reported to the Audit Committee or the Board, and within the next 135 days the Company does not reasonably expect to publicly disclose or report to the Audit Committee or the Board, a “significant deficiency”, “material weakness” (each as defined in Rule 12b-2 of the Exchange Act), adverse change in Internal Controls or fraud involving management or other employees who have a significant role in Internal Controls, or any violation of, or failure to comply with, the Securities Laws, which, if determined adversely, would have a Material Adverse Effect.

(x) Litigation. Except as disclosed in the Registration Statement and the Prospectus, there are no pending actions, suits or proceedings (including, to the Company’s knowledge, any inquiries or investigations by any court or governmental agency or body, domestic or foreign) against or affecting the Company, any of its subsidiaries or any of their respective properties that, if determined adversely to the Company or any of its subsidiaries, would, individually or in the aggregate, reasonably be expected to have a Material Adverse Effect, or would materially and adversely affect the ability of the Company to perform its obligations under this Agreement, or which are otherwise material in the context of the sale of the Common Shares; and no such actions, suits or proceedings (including, to the Company’s knowledge, any

inquiries or investigations by any court or governmental agency or body, domestic or foreign) are threatened or, to the Company's knowledge, contemplated.

(y) Financial Statements. The financial statements filed with the Commission as part of the Registration Statement and the Prospectus present fairly in all material respects the financial position of the Company and its consolidated subsidiaries as of the dates shown and their results of operations and cash flows for the periods shown, and such financial statements have been prepared in conformity with GAAP, applied on a consistent basis.

(z) Auditor Independence. PricewaterhouseCoopers LLP, who has certified certain financial statements of the Company, is an independent registered public accounting firm with respect to the Company within the applicable rules and regulations adopted by the Commission and the Public Company Accounting Oversight Board (United States) and as required by the Securities Act.

(aa) No Material Adverse Change. Except as disclosed in the Registration Statement and the Prospectus, since the end of the period covered by the latest audited financial statements incorporated by reference in the Registration Statement and the Prospectus, (i) there has been no change, nor any development or event involving a prospective change, that would reasonably be expected to result in a Material Adverse Effect, (ii) there has been no dividend or distribution of any kind declared, paid or made by the Company on any class of its capital stock and (iii) there has been no material adverse change in the capital stock, short-term indebtedness, long-term indebtedness, net current assets or net assets of the Company and its subsidiaries.

(bb) Investment Company Act. The Company is not and, after giving effect to the offering and sale of the Shares and the application of the proceeds thereof as described in the Prospectus, will not be an "investment company" as defined in the Investment Company Act of 1940, as amended (the "**Investment Company Act**").

(cc) Ratings. The Company does not have any debt securities or preferred stock that are rated by any "nationally recognized statistical rating agency" (as defined in Section 3(a)(62) of the Exchange Act).

(dd) Sanctions. Neither the Company nor any of its subsidiaries nor, to the knowledge of the Company, any of its directors, officers, employees, nor, to the knowledge of the Company, any agents or affiliates is currently the subject or the target of any U.S. sanctions administered by the Office of Foreign Assets Control of the U.S. Department of the Treasury ("**OFAC**") or the U.S. Department of State, the United Nations Security Council, the European Union, Her Majesty's Treasury of the United Kingdom, or other relevant sanctions authority (collectively, "**Sanctions**"); nor is the Company or any of its subsidiaries located, organized or resident in a country or territory that is the subject or the target of Sanctions, including, without limitation, Crimea, Cuba, Iran, North Korea, and Syria; and the Company will not directly or indirectly use the proceeds of this offering, or lend, contribute or otherwise make available such proceeds to any subsidiary, or any joint venture partner or other person or entity, for the purpose of financing the activities of or business with any person, or in any country or territory, that at the time of such financing, is the subject or the target of Sanctions or in any other manner that will result in a violation by any person (including any person participating in the transaction whether as underwriter, advisor, investor or otherwise) of applicable Sanctions. For the past five years, the Company and its subsidiaries have not knowingly engaged in and are not now knowingly engaged in any dealings or transactions with any person that at the time of the dealing or transaction is or was the subject or the target of Sanctions or with any Sanctioned Country.

(ee) Anti-Corruption and Anti-Bribery Laws. Neither the Company nor any of its subsidiaries nor any director or officer, nor to the knowledge of the Company, any employee of the Company or any of its subsidiaries any agent, affiliate or other person acting on behalf of the Company or any of its subsidiaries has, in the course of its actions for, or on behalf of, the Company or any of its subsidiaries (i) used any corporate funds for any unlawful contribution, gift, entertainment or other unlawful expenses relating to political activity; (ii) made or taken any act in furtherance of an offer, promise, or authorization of any direct or indirect unlawful payment or benefit to any foreign or domestic government official or employee, including of any government-owned or controlled entity or public international organization, or any political party, party official, or candidate for political office; (iii) violated or is in violation of any provision of the U.S. Foreign Corrupt Practices Act of 1977, as amended (the “**FCPA**”), the UK Bribery Act 2010, or any other applicable anti-bribery or anti-corruption law; or (iv) made, offered, authorized, requested, or taken an act in furtherance of any unlawful bribe, rebate, payoff, influence payment, kickback or other unlawful payment or benefit. The Company and its subsidiaries have instituted and maintain policies and procedures reasonably designed to ensure continued compliance therewith.

(ff) Money Laundering Laws. The operations of the Company and its subsidiaries are, and have been conducted at all times, in compliance with applicable financial recordkeeping and reporting requirements of the Currency and Foreign Transactions Reporting Act of 1970, as amended, the money laundering statutes of all applicable jurisdictions, the rules and regulations thereunder and any related or similar applicable rules, regulations or guidelines, issued, administered or enforced by any applicable governmental agency (collectively, the “**Money Laundering Laws**”) and no action, suit or proceeding by or before any court or governmental agency, authority or body or any arbitrator involving the Company or any of its subsidiaries with respect to the Money Laundering Laws is pending or, to the knowledge of the Company, threatened.

(gg) FDA. The Company has operated and currently is in compliance with all applicable rules, regulations and policies of the FDA, except where the failure to so operate or be in compliance would not reasonably be expected to have a Material Adverse Effect.

(hh) Clinical Trials. Any clinical trials and human studies conducted by the Company and, to the knowledge of the Company, any clinical trials and human studies conducted on behalf of the Company or in which the Company has participated, with respect to the Company’s product candidates, were, and if still pending are, being conducted in accordance with all applicable rules, regulations and policies of the FDA and comparable regulatory agencies outside of the United States to which the Company is subject and current Good Clinical Practices and Good Laboratory Practices, except where the failure to be so conducted would not reasonably be expected to have a Material Adverse Effect.

(ii) Taxes. The Company has filed all federal, state, local and non-U.S. tax returns that are required to be filed through the date of this Agreement or have obtained extensions thereof (except in any case in which the failure to file would not, individually or in the aggregate, reasonably be expected to have a Material Adverse Effect) and have paid all taxes required to be paid thereon, including any assessments, fines or penalties related thereto (except for any such taxes, assessments, fines or penalties being contested in good faith for which reserves required by GAAP have been created in the financial statements of the Company, or, except in any case in which the failure to file or pay would not, individually or in the aggregate, reasonably be expected to have a Material Adverse Effect); and no tax deficiency has been determined adversely to the Company which has had (nor does the Company have any notice or knowledge of any tax deficiency which could reasonably be expected to be determined adversely to the Company and which would reasonably be expected to have) a Material Adverse Effect.

(jj) Insurance. The Company is insured by insurers with appropriately rated claims paying abilities against such losses and risks and in such amounts as are prudent and customary for similarly sized

companies in the businesses in which it is engaged; all policies of insurance and fidelity or surety bonds insuring the Company or its business, assets, employees, officers and directors are in full force and effect, except as would not, individually or in the aggregate, reasonably be expected to result in a Material Adverse Effect; the Company is in compliance with the terms of such policies and instruments in all material respects; and there are no claims by the Company under any such policy or instrument as to which any insurance company is denying liability or defending under a reservation of rights clause; the Company has not been refused any insurance coverage sought or applied for; the Company does not have any reason to believe that it will not be able to renew its existing insurance coverage as and when such coverage expires or to obtain similar coverage from similar insurers as may be necessary to continue its business at a cost that would not reasonably be expected to have a Material Adverse Effect, except as disclosed in the Registration Statement and the Prospectus; and the Company has obtained directors' and officers' insurance in such amounts as is customary for similarly sized companies in the businesses in which it is engaged.

