Corvus Pharmaceuticals, Inc.
Form 10-K
March 07, 2019
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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, 2018

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	001-37719	46-4670809
(State or other jurisdiction of incorporation)	(Commission File Number)	(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	Name of each exchange on which registered
Common Stock, $0.0001 par value	The 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 if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§ 229.405) is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10- K.

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	Accelerated filer	Non accelerated filer	Small reporting company
			Emerging growth company

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

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

As of June 30, 2018, the aggregate market value of the 14,272,642 shares of Common Stock held by non-affiliates of the registrant was approximately $156.7 million, computed by reference to the closing price as reported on The Nasdaq Stock Market. Shares of the registrant's common stock held by each officer and director and each person known to the registrant to own 10% or more of the outstanding common stock of the registrant have been excluded in that such persons may be deemed affiliates. This determination of affiliate status is not a determination for other purposes. As of March 7, 2019, 29,326,900 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 2019 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.

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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,” “expec “plan,” “anticipate,” “believe,” “estimate,” “intend,” “predict,” “seek,” “contemplate,” “potential” or “continue” or the negative terms or other comparable terminology. These forward looking statements include, but are not limited to, statements about:

- 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 CPI 444, CPI 006 and CPI-818, 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 trial of CPI 444 and CPI-006 and the timing and availability of clinical data from such clinical trials;
- clinical and regulatory development plans with respect to CPI 444, CPI 006 and our other product candidates, including CPI-818;
- our expectations regarding the potential market size and the size of the patient populations for CPI 444, CPI 006 and our other product candidates, including CPI-818, if approved for commercial use;
- our ability to commercialize CPI 444 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 and our ability to enter into strategic arrangements;
- 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;

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· 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.

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Part I

Item 1. Business

Overview

We are a clinical stage biopharmaceutical company focused on the development and commercialization of precisely targeted oncology therapies. Since we began operations in November 2014, we have built a pipeline of five oncology programs Three of our programs are aimed at disabling cancer's ability to subvert immune attack by inhibiting adenosine in the tumor microenvironment or by blocking its production by tumors. Adenosine activates an immune checkpoint, the adenosine A2A receptor, that is used by the body to limit inflammation and immune responses. Adenosine accomplishes this by interacting with the A2A and A2B receptors expressed on several cells of the immune system; including T cells, natural killer ("NK") cells, macrophages, dendritic cells and myeloid derived suppressor cells, as well as other cells. We are developing small molecules that selectively inhibit the binding of adenosine to either A2A receptors or to A2B receptors. We also are developing injectable monoclonal antibodies that block the production of adenosine by tumors by inhibiting the cell surface enzyme CD73. Our fourth program is aimed at developing product candidates that regulate T cell activation and differentiation by inhibiting interleukin 2 inducible kinase ("ITK"). Several of our product candidates are orally administered small molecules, which may provide for easier administration and facilitate their use in combination with other anti cancer agents. Our oral product candidates are designed to be rapidly eliminated from the body, which, in turn, could reduce the potential for excessive toxicity when used in combination with other antibody based checkpoint inhibitors.

We currently expect to have three product candidates in clinical trials during 2019. Our lead product candidate, CPI 444, is an oral, small molecule antagonist of the A2A receptor for adenosine and is currently being studied in our amended Phase 1b/2 protocol as a monotherapy and in combination with Genentech, Inc.'s cancer immunotherapy, Tecentriq® (atezolizumab). Our second product candidate, CPI-006, is an anti CD73 monoclonal antibody that inhibits the production of adenosine and is currently being studied in a Phase 1/1b clinical trial in combination with CPI-444 and pembrolizumab. Our third product candidate, CPI-818, is a selective, covalent inhibitor of ITK. We plan to advance CPI-818 into a multi-center Phase 1/1b clinical trial in patients with various malignant T-cell lymphomas in March 2019. In addition, we expect to begin IND enabling studies in 2019 for the development candidate we selected for our third adenosine program, a small molecule antagonist of the A2B receptor, as well as a monoclonal antibody to a novel target in immuno oncology that we in-licensed in 2017. We believe the breadth and status of our pipeline demonstrates our management team's expertise in understanding and developing oncology 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.

Oncology therapies that stimulate or enhance immune responses to tumors are a new and emerging approach with several potential benefits over existing therapies. First, the immune system exhibits immunologic diversity and selectivity, which enables it to respond selectively to a large number of potential targets. Second, once triggered, the immune response can be amplified, offering the potential to enhance the efficacy of treatment. Third, once activated, the immune system possesses immunologic memory, potentially providing for a durable and long lasting response. Some of the most successful types of immuno oncology therapies are immune checkpoint inhibitors. Immune checkpoints are signaling molecules produced by or expressed on immune cells that act to shut down or block an immune response. In a healthy person, these checkpoints function to limit an immune response to ensure that the immune system does not overreact, which could lead to excessive inflammation and tissue damage, as occurs in patients with autoimmune diseases or allergies. Tumor cells have evolved to activate these checkpoints to shield the tumor from immune response attacks, but studies have shown that immune checkpoint inhibitors can counter these tumor protective measures and unleash the immune system's cancer destroying properties.

The FDA has approved agents that target specific immune checkpoints, including antibodies against the cytotoxic T lymphocyte associated antigen 4 ("CTLA 4"), programmed death 1 ("PD 1") receptors, and programmed death receptor ligand 1 ("PD L1"). These antibodies represent the first immune checkpoint inhibitors to demonstrate effectiveness in the clinic, and preclinical data suggest that there are many other immune checkpoints or targets that may be modulated to promote the activation of a patient's anti tumor immune system. To date, antibodies targeting immune checkpoints have been approved to treat melanoma, lung, renal cell, breast, bladder, head and neck and other cancers.

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Since we began operations in November 2014, we have built a pipeline of five oncology programs. Our oncology product candidate pipeline includes the following:

CPI 444 Adenosine A2A Receptor Antagonist. Our lead product candidate, CPI 444, 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. In January 2016, we began enrolling patients in a large expansion cohort trial for CPI 444. This Phase 1/1b clinical trial is designed to examine safety, tolerability, biomarkers and preliminary efficacy of CPI 444 in several solid tumor types, both as a single agent and in combination with Genentech, Inc.'s cancer immunotherapy, Tecentriq® (atezolizumab), a fully humanized monoclonal antibody targeting PD L1. In November 2016, we completed enrollment of 48 patients in the first step of the Phase 1/1b clinical trial, which was designed to determine the optimal dose of CPI 444 as both a single agent therapy and in combination with Tecentriq for use in the cohort expansion stage of the trial. The expansion cohort portion of the trial enrolled patients with non small cell lung cancer ("NSCLC"), renal cell cancer ("RCC"), melanoma ("MEL"), triple negative breast cancer ("TNBC") and other cancers including colorectal cancer, prostate cancer, head and neck cancer and bladder cancer at leading medical centers in the U.S., Australia and Canada. We have enrolled over 250 patients in this clinical trial to date. In 2017, both the single agent and combination arms of the NSCLC and RCC cohorts met the protocol defined criteria for expansion from 14 to 26 patients, and both arms of the RCC cohort further met the protocol defined criteria for expansion to 48 patients. In December 2017, Genentech began enrolling patients in a Phase 1b/2 trial that is evaluating CPI 444 in combination with Tecentriq in patients with NSCLC under an umbrella protocol known as Morpheus. In 2018, we amended our Phase 1/1b protocol to enroll up to 50 patients with RCC who have failed therapies with both anti-PD-(L)1 antibodies and tyrosine kinase inhibitors ("TKI") in a Phase 1b/2 clinical trial.

To date, the key findings from these clinical trials include:

- CPI-444 is well-tolerated at doses that achieve substantial receptor blockade;
- Evidence of anti-tumor activity as monotherapy and in combination with atezolizumab;
- Of cancers studied, RCC and NSCLC appeared most responsive to therapy; and
- Expression of adenosine induced genes may provide usful biomarkers for selection of patients in future clinical trials.

The issued U.S. patents that we in licensed from Vernalis are directed to the composition of matter of CPI 444 and its method of use for treating disorders treatable by purine receptor blocking. The composition of matter patent covering CPI 444 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 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 CPI 444. We have also filed patent applications covering the use of CPI 444 in combination with other checkpoint inhibitors, and the use of various biomarkers to select and monitor patients receiving therapy.

CPI-006 Anti CD73 Adenosine Production Inhibitor. Our second product candidate, CPI-006, is an anti CD73 monoclonal antibody that inhibits the production of adenosine that we in licensed from The Scripps Research Institute ("Scripps") in December 2014. CPI-006 was developed into a humanized anti CD73 monoclonal antibody from a mouse hybridoma clone expressing an anti human CD73 antibody. We have further modified CPI 006 to improve binding to CD73 and maximize its inhibition of catalytic activity. 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. In preclinical in vitro studies, our humanized monoclonal anti CD73 antibody has been shown to inhibit the catalytic activity of CD73, resulting in the blocking of extracellular adenosine production by tumor cells, which we believe could stimulate or enhance immune response to tumors. In February 2018, we initiated a Phase 1/1b clinical trial with CPI-006 administered alone and in combination with CPI-444 and pembrolizumab. To date, the key findings from this clinical trial include the observation that CPI-006 has been

well-tolerated and results in change in lymphocyte migration and activation in peripheral blood.

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We hold a non exclusive, world wide license 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 CPI 006.

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 prevents fibrosis. In 2018, we selected a development candidate for this program, a small molecule antagonist of the A2B receptor. We intend to conduct IND enabling studies for this product candidate in 2019 for potential use in cancer or fibrotic diseases.

We hold an exclusive, worldwide license under certain Vernalis patent rights and know how, including a limited right to grant sublicenses, for all fields of use to develop, manufacture and commercialize products containing such compounds that have been developed using the intellectual property rights that we in license from Vernalis.

CPI-818 ITK Inhibitor. We have developed a selective, covalent inhibitor of ITK. 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 also may be useful in the treatment of T cell lymphomas. We have selected CPI-818 which was designed to bind selectively to T cells as our development candidate. It is orally bioavailable and has been shown to achieve cellular occupancy of the target in vivo in various animal models. To date, the key findings from our pre-clinical studies have demonstrated that CPI-818 is well-tolerated in vivo and results in inhibition of T-cell activation. We plan to advance CPI-818 into a multi-center Phase 1/1b clinical trial in patients with various malignant T-cell lymphomas in March 2019.

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

Myeloid Suppression. In 2017, we in-licensed a monoclonal antibody to a novel target in immuno oncology. This antibody is now undergoing optimization and we intend to conduct IND enabling studies for this product candidate in 2019.

Our Company Origins and Team

Since we began operations in November 2014, our focus has been on improving and expanding upon the recent success achieved with immune checkpoint inhibitors and on developing agents to new targets in the evolving immuno oncology field. Our founders and management team consist of industry veterans who have played significant roles in the discovery and development of successful oncology and immunology antibodies and drugs, including rituximab and ibrutinib. Our co founders include our Chief Executive Officer, Richard A. Miller, M.D., our Chief Financial Officer, Leiv Lea, and our Executive Vice President, Discovery Research, Joseph Buggy, Ph.D. Dr. Miller previously co founded IDEC (which merged to form Biogen IDEC, now Biogen), where he led research efforts on lymphoma, culminating in the development of rituximab. Dr. Miller, an oncologist, also co founded and was the initial CEO of Pharmacyclics, Inc. where he and colleagues in licensed ibrutinib and, together with Dr. Buggy, led its development. Our Chief Financial Officer, Leiv Lea, has previously led finance teams for emerging biotechnology companies, including Pharmacyclics. Mr. Lea has extensive commercial and operating experience in addition to having completed a number of financial and strategic transactions. We have recruited industry veterans and experts to join our management team, and established collaborations with leading biotechnology companies, including Genentech, and collaborative relationships with many leading academic research institutions. With our management

team's expertise in developing both small molecule and antibody based oncology treatments, we believe we are well positioned to identify and develop novel therapeutic agents that have diverse but complementary mechanisms of action, allowing for their potential integration into oncology treatment regimens for a broad variety of cancers.