(kk) Cybersecurity; Data Privacy. (i) Except as disclosed in the Registration Statement and the Prospectus, to the Company's knowledge, there has been no security breach, attack or other compromise of or relating to any of the Company's information technology and computer systems, networks, hardware, software or data maintained by or on behalf of the Company (including the data of its customers, employees, suppliers, vendors and any other third party data maintained by or on behalf of the Company) (collectively, the "**IT Systems and Data**") that would not, individually or in the aggregate, reasonably be expected to result in a Material Adverse Effect; (ii) the Company has been in compliance with all applicable laws or statutes and all applicable judgments, orders, rules and regulations of any court or arbitrator or governmental or regulatory authority, internal policies and contractual obligations relating to (x) the privacy and security of the IT Systems and Data, (y) the protection of the IT Systems and Data from unauthorized use, access, misappropriation or modification and (z) the collection, use, transfer, processing, storage, disposal and disclosure by the Company of personally identifiable information and/or any other information collected from or provided by third parties, except as would not, in the case of this clause (ii), individually or in the aggregate, have a Material Adverse Effect; (iii) the Company has implemented commercially reasonable backup and disaster recovery and security plans, procedures and facilities for its business consistent with industry standards and practices; and (iv) the Company has taken commercially reasonable steps for its business consistent with industry standards and practices to protect the IT Systems and Data.

(ll) Other Underwriting Agreements. Other than that certain sales agreement between the Company and the Agent dated March 9, 2020, the Company is not a party to any agreement with an agent or underwriter for any other "at the market" or continuous equity transaction.

Any certificate signed by any officer or representative of the Company or any of its subsidiaries and delivered to the Agent or counsel for the Agent in connection with an issuance of Shares shall be deemed a representation and warranty by the Company to the Agent as to the matters covered thereby on the date of such certificate.

The Company acknowledges that the Agent and, for purposes of the opinions to be delivered pursuant to Section 4(q) and 5(a)(v) hereof, counsel to the Company and counsel to the Agent, will rely upon the accuracy and truthfulness of the foregoing representations and hereby consents to such reliance.

### **Section 3. ISSUANCE AND SALE OF COMMON SHARES**

(a) Sale of Securities. On the basis of the representations, warranties and agreements herein contained, but subject to the terms and conditions herein set forth, the Company and the Agent agree that the Company may from time to time seek to sell Shares through the Agent, acting as sales agent, or directly to the Agent, acting as principal, as follows, with an aggregate Sales Price of up to the Maximum Program

Amount, based on and in accordance with Issuance Notices as the Company may deliver, during the Agency Period.

(b) Mechanics of Issuances.

(i) Issuance Notice. Upon the terms and subject to the conditions set forth herein, on any Trading Day during the Agency Period on which the conditions set forth in Section 5(a) and Section 5(b) shall have been satisfied, the Company may exercise its right to request an issuance of Shares by delivering to the Agent an Issuance Notice; *provided, however*, that (A) in no event may the Company deliver an Issuance Notice to the extent that (I) the sum of (x) the aggregate Sales Price of the requested Issuance Amount, plus (y) the aggregate Sales Price of all Shares issued under all previous Issuance Notices effected pursuant to this Agreement, would exceed the Maximum Program Amount; and (B) prior to delivery of any Issuance Notice, the period set forth for any previous Issuance Notice shall have expired or been terminated. An Issuance Notice shall be considered delivered on the Trading Day that it is received by e-mail to the persons set forth in Schedule A hereto and confirmed by the Company by telephone (including a voicemail message to the persons so identified), with the understanding that, with adequate prior written notice, the Agent may modify the list of such persons from time to time.

(ii) Agent Efforts. Upon the terms and subject to the conditions set forth in this Agreement, upon the receipt of an Issuance Notice, the Agent will use its commercially reasonable efforts consistent with its normal sales and trading practices to place the Shares with respect to which the Agent has agreed to act as sales agent, subject to, and in accordance with the information specified in, the Issuance Notice, unless the sale of the Shares described therein has been suspended, cancelled or otherwise terminated in accordance with the terms of this Agreement. For the avoidance of doubt, the parties to this Agreement may modify an Issuance Notice at any time provided they both agree in writing to any such modification.

(iii) Method of Offer and Sale. The Shares may be offered and sold (A) in privately negotiated transactions with the consent of the Company; (B) as block transactions; or (C) by any other method permitted by law deemed to be an “at the market offering” as defined in Rule 415(a)(4) under the Securities Act, including sales made directly on the Principal Market or sales made into any other existing trading market of the Common Shares. Nothing in this Agreement shall be deemed to require either party to agree to the method of offer and sale specified in the preceding sentence, and (except as specified in clauses (A) and (B) above) the method of placement of any Shares by the Agent shall be at the Agent’s discretion.

(iv) Confirmation to the Company. If acting as sales agent hereunder, the Agent will provide written confirmation to the Company no later than the opening of the Trading Day next following the Trading Day on which it has placed Shares hereunder setting forth the number of Shares sold on such Trading Day, the corresponding Sales Price and the Issuance Price payable to the Company in respect thereof.

(v) Settlement. Each issuance of Shares will be settled on the applicable Settlement Date for such issuance of Shares and, subject to the provisions of Section 5, on or before each Settlement Date, the Company will, or will cause its transfer agent to, electronically transfer the Shares being sold by crediting the Agent or its designee’s account at The Depository Trust Company through its Deposit/Withdrawal At Custodian (DWAC) System, or by such other means of delivery as may be mutually agreed upon by the parties hereto and, upon receipt of such Shares, which in all cases shall be freely tradable, transferable, registered shares in good deliverable form, the Agent will deliver, by wire transfer of immediately available funds, the related Issuance Price in same day funds delivered to an account designated by the Company prior to the Settlement Date. The Company may sell Shares to the Agent as principal at a price agreed upon at each relevant time Shares are sold pursuant to this Agreement (each, a “**Time of Sale**”).

(vi) Suspension or Termination of Sales. Consistent with standard market settlement practices, the Company or the Agent may, upon notice to the other party hereto in writing (including by email correspondence to each of the individuals of the other party whose names are set forth on Schedule A) or by telephone (confirmed immediately by verifiable email), suspend any sale of Shares, and the period set forth in an Issuance Notice shall immediately terminate; *provided, however*, that (A) such suspension and termination shall not affect or impair either party's obligations with respect to any Shares placed or sold hereunder prior to the receipt of such notice; (B) if the Company suspends or terminates any sale of Shares after the Agent confirms such sale to the Company, the Company shall still be obligated to comply with Section 3(b)(v) with respect to such Shares; and (C) if the Company defaults in its obligation to deliver Shares on a Settlement Date, the Company agrees that it will hold the Agent harmless against any loss, claim, damage or expense (including, without limitation, penalties, interest and reasonable legal fees and expenses), as incurred, arising out of or in connection with such default by the Company. The parties hereto acknowledge and agree that, in performing its obligations under this Agreement, the Agent may borrow Common Shares from stock lenders in the event that the Company has not delivered Shares to settle sales as required by subsection (v) above, and may use the Shares to settle or close out such borrowings. The Company agrees that no such notice shall be effective against the Agent unless it is made to the persons identified in writing by the Agent pursuant to Section 3(b)(i).

(vii) No Guarantee of Placement, Etc. The Company acknowledges and agrees that (A) there can be no assurance that the Agent will be successful in placing Shares; (B) the Agent will incur no liability or obligation to the Company or any other Person if it does not sell Shares; and (C) the Agent shall be under no obligation to purchase Shares on a principal basis pursuant to this Agreement, except as otherwise specifically agreed by the Agent and the Company.

(viii) Material Non-Public Information. Notwithstanding any other provision of this Agreement, the Company and the Agent agree that the Company shall not deliver any Issuance Notice to the Agent, and the Agent shall not be obligated to place any Shares, during any period in which the Company is in possession of material non-public information.

(c) Fees. As compensation for services rendered, the Company shall pay to the Agent, on the applicable Settlement Date, the Selling Commission for the applicable Issuance Amount (including with respect to any suspended or terminated sale pursuant to Section 3(b)(vi)) by the Agent deducting the Selling Commission from the applicable Issuance Amount.

(d) Expenses. The Company agrees to pay all costs, fees and expenses incurred in connection with the performance of its obligations hereunder and in connection with the transactions contemplated hereby, including without limitation (i) all expenses incident to the issuance and delivery of the Shares (including all printing and engraving costs); (ii) all fees and expenses of the registrar and transfer agent of the Shares; (iii) all necessary issue, transfer and other stamp taxes in connection with the issuance and sale of the Shares; (iv) all fees and expenses of the Company's counsel, independent public or certified public accountants and other advisors; (v) all costs and expenses incurred in connection with the preparation, printing, filing, shipping and distribution of the Registration Statement (including financial statements, exhibits, schedules, consents and certificates of experts), the Prospectus, any Free Writing Prospectus (as defined below) prepared by or on behalf of, used by, or referred to by the Company, and all amendments and supplements thereto, and this Agreement; (vi) all filing fees, attorneys' fees and expenses incurred by the Company or the Agent in connection with qualifying or registering (or obtaining exemptions from the qualification or registration of) all or any part of the Shares for offer and sale under the state securities or blue sky laws or the provincial securities laws of Canada; (vii) the reasonable and documented fees and disbursements of the Agent's counsel, including the reasonable fees and expenses of counsel for the Agent in connection with, FINRA review, if any, and approval of the Agent's participation in the offering and distribution of the Shares; (viii) the filing fees incident to FINRA review, if any; (ix) the costs and expenses

of the Company relating to investor presentations on any “road show” undertaken in connection with the marketing of the offering of the Shares; and (x) the fees and expenses associated with listing the Shares on the Principal Market. The fees and disbursements of Agent’s counsel pursuant to subsections (vi) and (vii) above shall not exceed (A) \$50,000 in connection with the execution of this Agreement and (B) \$15,000 in connection with each Triggering Event Date (as defined below) on which the Company is required to provide a certificate pursuant to Section 4(q).

#### **Section 4. ADDITIONAL COVENANTS**

The Company covenants and agrees with the Agent as follows, in addition to any other covenants and agreements made elsewhere in this Agreement:

(a) Exchange Act Compliance. During the Agency Period, the Company shall (i) file, on a timely basis, with the Commission all reports and documents required to be filed under Section 13, 14 or 15 of the Exchange Act in the manner and within the time periods required by the Exchange Act; and (ii) either, in the Company’s sole discretion, (A) include in its quarterly reports on Form 10-Q and its annual reports on Form 10-K, a summary detailing, for the relevant reporting period, (1) the number of Shares sold, if any, through the Agent pursuant to this Agreement and (2) the net proceeds received, if any, by the Company from such sales or (B) prepare a prospectus supplement containing, or include in such other filing permitted by the Securities Act or Exchange Act (each an “**Interim Prospectus Supplement**”), such summary information and, at least once a quarter and subject to this Section 4, file such Interim Prospectus Supplement pursuant to Rule 424(b) under the Securities Act (and within the time periods required by Rule 424(b) and Rule 430B under the Securities Act).

(b) Securities Act Compliance. After the date of this Agreement, the Company shall promptly advise the Agent in writing (i) of the receipt of any comments of, or requests for additional or supplemental information from, the Commission; (ii) of the time and date of any filing of any post-effective amendment to the Registration Statement, any Rule 462(b) Registration Statement or any amendment or supplement to the Prospectus, or any Free Writing Prospectus; (iii) of the time and date that any post-effective amendment to the Registration Statement or any Rule 462(b) Registration Statement becomes effective; and (iv) of the issuance by the Commission of any stop order suspending the effectiveness of the Registration Statement or any post-effective amendment thereto, any Rule 462(b) Registration Statement or any amendment or supplement to the Prospectus or of any order preventing or suspending the use of any Free Writing Prospectus or the Prospectus, or of any proceedings to remove, suspend or terminate from listing or quotation the Common Shares from any securities exchange upon which they are listed for trading or included or designated for quotation, or of the threatening or initiation of any proceedings for any of such purposes. If the Commission shall enter any such stop order at any time, the Company will use its commercially reasonable efforts to obtain the lifting of such order as soon as practicable. Additionally, the Company agrees that it shall comply with the provisions of Rule 424(b) and Rule 433, as applicable, under the Securities Act and will use its reasonable efforts to confirm that any filings made by the Company under such Rule 424(b) or Rule 433 were received in a timely manner by the Commission.

(c) Amendments and Supplements to the Prospectus and Other Securities Act Matters. If any event shall occur or condition exist as a result of which it is necessary to amend or supplement the Prospectus so that the Prospectus does not include an untrue statement of a material fact or omit to state a material fact necessary in order to make the statements therein, in the light of the circumstances when the Prospectus is delivered to a purchaser, not misleading, or if in the opinion of the Agent or counsel for the Agent it is otherwise necessary to amend or supplement the Prospectus to comply with applicable law, including the Securities Act, the Company agrees (subject to Section 4(d) and 4(f)) to promptly prepare, file with the Commission and furnish at its own expense to the Agent, amendments or supplements to the Prospectus so that the statements in the Prospectus as so amended or supplemented will not include an

untrue statement of a material fact or omit to state a material fact necessary in order to make the statements therein, in the light of the circumstances when the Prospectus is delivered to a purchaser, be misleading or so that the Prospectus, as amended or supplemented, will comply with applicable law including the Securities Act. Neither the Agent's consent to, or delivery of, any such amendment or supplement shall constitute a waiver of any of the Company's obligations under Sections 4(d) and 4(f); *provided, however* that the only remedy the Agent shall have with respect to the failure by the Company to make such filing (other than the Agent's rights under Section 3(d) or Section 6 hereof) shall be to cease making sales under this Agreement until such amendment or supplement is filed; provided further, that the failure of the Company to file such amendment or supplement request shall not relieve the Company of any obligation or liability under Section 3(d) or Section 6 hereof, or affect the Agent's right to rely on the representations and warranties made by the Company in this Agreement. Notwithstanding the foregoing, the Company shall not be required to file such amendment or supplement if there is no pending Issuance Notice and the Company believes that it is in its best interest not to file such amendment or supplement.

(d) Agent's Review of Proposed Amendments and Supplements. During any period in which an Issuance Notice is pending, prior to amending or supplementing the Registration Statement (including any registration statement filed under Rule 462(b) under the Securities Act) or the Prospectus (excluding any amendment or supplement through incorporation of any report filed under the Exchange Act), insofar as such proposed amendment or supplement relates to the Shares or the transactions contemplated hereby, the Company shall furnish to the Agent for review, a reasonable amount of time prior to the proposed time of filing or use thereof, a copy of each such proposed amendment or supplement, and the Company shall not file or use any such proposed amendment or supplement without the Agent's prior consent, and the Company shall file with the Commission within the applicable period specified in Rule 424(b) under the Securities Act any prospectus required to be filed pursuant to such Rule.

(e) Use of Free Writing Prospectus. Neither the Company nor the Agent has prepared, used, referred to or distributed, or will prepare, use, refer to or distribute, without the other party's prior written consent, any "written communication" that constitutes a "free writing prospectus" as such terms are defined in Rule 405 under the Securities Act with respect to the offering contemplated by this Agreement (any such free writing prospectus being referred to herein as a "**Free Writing Prospectus**").

(f) Free Writing Prospectuses. During any period in which an Issuance Notice is pending, the Company shall furnish to the Agent for review, a reasonable amount of time prior to the proposed time of filing or use thereof, a copy of each proposed free writing prospectus or any amendment or supplement thereto to be prepared by or on behalf of, used by, or referred to by the Company insofar as such proposed amendment or supplement relates to the Shares or the transactions contemplated hereby, and the Company shall not file, use or refer to any proposed free writing prospectus or any amendment or supplement thereto without the Agent's consent. The Company shall furnish to the Agent, without charge, as many copies of any free writing prospectus prepared by or on behalf of, or used by the Company insofar as such proposed amendment or supplement relates to the Shares or the transactions contemplated hereby, as the Agent may reasonably request. If at any time when a prospectus is required by the Securities Act (including, without limitation, pursuant to Rule 173(d)) to be delivered in connection with sales of the Shares (but in any event if at any time through and including the date of this Agreement) there occurred or occurs an event or development as a result of which any free writing prospectus prepared by or on behalf of, used by, or referred to by the Company conflicted or would conflict with the information contained in the Registration Statement or included or would include an untrue statement of a material fact or omitted or would omit to state a material fact necessary in order to make the statements therein, in the light of the circumstances prevailing at that subsequent time, not misleading, the Company shall promptly amend or supplement such free writing prospectus to eliminate or correct such conflict or so that the statements in such free writing prospectus as so amended or supplemented will not include an untrue statement of a material fact or omit to state a material fact necessary in order to make the statements therein, in the light of the circumstances

prevailing at such subsequent time, not misleading, as the case may be; *provided, however*, that prior to amending or supplementing any such free writing prospectus, the Company shall furnish to the Agent for review, a reasonable amount of time prior to the proposed time of filing or use thereof, a copy of such proposed amended or supplemented free writing prospectus and the Company shall not file, use or refer to any such amended or supplemented free writing prospectus without the Agent's consent.

(g) Filing of Agent Free Writing Prospectuses. The Company shall not take any action that would result in the Agent or the Company being required to file with the Commission pursuant to Rule 433(d) under the Securities Act a free writing prospectus prepared by or on behalf of the Agent that the Agent otherwise would not have been required to file thereunder.

(h) Copies of Registration Statement and Prospectus. After the date of this Agreement through the last time that a prospectus is required by the Securities Act (including, without limitation, pursuant to Rule 173(d)) to be delivered in connection with sales of the Shares, the Company agrees to furnish the Agent with copies (which may be electronic copies) of the Registration Statement and each amendment thereto, and with copies (which may be electronic copies) of the Prospectus and each amendment or supplement thereto in the form in which it is filed with the Commission pursuant to the Securities Act or Rule 424(b) under the Securities Act, both in such quantities as the Agent may reasonably request from time to time; and, if the delivery of a prospectus is required under the Securities Act or under the blue sky or securities laws of any jurisdiction at any time on or prior to the applicable Settlement Date for any period set forth in an Issuance Notice in connection with the offering or sale of the Shares and if at such time any event has occurred as a result of which the Prospectus as then amended or supplemented would include an untrue statement of a material fact or omit to state any material fact necessary in order to make the statements therein, in the light of the circumstances under which they were made when such Prospectus is delivered, not misleading, or, if for any other reason it is necessary during such same period to amend or supplement the Prospectus or to file under the Exchange Act any document incorporated by reference in the Prospectus in order to comply with the Securities Act or the Exchange Act, to notify the Agent and to request that the Agent suspend offers to sell Shares (and, if so notified, the Agent shall cease such offers as soon as practicable); and if the Company decides to amend or supplement the Registration Statement or the Prospectus as then amended or supplemented, to advise the Agent promptly by telephone (with confirmation in writing) and to prepare and cause to be filed promptly with the Commission an amendment or supplement to the Registration Statement or the Prospectus as then amended or supplemented that will correct such statement or omission or effect such compliance; provided, however, that if during such same period the Agent is required to deliver a prospectus in respect of transactions in the Shares, the Company shall promptly prepare and file with the Commission such an amendment or supplement.