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Our Strategy

Our goal is to become a leader in the in the discovery and development of precisely targeted treatments for multiple cancer indications. Specific elements of our strategy are:

•Leverage our expertise in immunology and oncology to identify, develop and commercialize new product candidates. We have established development expertise and capabilities in synthetic chemistry, molecular biology, immunology and clinical oncology, which we believe will help us advance product candidates in the oncology field. We plan to become a leader in the development and commercialization of product candidates targeting adenosine in what is known as the adenosine cancer axis, a key mechanism used by tumors to evade immune attack. Three of our product programs, are focused on the development of product candidates targeting this axis, including an A2A receptor antagonist (CPI-444), an anti CD73 antibody (CPI-006) and an A2B receptor antagonist. We have also in licensed a monoclonal antibody to a novel immuno oncology target that is independent of the adenosine axis. In addition to our internal research programs, we intend to seek opportunities to in license other product candidates with a focus on the potential to address unmet needs within our areas of expertise.

•Utilize efficient clinical trial designs to enable us to identify the most promising clinical indications. Our Phase 1/1b clinical trials are designed to evaluate multiple variables, such as single agent and combination therapy, impact of prior therapy with immuno oncology agents and the role of various biomarkers, which may allow us to determine tumor types that are most responsive to treatment with CPI 444 and CPI-006, alone or in combination. This approach has the potential to shorten development time by quickly identifying the most promising clinical indications, which would then be evaluated in subsequent definitive pivotal trials. For instance, in 2017, both the single agent and combination arms of the NSCLC and RCC cohorts met the protocol defined criteria for expansion, and both arms of the RCC cohort further met the protocol defined criteria for additional expansion. We believe the expansion design of our protocol has allowed us to select the most promising development path to date.

•Advance product candidates for use alone or in combination with other oncology treatments. We intend to focus on product candidates with single agent activity, which are also designed to be combined synergistically with other cancer therapies. We believe that many immuno oncology therapeutic regimens will likely be built on a backbone of anti PD 1/PD L1 blockade, and our initial Phase 1/1b clinical trial includes the administration of CPI 444 in combination with Tecentriq. Our Phase 1/1b clinical trial with CPI-006 includes the administration of CPI-006 both alone and in combination with CPI-444 and pembrolizumab. Our product candidates are designed to target the patient's immune system rather than a specific type of malignant cell, and, if approved, could be suitable as a single agent as well as in combination with current and future immunotherapy agents as well as traditional cancer treatments, including chemotherapy, biologic therapy, targeted therapy and radiation therapy.

•Identify biomarkers to select patients and monitor treatment with our product candidates. Predicting optimal drug responses in patients requires the identification and validation of predictive biomarkers. We believe that developing the ability to identify patient subsets most likely to respond to our product candidates will increase the clinical benefit to patients and improve the probability of success of our clinical trials. Our Phase 1/1b clinical trials of CPI 444 and CPI-006 include the examination of numerous biomarkers to identify those that may correlate with clinical efficacy and increase our likelihood of success. For instance, from our clinical data we believe we have discovered a novel adenosine gene expression signature, which could identify patients most likely to respond to treatment with adenosine blockade with CPI-444.

•Pursue collaborative relationships, partnerships and in licensing opportunities to help advance and expand our product candidate portfolio. In addition to developing product candidates through preclinical and clinical stages of development, we plan to identify and pursue strategic collaborative relationships, partnerships and in licensing opportunities, which could enhance the development of our programs and product candidates. As evidenced by our

collaboration with Genentech for CPI 444, we intend to build

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upon our relationships with leading biotechnology companies and research institutions to identify new new opportunities in cancer treatment.

Cancer Treatment and Immuno oncology

Cancer is the second leading cause of mortality in the United States, accounting for nearly one in every four deaths. Approximately 40% of Americans will develop some form of cancer, and, according to the American Cancer Society, there were 1.7 million new cases of cancer and 600,000 deaths due to cancer in the United States in 2017. Cancer treatment has traditionally included chemotherapy, biologic therapy, radiation, surgery or a combination of these approaches. Treatment with targeted agents that block cell signaling pathways or inhibit driver mutations in cancer cells is becoming more widely used. These agents often react with specifically mutated proteins in cancer or signaling molecules involved in cellular activation and proliferation. Many different mutations are now known to occur in cancer and, in many cases, are responsible for driving tumor progression.

Immuno oncology is an approach to treating cancer that is based on stimulating or enhancing an immune response to the tumor and is founded on the findings that the mutations occurring in cancer cells may be immunogenic and capable of eliciting an immune response against the tumor. Immuno oncology therapies offer several potential advantages over existing cancer therapies due to the intrinsic features of the immune system. For instance, the immune system exhibits immunologic diversity and selectivity, which enables it to respond to a large number of potential targets. In addition, once triggered, the immune response can be amplified, offering the potential to enhance the efficacy of treatment. Furthermore, once activated, the immune system possesses immunologic memory, potentially providing for a durable and long lasting response. Finally, because immunotherapy mechanisms are indifferent to tissue origin and are instead focused on immunogenic mutations, which are often expressed across tumor types, immunotherapy may be widely applicable to many types of cancer and not limited to a particular tumor type. This allows for these agents to be potentially active in a multitude of cancer histologies.

Recently, the reasons for the historical failures of immunologic approaches to cancer treatment have become better understood. Tumors evolve sophisticated survival mechanisms, allowing them to avoid immune mediated destruction as occurs with pathogens, such as bacteria or viruses. These mechanisms include the activation of immune checkpoints on cells of the immune system, which act to block immune responses, and the reprogramming of T cells to create an inflammatory environment that inhibits immune response and favors tumor growth. Immune checkpoints are signaling molecules produced by or expressed on immune cells that shut down or block an immune response. In a healthy person, these checkpoints function to limit an immune response to ensure that the immune system does not overreact, which could lead to excessive inflammation and tissue damage, as occurs in patients with autoimmune diseases or allergies. Tumors have evolved to activate these checkpoints to shield them from immune response attacks. However, studies have shown that these mechanisms can be countered using immune checkpoint inhibitors, which can unleash the immune system's cancer destroying properties. The new found understanding of immune checkpoints has led to a revolution in cancer treatment and the growing field of immuno oncology. Specific immune checkpoint inhibitors, including antibodies against CTLA 4, PD 1 receptor or its ligand PD L1 have produced impressive results in the clinic in a range of cancers, leading to FDA approvals for ipilimumab (anti CTLA 4), nivolumab (anti PD 1), pembrolizumab (anti PD 1), Tecentriq (anti PD L1), durvalumab (anti PD L1) and avelumab (anti PD L1).

Despite their recent success, current checkpoint inhibitors suffer from several limitations. Only a subset of patients treated with checkpoint inhibitors exhibit robust anti tumor responses, and responses are often partial and temporary. Many patients initially respond, but then relapse due to the emergence of resistant pathways, which may occur due to tumor cell expression of other checkpoints. Some patients experience unusual toxicities related to an over exuberant immune response against normal tissues leading to pneumonitis, hepatitis, colitis and other autoimmune related disorders. These limitations have motivated a search for other immune checkpoint targets and the use of combinations

of various checkpoint inhibitors in an attempt to improve efficacy, reduce resistance and limit or reduce toxicity. To date, the use of combinations of immune checkpoint inhibitors has been limited by excessive and serious autoimmune toxicities.

The recent success of checkpoint inhibitors has stimulated increased interest in utilizing various immunotherapy approaches to treating cancer, including vaccines, cellular therapies and other immunomodulatory agents. These approaches include modulating the function of various immune cells.

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Product Pipeline

We are developing novel checkpoint inhibitors and targeted agents that we believe may overcome some of the limitations of current therapies. Three of our programs are aimed at disabling cancer's ability to subvert immune attack by inhibiting adenosine in the tumor microenvironment or by blocking its production by tumors. Our fourth program is aimed at developing product candidates that regulate T cell activation and differentiation by inhibiting ITK, an enzyme important in T-cell differentiation and function. We intend to commercialize any approved product candidates primarily in the United States and Europe for any oncology indications our product candidates are approved for. We expect cancer patients or their healthcare providers to be our primary customers for any approved product candidates and expect that our commercial sales of such product candidates will depend on the availability of adequate coverage and reimbursement from government health administration authorities, private health insurers and other third party payors.

The following chart summarizes key information regarding our current product candidate pipeline and expected milestones:

Adenosine Inhibitors

Adenosine Cancer Axis and Anti tumor 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. The first step is the catalytic conversion of adenosine triphosphate ("ATP") to adenosine monophosphate ("AMP") by the enzyme CD39. The second and rate limiting step is the conversion of AMP to adenosine by CD73, an enzyme expressed on the surface of several types of immune cells, tumor cells and cells of certain other tissues. Under normal circumstances, the level of adenosine is increased to protect a person from over injury in response to such stimuli as inflammation, infection or ischemia. However, as a self protective maneuver, many tumor types actively sustain increased levels of extracellular adenosine by production through CD73 or by direct secretion of adenosine. These increased levels of adenosine 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 system known as the adenosine cancer axis.

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The following figure provides an overview of adenosine production by tumors and its effects on the immune system:

Adenosine Cancer Axis

Immunosuppressive Effects of Adenosine Mediated through Multiple Pathways

The immune system is composed of several cellular components that mediate a variety of functions in response to tumor cells and foreign pathogens. For instance, macrophages and dendritic cells function primarily to process foreign antigens and tumor antigens. These cells then present such antigens to other cells, such as T cells. The presentation of these antigens to T cells stimulates cytotoxic T cells (also known as killer T cells) to destroy the tumor cells or foreign pathogens. Other cells, such as NK cells, are capable of destroying tumor cells without the need for antigen presentation from macrophages or dendritic cells. In addition, certain immune cells, such as myeloid derived suppressor cells and T regulatory cells, function to suppress or dampen immune responses. The various cellular components of the immune system work in a coordinated manner to recognize and destroy pathogens and tumor cells, and then return the tissue to its normal state.

Adenosine hinders the immune response to tumors by both blocking the activation and effectiveness of immune cells capable of destroying tumor cells, and by increasing the number of immune cells that act to suppress immune cells from responding to the tumor. For instance, adenosine reduces T cell and NK cell production of cytokines, such as interleukin 2 (“IL 2”) and gamma interferon (“IFNg”), which results in the blockade or reduction in the ability of such cells to destroy tumor cells. Adenosine also leads to activation and proliferation of T regulatory cells, which function to suppress or dampen immune responses. In addition, adenosine causes dendritic cells to both decrease the rate at which they present antigens to T cells, thereby inhibiting the ability of T cells to destroy tumor cells, and decrease their production of co stimulatory cytokines, which also has the effect of suppressing or dampening the immune response. Macrophages exposed to adenosine will similarly decrease their function, which results in the suppression of immune activity. Finally, adenosine stimulates and increases the number of myeloid derived suppressor cells in the tumor microenvironment, which suppresses immune responses to the tumor. As tumor cells evolve and form cancerous growths, they utilize these processes to evade immune attack and promote their survival. Many of the effects of adenosine on the immune system are mediated through binding to A2A receptors present on several immune cells. Much less is known about A2B receptors, but they have recently been found on certain immune cells, such as macrophages and myeloid derived suppressor cells, and adenosine binding to A2B receptors also appears to play a role in tumor induced immune suppression.

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Cancer cells also appear to directly utilize adenosine to promote their own growth. Many solid tumors upregulate CD73 for increased adenosine production. In some cases, it appears adenosine can stimulate growth in tumors by increasing a tumor's blood supply.

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. Treatment with anti CD73 antibodies has been shown to inhibit tumor growth in several pre clinical animal tumor models.

Lead Product Candidate: CPI 444, an A2A selective, orally administered antagonist of the adenosine A2A receptor

Overview

Our lead product candidate, CPI 444, is a selective oral adenosine A2A receptor antagonist that we licensed from Vernalis in February 2015. Since licensing CPI 444, we have conducted extensive laboratory studies in vitro and in vivo in animal models to evaluate CPI 444's immune enhancing and anti tumor properties. In these studies, orally administered CPI 444 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 CPI 444 binds potently and selectively to human activated T cells and blocks adenosine mediated immunosuppression by restoring T cell function. In addition, we have shown that there is anti tumor activity in mice for a significant time following oral administration, which appears to be mediated through a long lasting memory immune response. Furthermore, we have shown in animal models that the treatment is well tolerated. Our IND in oncology was filed in October 2015, and we began enrolling patients in a Phase 1/1b clinical trial in January 2016. Preclinical data with CPI-444 was published in the journal Cancer Immunology Research in October 2018 demontrating that CPI-444 was active as a monotherapy and in combination with other agents in several tumor models.