(i) Blue Sky Compliance. The Company shall cooperate with the Agent and counsel for the Agent to qualify or register the Shares for sale under (or obtain exemptions from the application of) the state securities or blue sky laws or Canadian provincial securities laws of those jurisdictions designated by the Agent, shall comply with such laws and shall continue such qualifications, registrations and exemptions in effect so long as required for the distribution of the Shares. The Company shall not be required to qualify as a foreign corporation or to take any action that would subject it to general service of process in any such jurisdiction where it is not presently qualified or where it would be subject to taxation as a foreign corporation. The Company will advise the Agent promptly of the suspension of the qualification or registration of (or any such exemption relating to) the Shares for offering, sale or trading in any jurisdiction or any initiation or threat of any proceeding for any such purpose, and in the event of the issuance of any order suspending such qualification, registration or exemption, the Company shall use its commercially reasonable efforts to obtain the withdrawal thereof as soon as practicable.

(j) Earnings Statement. As soon as practicable, the Company will make generally available to its security holders and to the Agent an earnings statement (which need not be audited) covering a period

of at least twelve months beginning with the first fiscal quarter of the Company occurring after the date of this Agreement which shall satisfy the provisions of Section 11(a) of the Securities Act and Rule 158 under the Securities Act.

(k) Listing; Reservation of Shares. (a) The Company will maintain the listing of the Shares on the Principal Market; and (b) the Company will reserve and keep available at all times, free of preemptive rights, Shares for the purpose of enabling the Company to satisfy its obligations under this Agreement.

(l) Transfer Agent. The Company shall engage and maintain, at its expense, a registrar and transfer agent for the Shares.

(m) Due Diligence. During the term of this Agreement, the Company will reasonably cooperate with any reasonable due diligence review conducted by the Agent in connection with the transactions contemplated hereby, including, without limitation, providing information and making available documents and senior corporate officers, during normal business hours and at the Company's principal offices, as the Agent may reasonably request from time to time.

(n) Representations and Warranties. The Company acknowledges that each delivery of an Issuance Notice and each delivery of Shares on a Settlement Date shall be deemed to be (i) an affirmation to the Agent that the representations and warranties of the Company contained in or made pursuant to this Agreement are true and correct as of the date of such Issuance Notice or of such Settlement Date, as the case may be, as though made at and as of each such date, except as may be disclosed in the Prospectus (including any documents incorporated by reference therein and any supplements thereto); and (ii) an undertaking that the Company will advise the Agent if any of such representations and warranties will not be true and correct as of the Settlement Date for the Shares relating to such Issuance Notice, as though made at and as of each such date (except that such representations and warranties shall be deemed to relate to the Registration Statement and the Prospectus as amended and supplemented relating to such Shares).

(o) Deliverables at Triggering Event Dates; Certificates. The Company agrees that on or prior to the date of the first Issuance Notice and, during the term of this Agreement after the date of the first Issuance Notice, upon:

(A) the filing with the Commission of an amendment or supplement of any Registration Statement or Prospectus (other than a prospectus supplement relating solely to an offering of securities other than the Shares or a prospectus filed pursuant to Section 4(a)(ii)(B)), by means of a post-effective amendment, sticker or supplement, but not by means of incorporation of documents by reference into the Registration Statement or Prospectus;

(B) the filing with the Commission of an annual report on Form 10-K or a quarterly report on Form 10-Q, in each case, of the Company;

(C) the filing with the Commission of any Form 10-K/A or Form 10-Q/A containing amended financial information or a material amendment to the previously filed annual report on Form 10-K or quarterly report on Form 10-Q, in each case, of the Company; or

(D) the filing with the Commission of a current report on Form 8-K of the Company containing amended financial information (other than information "furnished" pursuant to Item 2.02 or 7.01 of Form 8-K or to provide disclosure pursuant to Item 8.01 of Form 8-K relating to reclassification of certain properties as discontinued operations in accordance with Statement of Financial Accounting Standards No. 144) that the Agent reasonably determines is material to the offering of securities of the Company;

(any such event described in clauses (A) through (D) above, a “**Triggering Event Date**”), the Company shall furnish the Agent (but in the case of clauses (C) or (D) above, only if the Agent reasonably determines that the information contained in such amendment to Form 10-K or Form 10-Q or such current report on Form 8-K of the Company is material to a holder of Common Shares and the Agent requests such certification after the filing of such amendment or Form 8-K with the Commission) with a certificate as of the Triggering Event Date, in the form attached as Exhibit B hereto executed by the Chief Executive Officer, President or Chief Financial Officer of the Company. The requirement to provide a certificate under this Section 4(o) shall be automatically waived for any Triggering Event Date occurring at a time when no Issuance Notice is pending or a suspension is in effect, which waiver shall continue until the earlier to occur of the date the Company delivers instructions for the sale of Shares hereunder (which for such calendar quarter shall be considered a Triggering Event Date) and the next occurring Triggering Event Date. Notwithstanding the foregoing, if the Company subsequently decides to sell Shares following a Triggering Event Date when a suspension was in effect and did not provide the Agent with a certificate under this Section 4(o), then before the Company delivers the instructions for the sale of Shares or the Agent sells any Shares pursuant to such instructions, the Company shall provide the Agent with a certificate in conformity with this Section 4(o) dated as of the date that the instructions for the sale of Shares are issued.

(p) Legal Opinions. On or prior to the date of the first Issuance Notice and on or prior to each Triggering Event Date with respect to which the Company is obligated to deliver a certificate pursuant to Section 4(o) for which no waiver is applicable and excluding the date of this Agreement, the Company shall cause Latham & Watkins LLP, counsel to the Company, to furnish its negative assurances letter and written legal opinion, each dated the date of delivery, in form and substance reasonably satisfactory to Agent and its counsel, substantially similar to the form previously provided to the Agent and its counsel, modified, as necessary, to relate to the Registration Statement and the Prospectus as then amended or supplemented. In lieu of such opinions for subsequent periodic filings, in the discretion of the Agent, the Company may furnish a reliance letter from such counsel to the Agent, permitting the Agent to rely on a previously delivered opinion letter, modified as appropriate for any passage of time or Triggering Event Date (except that statements in such prior opinion shall be deemed to relate to the Registration Statement and the Prospectus as amended or supplemented as of such Triggering Event Date). The Company shall be required to furnish no more than one opinion letter and negative assurance letter per counsel hereunder per filing of an annual report on Form 10-K or quarterly report on Form 10-Q.

(q) Comfort Letter. On or prior to the date of the first Issuance Notice and on or prior to each Triggering Event Date with respect to which the Company is obligated to deliver a certificate pursuant to Section 4(o) for which no waiver is applicable and excluding the date of this Agreement, the Company shall cause PricewaterhouseCoopers LLP, the independent registered public accounting firm who has audited the financial statements included or incorporated by reference in the Registration Statement, to furnish the Agent a comfort letter, dated the date of delivery, in form and substance reasonably satisfactory to the Agent and its counsel, substantially similar to the form previously provided to the Agent and its counsel; provided, however, that any such comfort letter will only be required on the Triggering Event Date specified to the extent that it contains financial statements filed with the Commission under the Exchange Act and incorporated or deemed to be incorporated by reference into a Prospectus. The Company shall be required to furnish no more than one comfort letter hereunder per filing of an annual report on Form 10-K or quarterly report on Form 10-Q.

(r) Secretary’s Certificate. On or prior to the date of the first Issuance Notice and on or prior to each Triggering Event Date with respect to which the Company is obligated to deliver a certificate pursuant to Section 4(o) for which no waiver is applicable and excluding the date of this Agreement, the Company shall furnish the Agent a certificate executed by the Secretary of the Company, signing in such capacity, dated the date of delivery (i) certifying that attached thereto are true and complete copies of the resolutions duly adopted by the Board of Directors of the Company authorizing the execution and delivery of this

Agreement and the consummation of the transactions contemplated hereby (including, without limitation, the issuance of the Shares pursuant to this Agreement), which authorization shall be in full force and effect on and as of the date of such certificate and (ii) certifying and attesting to the office, incumbency, due authority and specimen signatures of each Person who executed this Agreement for or on behalf of the Company, along with such certificates of good standing or other certificates of public officials as may be reasonably requested by Company Counsel or Agent Counsel (as defined below) in connection with the rendering of their opinions and negative assurance letters as contemplated by Sections 4(p) and 5(a)(v).