CPI 444 Clinical Development Plan

In January 2016, we began enrolling patients in a Phase 1/1b, open label, expansion cohort design clinical trial for patients with selected advanced, incurable cancers. The trial is examining oral CPI 444 administered as both a single agent and in combination with Tecentriq. Under our clinical trial collaboration agreement with Genentech, we are responsible for the design, conduct and cost of the relevant studies, which are under the review of a joint development committee made up of our representatives and representatives of Genentech. Genentech supplies Tecentriq. Pre treatment and on treatment tissue, blood and serum samples are collected and tested for a wide range of biomarkers including the characteristics of immune cell infiltrates and expression of numerous genes in tumor tissue samples.

We are currently conducting the trial at leading medical centers in the United States, Australia and Canada. We have enrolled over 250 patients to date. Patients with NSCLC, MEL, RCC, TNBC, bladder cancer, prostate cancer or colorectal cancer with high mutation rates are eligible for participation. Studies by others, utilizing anti CTLA 4 therapies, anti PD 1 therapies and anti PD L1 therapies have shown that these tumors are more likely to possess immunogenic proteins that are capable of eliciting anti tumor immune responses. As a result, we believe that selecting patients with these types of tumors will enhance our chances of identifying patients responsive to CPI 444 therapy.

The primary objectives of our clinical trial for CPI 444, as a single agent and in combination with Tecentriq, are to:

•evaluate the safety and tolerability of CPI 444 in cancer patients;

•determine optimum dosage based on safety, pharmacokinetic and pharmacodynamic data;

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•assess primary efficacy endpoints: overall response rate, duration of clinical benefit defined as complete response, partial response and stable disease (stable disease defined as no disease progression for at least 3 months).

•assess secondary efficacy endpoints: include progression free survival, duration of response, and overall survival; and

•assess the potential role of various biomarkers to predict or monitor response to therapy.

We are conducting the clinical trial of CPI 444 in two steps:

•Step 1—Dose Selection: We initiated the first step of the clinical trial in January 2016. During this step, we determined the appropriate dosing based on safety, pharmacokinetic and biomarker studies. We randomized patients into one of four cohorts, with up to twelve patients per cohort. In three of the cohorts, we tested single agent CPI 444 at three different doses and schedules as follows: 100 mg twice per day for 14 days, 200 mg once per day for 14 days and 100 mg twice per day for 28 days. Treatment cycles are 28 days and patients continue on therapy until disease progression and/or toxicity. In the fourth cohort, we evaluated 100 mg twice per day for 14 days and then for 28 days in combination with a fixed dose of Tecentriq. In each case, patients continued the therapy until there was evidence of disease progression and/or toxicity. We completed the first step of the clinical trial in November 2016, after enrolling 48 patients, 47 of whom received study treatment and one of whom withdrew from the study prior to receiving any therapy. The optimum dose of CPI 444 selected for step 2 was based on safety and pharmacodynamics.

•Step 2—Dose Expansion: We initiated this portion of the clinical trial in November 2016. During this step, we have evaluated and plan to further evaluate the selected dose and schedule of CPI 444 as a single agent and in combination with Tecentriq in disease specific expansion cohorts. This phase of the study has ten cohorts, with five cohorts receiving single agent CPI 444 at a dose of 100mg twice per day for 28 days and five cohorts receiving the combination of CPI 444 at a dose of 100 mg twice per day for 28 days and Tecentriq. Patients are placed into disease specific cohorts based on type of cancer and prior exposure to an anti PD 1 or anti PD L1 antibody. Each cohort enrolled up to 14 patients, with cohorts expanded if evidence of anti tumor activity was shown. If a response (defined as partial or complete tumor response or disease stabilization for three months or more) in one or more patients out of 14 patients in a cohort was observed, then we expanded that cohort by twelve additional patients to a total of 26 patients. If a response in five or more patients out of 26 patients in the expanded cohort was observed, then expanded that cohort again by an additional 22 patients, for a total of 48 patients. To date, both the single agent and combination arms of the NSCLC and RCC cohorts met the protocol defined criteria for expansion from 14 to 26 patients, and both arms of the RCC cohort further met the protocol defined criteria for expansion to 48 patients. We have discontinued enrollment of NSCLC patients since the Morpheus trial began enrolling NSCLC paients. RCC patients are being enrolled pursuant to a protocol amendment that allows the enrollment of earlier stage RCC patients.

Evaluation of responses will be made according to the Response Evaluation Criteria in Solid Tumors (“RECIST”) criteria. RECIST is a set of published rules that define when tumors in cancer patients improve (respond), stay the same (stabilize), or worsen (progress) during treatments. The criteria were published in February 2000 by an international collaboration including the European Organization for Research and Treatment of Cancer, National Cancer Institute of the United States, and the National Cancer Institute of Canada Clinical Trials Group. The efficacy endpoints of the study were response rate and disease control rate (defined as complete response, partial response or stable disease). Partial response (“PR”) is defined as tumor regression of more than 30% of the tumor volume. Disease control is PR plus stable disease (“SD”). SD is reduction in tumor volume of less than 30% and no more than 20% increase in tumor volume.

The following is a schematic of the overall study design of our Phase 1/1b clinical trial showing three CPI 444 single agent dose selection cohorts and one combination CPI 444 and Tecentriq cohort followed by disease specific expansion cohorts that will receive single agent CPI 444 or CPI 444 combined with Tecentriq. The disease cohorts

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include NSCLC, MEL, RCC, TNBC and one additional cohort ("Other"), which includes bladder cancer, prostate cancer and colorectal cancer with high mutation rates.

Phase 1/lb Clinical Trial Protocol

CPI 444 Preliminary Clinical Trial Results

Results Presented at the Society for Immunotherapy of Cancer Annual Meeting—November 2018

Updated clinical and biomarker data in 68 patients with RCC from our Phase 1/1b clinical trial were presented in November 2018 at the Society for Immunotherapy of Cancer Annual Meeting. Data from 33 patients receiving CPI-444 as a monotherapy and 35 receiving CPI-444 in combination with atezolizumab who were evaluable for response were reported.

Updated results in patients with treatment-refractory RCC demonstrated an overall survival ("OS") of 88% at more than 20 months follow-up with CPI-444 administered in combination with atezolizumab. The OS for patients receiving CPI-444 alone was over 60% at 16 months. At the time of enrollment, study participants had advanced refractory disease and a poor prognosis. They had been treated with a median of three prior therapies (range: 1 to 5), and approximately 72% had failed prior anti-PD-(L)1 therapy. For more than 60% of patients, the protocol treatment represented a fourth, fifth or sixth line of therapy. Although activity was seen in other tumors studied, we are currently not pursuing those other indications.

A summary of the results are:

· Disease control for more than 6 months was observed in 35% and 17% of patients receiving combination therapy and monotherapy, respectively.

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- For patients receiving combination therapy, 11% experienced a confirmed 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 5.9 months with combination therapy and 4.0 months with monotherapy.
- OS was 88% at 20 or more months with combination therapy and 65% at 16 or more months with monotherapy.
- Combination therapy was superior to monotherapy with respect to OS, response rate, disease control rate and progression-free survival.
- Evaluation of pre- and on-treatment tumor biopsies showed a statistically significant correlation between treatment-induced CD8+ T-cell infiltration in tumors and response ($p<0.016$).
- The recently described adenosine signature showed a statistically significant correlation with tumor response and disease control rates ($p<0.008$).
- CPI-444 continues to be well tolerated to date. In the combination arm, adverse events were generally consistent with other anti-PD-L1 therapies. In the monotherapy arm, grade 3 adverse events were infrequent (less than 5%) and reversible.

These studies support the tumor immune enhancing potential of adenosine pathway blockade. The unique mechanism of action and safety suggest that this treatment 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 exhibits high levels of adenosine pathway related genes. We expect to be able to utilize this biomarker in future studies to target patients most likely to benefit from therapy with CPI-444.

Additional CPI 444 Clinical Trials

We believe the preliminary data from our clinical trial indicate that CPI 444 has single agent activity in multiple tumor histologies and in patients refractory to prior therapies with anti PD (L)1 antibodies. Based on these results, we have entered into a second collaboration agreement with Genentech, pursuant to which it will evaluate CPI 444 in combination with atezolizumab in patients with NSCLC that have previously failed a platinum containing chemotherapy regimen and an anti PD (L)1. This Phase 1b/2 clinical trial, which is currently enrolling patients, will be conducted under an umbrella protocol known as Morpheus. Up to 65 patients will be enrolled in this trial and compared to a control arm of patients receiving docetaxel, an approved treatment for NSCLC. We have also amended our ongoing Phase 1/1b protocol to enroll up to 50 patients with RCC that have failed only an anti PD (L)1 and a tyrosine kinase inhibitor.

Product Candidate: CPI-006, A monoclonal anti CD73 antibody for cancer

Overview

In December 2014, we in licensed from Scripps a mouse anti human CD73 antibody, CPI 006. We have genetically engineered CPI 006 to be humanized by replacing the immunoglobulin (“Ig”) heavy and light chain constant regions, and by replacing the murine variable framework regions with human heavy and light chain Ig frameworks. In

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addition, we have further engineered CPI 006 to enhance binding to CD73 and to block its catalytic activity, which we expect will inhibit conversion of AMP to adenosine by tumor cells.

The Role of CD73 in Cancer

CD73 is an enzyme expressed on lymphocytes and tumor cells that regulates immune responses by producing immunosuppressive adenosine. The catalytic production of adenosine by CD73 may play an important role in tumor immune suppression by increasing the concentration of adenosine in the tumor microenvironment. CD73 is overexpressed in many cancers, and high levels of CD73 have been shown to be associated with poor disease prognosis. CD73 expression on tumor cells as well as on the host immune cells has been shown to promote tumor immune suppression and metastasis in mice. Other studies in mice have shown that the targeted blockade of CD73 with antibodies can enhance the therapeutic activity of anti PD 1 and anti CTLA 4 checkpoint blockade. We believe CD73 and the adenosine cancer axis may play a role in acquired resistance to anti PD (L)1 therapies.

Preclinical Proof of Concept

In preclinical studies using tumor cells that express the CD73 enzyme, the addition of various concentrations of CPI 006 to such cells in culture substantially inhibited the catalytic activity of the enzyme to background levels of the assay. This was studied by measuring the conversion of AMP to adenosine. These studies demonstrated that at concentrations of 10 μg/ml, CPI 006 was capable of substantially inhibiting the production of adenosine, which indicates that CPI 006 binds to a critical site in the CD73 enzyme necessary for its function. By blocking the cellular production of adenosine, we believe CPI 006 could lead to enhancement of the anti tumor immune response by lowering the amount of adenosine in the tumor environment. As compared to other reported anti CD73 antibodies, CPI 006 has been shown in these preclinical studies to react with the active site of the CD73 enzyme and has not caused internalization of CD73. We believe this means it will act as a more potent blockade of the enzyme. In in vitro studies with human lymphocytes, CPI 006 has been shown to restore T-cell activation in the presence of AMP, indicating blockade of CD73 activity. CPI-006 has been found to possess other properties that are independent of adenosine. Its binding to CD73 results in activation of some lymphocytes and redistribution from blood to other lymphoid tissues. Other preclinical studies we conducted have shown that CPI 006 binds to a variety of different types of cancer cell lines in vitro, including those derived from human breast cancer, lung cancer, lymphoma, leukemias and sarcomas.

Anti CD73 Development Plan

In February 2018, we began enrollment in a multicenter Phase 1/1b expansion design trial that will evaluate CPI 006 as a single agent, in combination with our adenosine antagonist, CPI 444, and in combination with pembrolizumab (anti PD 1) in three arms, enrolling up to 350 patients. In each arm, CPI 006 will be administered in increasing doses to cohorts of patients until a maximally tolerated dose is determined for each arm. This will be followed by an expansion stage that will evaluate various tumor types, including RCC and NSCLC.

Thus far, we have dosed patients in the single agent arm of the trial and in the CPI-006 combination arm with CPI-444. No dose limiting toxicity has been observed to date. Initial data from the single-agent arm of the trial has demonstrated that CPI-006 blocked production of adenosine by inhibiting the enzymatic active site of CD73, activated peripheral blood B cells, and affected B lymphocyte trafficking in the blood.