(s) Agent's Own Account; Clients' Account. The Company consents to the Agent trading, in compliance with applicable law, in the Common Shares for the Agent's own account and for the account of its clients at the same time as sales of the Shares occur pursuant to this Agreement.

(t) Investment Limitation. The Company shall not invest, or otherwise use the proceeds received by the Company from its sale of the Shares in such a manner as would require the Company or any of its subsidiaries to register as an investment company under the Investment Company Act.

(u) Market Activities. The Company will not take, directly or indirectly, any action designed to or that might be reasonably expected to cause or result in stabilization or manipulation of the price of the Shares or any other reference security, whether to facilitate the sale or resale of the Shares or otherwise, and the Company will, and shall cause each of its affiliates to, comply with all applicable provisions of Regulation M. If the limitations of Rule 102 of Regulation M ("**Rule 102**") do not apply with respect to the Shares or any other reference security pursuant to any exception set forth in Section (d) of Rule 102, then promptly upon notice from the Agent (or, if later, at the time stated in the notice), the Company will, and shall cause each of its affiliates to, comply with Rule 102 as though such exception were not available but the other provisions of Rule 102 (as interpreted by the Commission) did apply. The Company shall promptly notify the Agent if it no longer meets the requirements set forth in Section (d) of Rule 102.

(v) Notice of Other Sale. Without the written consent of the Agent, the Company will not, directly or indirectly, offer to sell, sell, contract to sell, grant any option to sell or otherwise dispose of any Common Shares or securities convertible into or exchangeable for Common Shares (other than Shares hereunder), warrants or any rights to purchase or acquire Common Shares, during the period beginning on the third Trading Day immediately prior to the date on which any Issuance Notice is delivered to the Agent hereunder and ending on the earlier of (x) the third Trading Day immediately following the Settlement Date with respect to Shares sold pursuant to such Issuance Notice and (y) the date the Company notifies the Agent of the withdrawal of such Issuance Notice; and will not directly or indirectly enter into any other "at the market" or continuous equity transaction pursuant to which the Company (including through another person as agent or principal) offers to sell, sells, contracts to sell, grants any option to sell or otherwise disposes of any Common Shares (other than the Shares offered pursuant to this Agreement) or securities convertible into or exchangeable for Common Shares, warrants or any rights to purchase or acquire, Common Shares prior to the termination of this Agreement; provided, however, that such restrictions will not be required in connection with the Company's (i) issuance or sale of Common Shares, options to purchase Common Shares or Common Shares issuable upon the exercise of options or other equity awards pursuant to any employee or director share option, incentive or benefit plan, share purchase or ownership plan, long-term incentive plan, dividend reinvestment plan, inducement award under Nasdaq rules or other compensation plan of the Company or its subsidiaries, whether now in effect or hereafter implemented, (ii) issuance or sale of Common Shares issuable upon exchange, conversion or redemption of securities or the exercise or vesting of warrants, options or other equity awards disclosed in filings by the Company available on EDGAR or otherwise in writing to the Agent, (iii) modification of any outstanding options, warrants or any rights to purchase or acquire Common Shares, and (iv) Common Shares or securities convertible into or exchangeable for Common Shares as consideration for mergers, acquisitions, other business combinations, collaboration agreements or strategic alliances occurring after the date of this Agreement

which are not issued primarily for capital raising purposes; provided, however, that if any Issuance Notice is pending, the Company will not issue Common Shares pursuant to clause (iv) of this Section 4(v) while such Issuance Notice is pending if, following such issuance, the number of Common Shares issued or issuable in connection with all such issuances pursuant to clause (iv) would exceed 5% of the aggregate number of shares of Common Stock outstanding as of the date of this Agreement.

## Section 5. CONDITIONS TO DELIVERY OF ISSUANCE NOTICES AND TO SETTLEMENT

(a) Conditions Precedent to the Right of the Company to Deliver an Issuance Notice and the Obligation of the Agent to Sell Shares. The right of the Company to deliver an Issuance Notice hereunder is subject to the satisfaction, on the date of delivery of such Issuance Notice, and the obligation of the Agent to use its commercially reasonable efforts to place Shares during the applicable period set forth in the Issuance Notice is subject to the satisfaction, on each Trading Day during the applicable period set forth in the Issuance Notice, of each of the following conditions:

- (i) Accuracy of the Company's Representations and Warranties; Performance by the Company. The Company shall have delivered the certificate required to be delivered pursuant to Section 4(o) on or before the date on which delivery of such certificate is required pursuant to Section 4(o). The Company shall have performed, satisfied and complied with all covenants, agreements and conditions required by this Agreement to be performed, satisfied or complied with by the Company at or prior to such date, including, but not limited to, the covenants contained in Section 4(m), Section 4(q) and Section 4(r).
- (ii) No Injunction. No statute, rule, regulation, executive order, decree, ruling or injunction shall have been enacted, entered, promulgated or endorsed by any court or governmental authority of competent jurisdiction or any self-regulatory organization having authority over the matters contemplated hereby that prohibits or directly and materially adversely affects any of the transactions contemplated by this Agreement, and no proceeding shall have been commenced that may have the effect of prohibiting or materially adversely affecting any of the transactions contemplated by this Agreement.
- (iii) Material Adverse Changes. Except as disclosed in the Prospectus and the Time of Sale Information, since the respective date as of which information is given in the Registration Statement and the Prospectus, in the judgment of the Agent there shall not have occurred any Material Adverse Effect.
- (iv) No Suspension of Trading in or Delisting of Common Shares; Other Events. The trading of the Common Shares (including without limitation the Shares) shall not have been suspended by the Commission, the Principal Market or FINRA and the Common Shares (including without limitation the Shares) shall have been approved for listing or quotation on and shall not have been delisted from the Nasdaq Stock Market, the New York Stock Exchange or any of their constituent markets. There shall not have occurred (and be continuing in the case of occurrences under clauses (i) and (ii) below) any of the following: (i) trading or quotation in any of the Company's securities shall have been suspended or limited by the Commission or by the Principal Market or trading in securities generally on either the Principal Market shall have been suspended or limited, or minimum or maximum prices shall have been generally established on any of such stock exchanges by the Commission or the FINRA; (ii) a general banking moratorium shall have been declared by any of federal or New York, authorities; or (iii) there shall have occurred any outbreak or escalation of national or international hostilities or any crisis or calamity, or any change in the United States or international financial markets, or any substantial change or

development involving a prospective substantial change in United States' or international political, financial or economic conditions, as in the judgment of the Agent is material and adverse and makes it impracticable to market the Shares in the manner and on the terms described in the Prospectus or to enforce contracts for the sale of securities.

- (v) **Agent Counsel Opinion and Negative Assurances Letter.** On or prior to the date of the first Issuance Notice and on or prior to each Triggering Event Date with respect to which the Company is obligated to deliver a certificate pursuant to Section 4(o) for which no waiver is applicable and excluding the date of this Agreement, Davis Polk & Wardwell LLP, counsel to the Agent ("Agent Counsel"), shall have furnished to the Agent a negative assurances letter and the written legal opinion, each dated the date of delivery, in form and substance reasonably satisfactory to the Agent, modified, as necessary, to relate to the Registration Statement and the Prospectus as then amended or supplemented. In lieu of such opinion for subsequent periodic filings, Agent Counsel may furnish a reliance letter, permitting the Agent to rely on a previously delivered opinion letter, modified as appropriate for any passage of time or Triggering Event Date (except that statements in such prior opinion shall be deemed to relate to the Registration Statement and the Prospectus as amended or supplemented as of such Triggering Event Date).

(b) **Documents Required to be Delivered on each Issuance Notice Date.** The Agent's obligation to use its commercially reasonable efforts to place Shares hereunder shall additionally be conditioned upon the delivery to the Agent on or before the Issuance Notice Date of a certificate in form and substance reasonably satisfactory to the Agent, executed by the Chief Executive Officer, President or Chief Financial Officer of the Company, to the effect that all conditions to the delivery of such Issuance Notice shall have been satisfied as at the date of such certificate as required to be delivered pursuant to Section 4(o) (which certificate shall not be required if the foregoing representations shall be set forth in the Issuance Notice).

(c) **No Misstatement or Material Omission.** Agent shall not have advised the Company that the Registration Statement, the Prospectus or the Times of Sales Information, or any amendment or supplement thereto, contains an untrue statement of fact that in the Agent's reasonable opinion is material, or omits to state a fact that in the Agent's reasonable opinion is material and is required to be stated therein or is necessary to make the statements therein not misleading.

## **Section 6. INDEMNIFICATION AND CONTRIBUTION**

(a) **Indemnification of the Agent.** The Company agrees to indemnify and hold harmless the Agent, its officers and employees, and each person, if any, who controls the Agent within the meaning of the Securities Act or the Exchange Act against any loss, claim, damage, liability or expense, as incurred, to which the Agent or such officer, employee or controlling person may become subject, under the Securities Act, the Exchange Act, other federal or state statutory law or regulation, or the laws or regulations of foreign jurisdictions where Shares have been offered or sold or at common law or otherwise (including in settlement of any litigation), insofar as such loss, claim, damage, liability or expense (or actions in respect thereof as contemplated below) arises out of or is based upon (i) any untrue statement or alleged untrue statement of a material fact contained in the Registration Statement, or any amendment thereto, including any information deemed to be a part thereof pursuant to Rule 430B under the Securities Act, or the omission or alleged omission therefrom of a material fact required to be stated therein or necessary to make the statements therein not misleading; (ii) any untrue statement or alleged untrue statement of a material fact contained in any Free Writing Prospectus that the Company has used, referred to or filed, or is required to file, pursuant to Rule 433(d) of the Securities Act or the Prospectus (or any amendment or supplement thereto), or the omission or alleged omission therefrom of a material fact necessary in order to make the

statements therein, in the light of the circumstances under which they were made, not misleading; or (iii) any act or failure to act or any alleged act or failure to act by the Agent in connection with, or relating in any manner to, the Common Shares or the offering contemplated hereby, and which is included as part of or referred to in any loss, claim, damage, liability or action arising out of or based upon any matter covered by clause (i) or (ii) above, provided that the Company shall not be liable under this clause (iii) to the extent that a court of competent jurisdiction shall have determined by a final judgment that such loss, claim, damage, liability or action resulted directly from any such acts or failures to act undertaken or omitted to be taken by the Agent through its bad faith or willful misconduct, and to reimburse the Agent and each such officer, employee and controlling person for any and all reasonable and documented expenses (including the reasonable and documented fees and disbursements of counsel chosen by the Agent) as such expenses are reasonably incurred by the Agent or such officer, employee or controlling person in connection with investigating, defending, settling, compromising or paying any such loss, claim, damage, liability, expense or action; provided, however, that the foregoing indemnity agreement shall not apply to any loss, claim, damage, liability or expense to the extent, but only to the extent, arising out of or based upon any untrue statement or alleged untrue statement or omission or alleged omission made in reliance upon and in conformity with written information furnished to the Company by the Agent expressly for use in the Registration Statement, any such Free Writing Prospectus or the Prospectus (or any amendment or supplement thereto), it being understood and agreed that the only such information furnished by the Agent to the Company consists the tenth paragraph under the caption "Plan of Distribution" in the Prospectus beginning with the words: "A prospectus supplement and the accompanying prospectus in electronic format. . ." (the "**Agent Information**"). The indemnity agreement set forth in this Section 6(a) shall be in addition to any liabilities that the Company may otherwise have.

(b) Indemnification of the Company, its Directors and Officers. The Agent agrees to indemnify and hold harmless the Company, each of its directors, each of its officers who signed the Registration Statement and each person, if any, who controls the Company within the meaning of the Securities Act or the Exchange Act against any loss, claim, damage, liability or expense, as incurred, to which the Company or any such director, officer or controlling person may become subject, under the Securities Act, the Exchange Act, or other federal or state statutory law or regulation, or the laws or regulations of foreign jurisdictions where Shares have been offered or sold or at common law or otherwise (including in settlement of any litigation), insofar as such loss, claim, damage, liability or expense (or actions in respect thereof as contemplated below) arises out of or is based upon (i) any untrue statement or alleged untrue statement of a material fact contained in the Registration Statement, or any amendment thereto, including any information deemed to be a part thereof pursuant to Rule 430B under the Securities Act, or the omission or alleged omission therefrom of a material fact required to be stated therein or necessary to make the statements therein not misleading; or (ii) any untrue statement or alleged untrue statement of a material fact contained in any Free Writing Prospectus that the Company has used, referred to or filed, or is required to file, pursuant to Rule 433(d) of the Securities Act or the Prospectus (or any amendment or supplement thereto), or the omission or alleged omission therefrom of a material fact necessary in order to make the statements therein, in the light of the circumstances under which they were made, not misleading; and to reimburse the Company and each such director, officer and controlling person for any and all expenses (including the and disbursements of counsel chosen by the Company) as such expenses are reasonably incurred by the Company or such officer, director or controlling person in connection with investigating, defending, settling, compromising or paying any such loss, claim, damage, liability, expense or action; *provided, however*, that the foregoing indemnity agreement shall only apply to any loss, claim, damage, liability or expense to the extent, but only to the extent, arising out of or based upon any untrue statement or alleged untrue statement or omission or alleged omission made in reliance upon and in conformity with the Agent Information expressly for use in the Registration Statement, any such Free Writing Prospectus or the Prospectus (or any amendment or supplement thereto). The indemnity agreement set forth in this Section 6(b) shall be in addition to any liabilities that the Agent or the Company may otherwise have.

(c) Notifications and Other Indemnification Procedures. Promptly after receipt by an indemnified party under this Section 6 of notice of the commencement of any action, such indemnified party will, if a claim in respect thereof is to be made against an indemnifying party under this Section 6, notify the indemnifying party in writing of the commencement thereof, but the omission to so notify the indemnifying party will not relieve it from any liability which it may have to any indemnified party for contribution or otherwise than under the indemnity agreement contained in this Section 6 or to the extent it is not prejudiced as a proximate result of such failure. In case any such action is brought against any indemnified party and such indemnified party seeks or intends to seek indemnity from an indemnifying party, the indemnifying party will be entitled to participate in, and, to the extent that it shall elect, jointly with all other indemnifying parties similarly notified, by written notice delivered to the indemnified party promptly after receiving the aforesaid notice from such indemnified party, to assume the defense thereof with counsel reasonably satisfactory to such indemnified party; provided, however, if the defendants in any such action include both the indemnified party and the indemnifying party and the indemnified party shall have reasonably concluded based on the advice of counsel that a conflict may arise between the positions of the indemnifying party and the indemnified party in conducting the defense of any such action or that there may be legal defenses available to it and/or other indemnified parties which are different from or additional to those available to the indemnifying party, the indemnified party or parties shall have the right to select separate counsel to assume such legal defenses and to otherwise participate in the defense of such action on behalf of such indemnified party or parties. Upon receipt of notice from the indemnifying party to such indemnified party of such indemnifying party's election so to assume the defense of such action and approval by the indemnified party of counsel, the indemnifying party will not be liable to such indemnified party under this Section 6 for any reasonable and documented legal or other expenses subsequently incurred by such indemnified party in connection with the defense thereof unless (i) the indemnified party shall have employed separate counsel in accordance with the proviso to the preceding sentence (it being understood, however, that the indemnifying party shall not be liable for the fees and expenses of more than one separate counsel (together with local counsel), representing the indemnified parties who are parties to such action), which counsel (together with any local counsel) for the indemnified parties shall be selected by the Agent (in the case of counsel for the indemnified parties referred to in Section 6(a) above) or the Company (in the case of counsel for the indemnified parties referred to in Section 6(b) above), (ii) the indemnifying party shall not have employed counsel satisfactory to the indemnified party to represent the indemnified party within a reasonable time after notice of commencement of the action or (iii) the indemnifying party has authorized in writing the employment of counsel for the indemnified party at the expense of the indemnifying party, in each of which cases the fees and expenses of counsel shall be at the expense of the indemnifying party and shall be paid as they are incurred.

(d) Settlements. The indemnifying party under this Section 6 shall not be liable for any settlement of any proceeding effected without its written consent, but if settled with such consent or if there be a final judgment for the plaintiff, the indemnifying party agrees to indemnify the indemnified party against any loss, claim, damage, liability or expense by reason of such settlement or judgment. Notwithstanding the foregoing sentence, if at any time an indemnified party shall have requested an indemnifying party to reimburse the indemnified party for fees and expenses of counsel as contemplated by Section 6(c) hereof, the indemnifying party agrees that it shall be liable for any settlement of any proceeding effected without its written consent if (i) such settlement is entered into more than 30 days after receipt by such indemnifying party of the aforesaid request; and (ii) such indemnifying party shall not have reimbursed the indemnified party in accordance with such request prior to the date of such settlement. No indemnifying party shall, without the prior written consent of the indemnified party, effect any settlement, compromise or consent to the entry of judgment in any pending or threatened action, suit or proceeding in respect of which any indemnified party is or could have been a party and indemnity was or could have been sought hereunder by such indemnified party, unless such settlement, compromise or consent includes an unconditional release of such indemnified party from all liability on claims that are the subject matter of such action, suit or proceeding.