Product Candidate: An antagonist of the adenosine A2B receptor

We are synthesizing and have identified A2B receptor antagonists from our internal research program. Adenosine A2B receptors have recently been found to play an important role in the immune response to tumors. Similar to

adenosine A2A receptors, adenosine binds to adenosine A2B receptors, which leads to immunosuppression. However, adenosine A2B receptor expression is found on different immune cells, and its function in tumor induced immune suppression is not yet well understood. We have selected a development candidate for our third adenosine program, a small molecule antagonist of the A2B receptor and expect to begin IND enabling studies in 2019 for potential use in cancer and fibrotic diseases.

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ITK Inhibitor

ITK and Anti tumor Immune Response

ITK is an enzyme expressed predominantly in T cells where it plays a key role in T cell signaling. 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 IFNg, 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.

Product Candidate: CPI-818, An ITK kinase inhibitor

CPI-818 is a selective, small molecule covalent inhibitor of ITK that we have selected as our lead development candidate for our ITK program. We identified ITK as a product candidate target because it plays a key role in T cell receptor signaling and in the differentiation of T cells responsible for tumor immunity. Small molecule inhibitors of ITK, such as ibrutinib, have been shown to shift the balance in signaling to enhance anti tumor immune responses in combination with a checkpoint inhibitor. While this observation provides important target validation, ibrutinib is primarily a BTK inhibitor and lacks the necessary potency and selectivity for ITK, which is believed to limit the clinical use of ibrutinib as an ITK inhibitor in this setting.

We have developed CPI-818 by targeting the cysteine amino acid residue at position 442 in the ITK protein. Covalent targeting of ITK is expected 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 co founders to generate ibrutinib. It is anticipated that the selectivity of CPI-818 will mimic the immune properties seen in ITK knockout mice and skew the immune response toward a more favorable anti tumor immune response.

In January 2018, we announced new preclinical data on CPI-818. These preclinical study results showed that orally administered CPI-818 achieved objective tumor responses in companion dogs with spontaneous, naturally occurring T-cell lymphomas, without significant toxicity. Data from in vitro studies of CPI-818 also demonstrated:

- Cytotoxicity against several types of human and mouse T-cell lymphomas at concentrations that do not harm normal T-cells.
- Evidence of Th1 skewing in human and mouse lymphocytes, indicating that CPI-818 induces the differentiation of T-cells to cytotoxic (killer) T-cells, which is thought to be an important component of the immune system's destruction of cancer cells.

We plan to advance CPI-818 into a Phase 1/1b clinical trial in March 2019 in patients with several types of T cell lymphomas including peripheral T-cell lymphoma ("PTCL"), cutaneous T-cell lymphoma ("CTCL"), angioimmunoblastic T-cell lymphoma ("AITL") and others.

Myeloid Suppression

In 2017, we in-licensed a monoclonal antibody to a novel target in immuno oncology. This antibody is now undergoing optimization and we intend to conduct IND enabling studies for this product candidate in 2019.

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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 CPI 444 and CPI-818 molecules and rely on one manufacturer for CPI-006 drug substance.

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 to develop and maintain strong intellectual property positions. We believe that the development experience of our scientific and management team, as well as the strength and promise of our product candidates, provide 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.

We are aware of companies that have advanced adenosine A2A receptor antagonists into early or late stage clinical development for non oncology indications, primarily Parkinson's disease. These companies include Merck & Co., Inc. that has evaluated preladenant in Parkinson's disease. In addition, Kyowa Hakko Kirin Pharma, Inc. has approval in Japan for an adenosine A2A receptor antagonist for use in Parkinson's disease and is currently conducting a Phase 3 study in the United States for Parkinson's disease. Within oncology, Novartis has announced an exclusive licensing agreement with Palobiofarma SL and is conducting a Phase 1 trial. AstraZeneca plc has licensed a preclinical A2A antagonist for use in cancer therapy from Heptares, Inc. 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 Squib, and Novartis in partnership with Surface Oncology, Inc. have initiated clinical trials with anti-CD73 antibodies in cancer patients. More generally, in the field of immuno-oncology, 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, Inc. and AbbVie Inc. 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. We do not yet own any issued patents relating to our product candidates. 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

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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 February 12, 2019, our owned, co owned, and licensed patent portfolio consisted of eleven licensed U.S. issued patents, three licensed U.S. pending patent applications, nine owned U.S. pending patent applications, thirteen owned or co owned U.S. provisional patent applications, and ten owned or co owned PCT International patent applications directed to CPI 444, CPI 006, and CPI-818, and certain of our other proprietary technology, inventions, improvements or other potential product candidates. In addition, our owned and licensed patent portfolio included forty four licensed patents, six licensed patent applications, and thirty-seven 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 CPI 444 and its method of use for treating disorders treatable by purine receptor blocking are expected to expire between January 2022 and July 2029, excluding any patent term extension that may be available. The pending U.S. 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 CPI 006 are expected to expire between December 2036 and June 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

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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 CPI 444. The issued U.S. patents that we in licensed from Vernalis pursuant to this agreement are directed to the composition of matter of CPI 444 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 CPI 444. We also must use commercially reasonable efforts to conduct certain preclinical and clinical studies to support the use of CPI 444 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 CPI 444 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 CPI 444 on a product by product and country by country basis, subject to certain offsets and reductions. The tiered royalty rates for products containing CPI 444 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 CPI 444 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

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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 CPI-006. 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 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 CPI-006) 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 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.

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 CPI 444 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. 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 CPI 444 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 CPI 444. Should we not reach agreement on the terms of such a license within a specified time period, we retain the right to enter into a license with another third party.

We and Genentech each have the right to terminate the agreement for material breach by the other party. In addition, the agreement may be terminated by either party due to safety considerations, if directed by a regulatory authority or if development of CPI 444 or Tecentriq is discontinued. Further, the agreement will expire after a set period of time following the provision by us of the final clinical study report to Genentech.