(e) Contribution. If the indemnification provided for in this Section 6 is for any reason held to be unavailable to or otherwise insufficient to hold harmless an indemnified party in respect of any losses, claims, damages, liabilities or expenses referred to therein, then each indemnifying party shall contribute to the aggregate amount paid or payable by such indemnified party, as incurred, as a result of any losses, claims, damages, liabilities or expenses referred to therein (i) in such proportion as is appropriate to reflect the relative benefits received by the Company, on the one hand, and the Agent, on the other hand, from the offering of the Shares pursuant to this Agreement; or (ii) if the allocation provided by clause (i) above is not permitted by applicable law, in such proportion as is appropriate to reflect not only the relative benefits referred to in clause (i) above but also the relative fault of the Company, on the one hand, and the Agent, on the other hand, in connection with the statements or omissions which resulted in such losses, claims, damages, liabilities or expenses, as well as any other relevant equitable considerations. The relative benefits received by the Company, on the one hand, and the Agent, on the other hand, in connection with the offering of the Shares pursuant to this Agreement shall be deemed to be in the same respective proportions as the net proceeds from the offering of the Shares (net of commissions to the Agent but before deducting expenses) received by the Company bear to the total commissions received by the Agent. The relative fault of the Company, on the one hand, and the Agent, on the other hand, shall be determined by reference to, among other things, whether any such untrue or alleged untrue statement of a material fact or omission or alleged omission to state a material fact relates to information supplied by the Company, on the one hand, or the Agent, on the other hand, and the parties' relative intent, knowledge, access to information and opportunity to correct or prevent such statement or omission.

The amount paid or payable by a party as a result of the losses, claims, damages, liabilities and expenses referred to above shall be deemed to include, subject to the limitations set forth in Section 6(c), any reasonable and documented legal or other fees or expenses reasonably incurred by such party in connection with investigating or defending any action or claim. The provisions set forth in Section 6(c) with respect to notice of commencement of any action shall apply if a claim for contribution is to be made under this Section 6(e); *provided, however*, that no additional notice shall be required with respect to any action for which notice has been given under Section 6(c) for purposes of indemnification.

The Company and the Agent agree that it would not be just and equitable if contribution pursuant to this Section 6(e) were determined by pro rata allocation or by any other method of allocation which does not take account of the equitable considerations referred to in this Section 6(e).

Notwithstanding the provisions of this Section 6(e), the Agent shall not be required to contribute any amount in excess of the agent fees received by the Agent in connection with the offering contemplated hereby. No person guilty of fraudulent misrepresentation (within the meaning of Section 11(f) of the Securities Act) shall be entitled to contribution from any person who was not guilty of such fraudulent misrepresentation. For purposes of this Section 6(e), each officer and employee of the Agent and each person, if any, who controls the Agent within the meaning of the Securities Act or the Exchange Act shall have the same rights to contribution as the Agent, and each director of the Company, each officer of the Company who signed the Registration Statement, and each person, if any, who controls the Company with the meaning of the Securities Act and the Exchange Act shall have the same rights to contribution as the Company.

## **Section 7. TERMINATION & SURVIVAL**

(a) Term. Subject to the provisions of this Section 7, the term of this Agreement shall continue from the date of this Agreement until the end of the Agency Period, unless earlier terminated by the parties to this Agreement pursuant to this Section 7.

(b) Termination; Survival Following Termination.

- (i) Either party may terminate this Agreement prior to the end of the Agency Period, by giving written notice as required by this Agreement, upon ten (10) days notice to the other party; provided that, (A) if the Company terminates this Agreement after the Agent confirms to the Company any sale of Shares, the Company shall remain obligated to comply with Section 3(b)(v) with respect to such Shares and (B) Section 2, Section 6, Section 7 and Section 8 shall survive termination of this Agreement. If termination shall occur prior to the Settlement Date for any sale of Shares, such sale shall nevertheless settle in accordance with the terms of this Agreement.
- (ii) In addition to the survival provision of Section 7(b)(i), the respective indemnities, agreements, representations, warranties and other statements of the Company, of its officers and of the Agent set forth in or made pursuant to this Agreement will remain in full force and effect, regardless of any investigation made by or on behalf of the Agent or the Company or any of its or their partners, officers or directors or any controlling person, as the case may be, and, anything herein to the contrary notwithstanding, will survive delivery of and payment for the Shares sold hereunder and any termination of this Agreement.

## **Section 8. MISCELLANEOUS**

(a) Press Releases and Disclosure. The Company may issue a press release describing the material terms of the transactions contemplated hereby as soon as practicable following the date of this Agreement, and may file with the Commission a Current Report on Form 8-K, with this Agreement attached as an exhibit thereto, describing the material terms of the transactions contemplated hereby, and the Company shall consult with the Agent prior to making such disclosures, and the parties hereto shall use all commercially reasonable efforts, acting in good faith, to agree upon a text for such disclosures that is reasonably satisfactory to all parties hereto. No party hereto shall issue thereafter any press release or like public statement related to this Agreement or any of the transactions contemplated hereby without the prior written approval of the other party hereto, except as may be necessary or appropriate in the reasonable opinion of the party seeking to make disclosure to comply with the requirements of applicable law or stock exchange rules, including, any disclosure regarding sales of Common Shares pursuant hereto on current reports on Form 8-K, quarterly reports on Form 10-Q or annual reports on Form 10-K. If any such press release or like public statement is so required (other than disclosure regarding sales of Common Shares pursuant hereto on current reports on Form 8-K, quarterly reports on Form 10-Q or annual reports on Form 10-K), the party making such disclosure shall consult with the other party prior to making such disclosure, and the parties shall use all commercially reasonable efforts, acting in good faith, to agree upon a text for such disclosure that is reasonably satisfactory to all parties hereto.

(b) No Advisory or Fiduciary Relationship. The Company acknowledges and agrees that (i) the transactions contemplated by this Agreement, including the determination of any fees, are arm's-length commercial transactions between the Company and the Agent, (ii) when acting as a principal under this Agreement, the Agent is and has been acting solely as a principal and is not the agent or fiduciary of the Company, or its stockholders, creditors, employees or any other party, (iii) the Agent has not assumed nor will assume an advisory or fiduciary responsibility in favor of the Company with respect to the transactions contemplated hereby or the process leading thereto (irrespective of whether the Agent has advised or is currently advising the Company on other matters) and the Agent does not have any obligation to the Company with respect to the transactions contemplated hereby except the obligations expressly set forth in this Agreement, (iv) the Agent and its respective affiliates may be engaged in a broad range of transactions that involve interests that differ from those of the Company, and (v) the Agent has not provided any legal, accounting, regulatory or tax advice with respect to the transactions contemplated hereby and the Company has consulted its own legal, accounting, regulatory and tax advisors to the extent it deemed appropriate.

(c) Research Analyst Independence. The Company acknowledges that the Agent's research analysts and research departments are required to and should be independent from their respective investment banking divisions and are subject to certain regulations and internal policies, and as such the Agent's research analysts may hold views and make statements or investment recommendations and/or publish research reports with respect to the Company or the offering that differ from the views of their respective investment banking divisions. The Company understands that the Agent is a full service securities firm and as such from time to time, subject to applicable securities laws, may effect transactions for its own account or the account of its customers and hold long or short positions in debt or equity securities of the companies that may be the subject of the transactions contemplated by this Agreement.

(d) Notices. All communications hereunder shall be in writing and shall be mailed, hand delivered or telecopied and confirmed to the parties hereto as follows:

If to the Agent:

Jefferies LLC  
520 Madison Avenue  
New York, NY 10022  
Attention: General Counsel

with a copy (which shall not constitute notice) to:

Davis Polk & Wardwell LLP  
1600 El Camino Real  
Menlo Park, CA 94025  
Attention: Alan F. Denenberg; Emily Roberts  
Email: alan.denenberg@davispolk.com; emily.roberts@davispolk.com

If to the Company:

Corvus Pharmaceuticals, Inc.  
863 Mitten Road, Suite 102  
Burlingame, California 94010  
Attention: Chief Financial Officer

with a copy (which shall not constitute notice) to:

Latham & Watkins LLP  
140 Scott Drive  
Menlo Park, California 94025  
Attention: Phillip Stoup  
Email: phillip.stoup@lw.com

Any party hereto may change the address for receipt of communications by giving written notice to the others in accordance with this Section 8(d).

(e) Successors. This Agreement will inure to the benefit of and be binding upon the parties hereto, and to the benefit of the employees, officers and directors and controlling persons referred to in Section 6, and in each case their respective successors, and no other person will have any right or obligation hereunder. The term "successors" shall not include any purchaser of the Shares as such from the Agent merely by reason of such purchase.

(f) Partial Unenforceability. The invalidity or unenforceability of any Article, Section, paragraph or provision of this Agreement shall not affect the validity or enforceability of any other Article, Section, paragraph or provision hereof. If any Article, Section, paragraph or provision of this Agreement is for any reason determined to be invalid or unenforceable, there shall be deemed to be made such minor changes (and only such minor changes) as are necessary to make it valid and enforceable.

(g) Governing Law Provisions. This Agreement shall be governed by and construed in accordance with the internal laws of the State of New York applicable to agreements made and to be performed in such state. Any legal suit, action or proceeding arising out of or based upon this Agreement or the transactions contemplated hereby (“**Related Proceedings**”) may be instituted in the federal courts of the United States of America located in the Borough of Manhattan in the City of New York or the courts of the State of New York in each case located in the Borough of Manhattan in the City of New York (collectively, the “**Specified Courts**”), and each party irrevocably submits to the exclusive jurisdiction (except for proceedings instituted in regard to the enforcement of a judgment of any such court (a “**Related Judgment**”), as to which such jurisdiction is non-exclusive) of such courts in any such suit, action or proceeding. Service of any process, summons, notice or document by mail to such party’s address set forth above shall be effective service of process for any suit, action or other proceeding brought in any such court. The parties irrevocably and unconditionally waive any objection to the laying of venue of any suit, action or other proceeding in the Specified Courts and irrevocably and unconditionally waive and agree not to plead or claim in any such court that any such suit, action or other proceeding brought in any such court has been brought in an inconvenient forum.

(h) General Provisions. This Agreement constitutes the entire agreement of the parties to this Agreement and supersedes all prior written or oral and all contemporaneous oral agreements, understandings and negotiations with respect to the subject matter hereof. This Agreement may be executed in two or more counterparts, each one of which shall be an original, with the same effect as if the signatures thereto and hereto were upon the same instrument, and may be delivered by facsimile transmission or by electronic delivery of a portable document format (PDF) file. This Agreement may not be amended or modified unless in writing by all of the parties hereto, and no condition herein (express or implied) may be waived unless waived in writing by each party whom the condition is meant to benefit. The Article and Section headings herein are for the convenience of the parties only and shall not affect the construction or interpretation of this Agreement.

(i) Recognition of the U.S. Special Resolution Regimes.

(a) In the event that the Agent is a Covered Entity and becomes subject to a proceeding under a U.S. Special Resolution Regime, the transfer from the Agent of this Agreement, and any interest and obligation in or under this Agreement, will be effective to the same extent as the transfer would be effective under the U.S. Special Resolution Regime if this Agreement, and any such interest and obligation, were governed by the laws of the United States or a state of the United States.

(b) In the event that the Agent is a Covered Entity or a BHC Act Affiliate of the Agent becomes subject to a proceeding under a U.S. Special Resolution Regime, Default Rights under this Agreement that may be exercised against the Agent are permitted to be exercised to no greater extent than such Default Rights could be exercised under the U.S. Special Resolution Regime if this Agreement were governed by the laws of the United States or a state of the United States.

(c) As used in this Section 8(i):

“BHC Act Affiliate” has the meaning assigned to the term “affiliate” in, and shall be interpreted in accordance with, 12 U.S.C. § 1841(k).

“Covered Entity” means any of the following:

(i) a “covered entity” as that term is defined in, and interpreted in accordance with, 12 C.F.R. § 252.82(b);

(ii) a “covered bank” as that term is defined in, and interpreted in accordance with, 12 C.F.R. § 47.3(b); or

(iii) a “covered FSI” as that term is defined in, and interpreted in accordance with, 12 C.F.R. § 382.2(b).

“Default Right” has the meaning assigned to that term in, and shall be interpreted in accordance with, 12 C.F.R. §§ 252.81, 47.2 or 382.1, as applicable.

“U.S. Special Resolution Regime” means each of (i) the Federal Deposit Insurance Act and the regulations promulgated thereunder and (ii) Title II of the Dodd-Frank Wall Street Reform and Consumer Protection Act and the regulations promulgated thereunder.

*[Signature Page Immediately Follows]*

If the foregoing is in accordance with your understanding of our agreement, kindly sign and return to the Company the enclosed copies hereof, whereupon this instrument, along with all counterparts hereof, shall become a binding agreement in accordance with its terms

Very truly yours,

**CORVUS PHARMACEUTICALS, INC.**

By: /s/ Leiv Lea

Name: Leiv Lea

Title: Chief Financial Officer

The foregoing Agreement is hereby confirmed and accepted by the Agent in New York, New York as of the date first above written.

**JEFFERIES LLC**

By: /s/ Michael Magarro

Name: Michael Magarro

Title: Managing Director

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**EXHIBIT A**

ISSUANCE NOTICE

[Date]

Jefferies LLC  
520 Madison Avenue  
New York, New York 10022

Attn: [\_\_\_\_\_]

Reference is made to the Open Market Sale Agreement between Corvus Pharmaceuticals, Inc. (the “**Company**”) and Jefferies LLC (the “**Agent**”) dated as of November 1, 2021. The Company confirms that all conditions to the delivery of this Issuance Notice are satisfied as of the date hereof.

Date of Delivery of Issuance Notice (determined pursuant to Section 3(b)(i)):

\_\_\_\_\_

Issuance Amount (equal to the total Sales Price for such Shares):

Number of days in selling period: \$ \_\_\_\_\_

First date of selling period: \_\_\_\_\_

Last date of selling period: \_\_\_\_\_

Settlement Date(s) if other than standard T+2 settlement:

\_\_\_\_\_

Floor Price Limitation (in no event less than \$1.00 without the prior written consent of the Agent, which consent may be withheld in the Agent’s sole discretion): \$ \_\_\_\_ per share

Comments: \_\_\_\_\_

\_\_\_\_\_  
By: \_\_\_\_\_  
Name:  
Title:



## Schedule A

### Notice Parties

#### The Company

Leiv Lea  
LLea@corvuspharma.com  
650-900-4522

#### The Agent

Michael Magarro  
mmagarro@jefferies.com  
(917) 421-1963

Donald Lynaugh  
dlynaugh@jefferies.com  
(917) 421-1946

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OFFICER'S CERTIFICATE

\_\_\_\_\_, 20\_\_

Reference is made to that certain Sale Agreement, dated as of November 1, 2021 (the "**Agreement**"), by and between Corvus Pharmaceuticals, Inc., a Delaware corporation (the "**Company**"), and Jefferies LLC. Capitalized terms used without definition herein shall have the meanings assigned thereto in the Agreement.

The undersigned, being the \_\_\_\_\_ of the Company, hereby certifies on behalf of the Company and not in a personal capacity (and with no personal liability therefor) as follows:

1. No stop order suspending the effectiveness of the Registration Statement is in effect, and no proceedings for such purpose are pending before or, to the best of my knowledge, threatened by the Commission.
2. The representations and warranties of the Company in Section 2 of the Agreement are true and correct on and as of the date hereof with the same force and effect as if expressly made on and as of the date hereof, except for those representations and warranties that speak solely as of a specific date and which were true and correct as of such date.
3. The Company has performed all of its obligations under the Agreement to be performed on or prior to the date hereof.

*[Signature Page Immediately Follows]*

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IN WITNESS WHEREOF, the undersigned has caused this certificate to be executed as of the date first written above.

\_\_\_\_\_  
Name:

Title:

\_\_\_\_\_

**List of Subsidiaries**

The following is a list of subsidiaries of the Company as of December 31, 2021:

<b>Subsidiary Legal Name</b>	<b>State or other Jurisdiction of Incorporation</b>
Corvus Biopharmaceuticals, Ltd.	Cayman Islands
Corvus Hong Kong Limited	Hong Kong

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**CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM**

We hereby consent to the incorporation by reference in the Registration Statements on Form S-3 (No. 333-237040), and Form S-8 (Nos. 333-255614, 333-223622, 333-216590, 333-210456, 333-231331 and 333-237933) of Corvus Pharmaceuticals, Inc. of our report dated March 25, 2021 relating to the financial statements, which appear in this Form 10-K.

/s/ PricewaterhouseCoopers LLP  
San Jose, California  
March 10, 2022

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## CERTIFICATIONS

I, Richard A. Miller, certify that:

1. I have reviewed this Annual Report on Form 10-K of Corvus Pharmaceuticals, Inc. for the year ended December 31, 2021;
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 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 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 10, 2022

/s/ RICHARD A. MILLER  
Richard A. Miller, M.D.  
*President and Chief Executive Officer*  
*(Principal Executive Officer)*

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## CERTIFICATIONS

I, Leiv Lea, certify that:

1. I have reviewed this Annual Report on Form 10-K of Corvus Pharmaceuticals, Inc. for the year ended December 31, 2021;
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 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 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 10, 2022

/s/ LEIV LEA

Leiv Lea

Chief Financial Officer

(Principal Financial and Accounting Officer)

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## SECTION 1350 CERTIFICATIONS\*

In connection with the Annual Report of Corvus Pharmaceuticals, Inc. (the “Company”) on Form 10-K for the fiscal year ended December 31, 2021, as filed with the Securities and Exchange Commission (the “Report”), Richard A. Miller, President and Chief Executive Officer (*Principal Executive Officer*) of the Company, and Leiv Lea, Chief Financial Officer (*Principal Financial and Accounting Officer*) of the Company, each hereby certifies, pursuant to the requirement set forth in Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended (the “Exchange Act”), and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. § 1350), that, to the best of his knowledge:

1. The Report, to which this Certification is attached as Exhibit 32.1, fully complies with the requirements of Section 13(a) or 15(d) of the Exchange Act; and
2. The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company for the period covered by the Report.

Dated: March 10, 2022

/s/ RICHARD A. MILLER

Richard A. Miller, M.D.

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

/s/ LEIV LEA

Leiv Lea

*Chief Financial Officer*  
(*Principal Financial and Accounting Officer*)

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\* This certification accompanies the Annual Report on Form 10-K, 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 the Company 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 Form 10-K), irrespective of any general incorporation language contained in such filing.

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