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In May 2017, we entered into a second clinical trial collaboration agreement with Genentech. Under the new agreement, CPI 444 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. It is anticipated that the study will enroll up to 65 patients in the treatment arm. Genentech will be 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 CPI 444 and retain global development and commercialization rights to CPI 444. We and Genentech each have the right to terminate the agreement for material breach by the other party. In addition, the agreement may be terminated by either party due to safety considerations, if directed by a regulatory authority or if development of CPI 444 or Tecentriq is discontinued. Further, the agreement will expire after a set period of time following the provision by us of the final clinical study report to Genentech.

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 NDA process and a new biologic must be approved by the FDA through the 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 GLP regulations and other applicable regulations;
- submission to the FDA of an IND, which must become effective before human clinical trials may begin;
- 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 for its intended use;
- submission to the FDA of an NDA or BLA;
- 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 Practices (cGMP) requirements to assure that the facilities, methods and controls are adequate to preserve the drug’s identity, strength, quality and purity; and
- FDA review and approval of the NDA or BLA.

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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 first phase of the clinical trial, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated, if the first phase 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 institutional review board ("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. Sponsors sometimes designate their Phase 1 trials as Phase 1a or Phase 1b. Phase 1b trials are typically aimed at confirming dosing, pharmacokinetics and safety in larger number of patients. Some Phase 1b studies evaluate biomarkers or surrogate markers that may be associated with efficacy in patients with specific types of diseases.
- Phase 2: This phase involves clinical trials 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: Clinical trials are undertaken to further evaluate dosage, clinical efficacy and safety in an expanded patient population at geographically dispersed clinical study sites. These clinical trials are intended to establish the overall risk benefit ratio of the product candidate and provide, if appropriate, 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.

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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 and before approval, progress reports summarizing the results of the clinical trials and nonclinical studies performed since the last progress report 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. Information related to the product, patient population, phase of investigation, trial sites and investigators and other aspects of the clinical trial is then made public as part of the registration. Sponsors are also obligated to discuss the results of their clinical trials after completion.

Disclosure of the results of these trials can be delayed until the new product or new indication being studied has been approved.

United States Review and Approval Process

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.

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 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. The approval process is lengthy and often difficult, and

the FDA may refuse to approve an NDA or BLA if the applicable regulatory criteria are not satisfied or may require additional clinical or other data and information. Even if such data and information are submitted, the FDA may ultimately decide that the NDA or BLA does not satisfy the criteria for approval. 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

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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.

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 pivotal Phase 3 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.

The Food and Drug Administration Safety and Innovation Act ("FDASIA") made permanent 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 indication for

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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 one of our product candidates for seven years if a competitor obtains approval of the same drug or biologic as defined by the FDA or if our 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. Orphan drug status in the European Union has similar but not identical benefits in that jurisdiction.

Although we have not sought or obtained orphan designation for any of our product candidates, we may pursue such designation in the future if we determine that our proposed indications meet the qualifying criteria for such designation.

Expedited Development and Review Programs

The FDA has a Fast Track program that is intended to expedite or facilitate the process for reviewing new drug products that meet certain criteria. Specifically, new drugs are eligible for Fast Track designation if they are intended to treat a serious or life threatening disease or condition and demonstrate the potential to address unmet medical needs for the disease or condition. Fast Track designation applies to the combination of the product and the specific indication for which it is being studied. Unique to a Fast Track product, the FDA may consider for review sections of the NDA or BLA 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.

Any product submitted to the FDA for approval, including a product with a Fast Track 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 product is eligible for priority review if it has the potential to provide safe and effective therapy where no satisfactory alternative therapy exists or a significant improvement in the treatment, diagnosis or prevention of a disease compared to marketed products. The FDA will attempt to direct additional resources to the evaluation of an application for a new drug 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 may be eligible for accelerated approval. Drug and biologic products intended to treat serious or life threatening diseases or conditions may be eligible for accelerated approval upon a determination that the product 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 receiving accelerated approval perform adequate and well controlled post marketing clinical trials. 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, priority review and accelerated approval do not change the standards for approval but may expedite the development or approval process.

FDASIA established a new category of drugs and biologics referred to as “breakthrough therapies” that may be eligible to receive Breakthrough Therapy Designation. A sponsor may seek FDA designation of a drug or biologic candidate as a “breakthrough therapy” if the product is intended, alone or in combination with one or more other products, to treat a serious or life threatening disease or condition and preliminary clinical evidence indicates that the product 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

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the Fast Track program features, as well as more intensive FDA interaction and guidance. The Breakthrough Therapy Designation is a distinct status from both accelerated approval and priority review, which can also be granted to the same drug if relevant criteria are met. If a product is designated as breakthrough therapy, the FDA will expedite the development and review of such drug. All requests for breakthrough therapy designation will be reviewed within 60 days of receipt, and the FDA will either grant or deny the request.

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 by us or our partners 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.

Patent Term Restoration and Marketing Exclusivity

Depending upon the timing, duration and specifics of FDA approval of our product candidates, some of the U.S. patents that we may be granted in the future may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the 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, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date. The patent term restoration period is generally one half the time between the effective date of an IND and the submission date of an NDA or BLA, plus the time between the submission date of an NDA or BLA and the approval of that application, less any time the applicant did not act with due diligence. Only one patent applicable to an approved drug is eligible for the extension, and the extension must be applied for prior to expiration of the patent. The United States Patent and Trademark

Office, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. In the future, we intend to apply for restorations of patent term for patents that may be issued to us, depending on the expected length of clinical trials and other factors involved in the filing of the relevant marketing application.

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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 marketing 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 ("BPCA") 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. To date, few biosimilars have been licensed under the BPCIA, although numerous biosimilars have been approved in Europe. 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. However, complexities associated with the larger, and often more complex, structures of biological products, as well as the processes by which such products are manufactured, pose significant hurdles to implementation of the abbreviated approval pathway that are still being addressed by the FDA.

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

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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.

The BPCIA is complex and continues to be interpreted and implemented by the FDA. In addition, recent government proposals have sought to reduce the twelve year reference product exclusivity period. Other aspects of the BPCIA, some of which may impact the BPCIA exclusivity provisions, have also been the subject of recent litigation. As a result, the ultimate impact, implementation and meaning of the BPCIA is subject to significant uncertainty.

Government Regulation Outside of the United States

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

Whether or not we obtain FDA approval for a product candidates, we must obtain the requisite approvals from regulatory authorities in foreign countries prior to the commencement of clinical studies or marketing of the product candidates in those countries. 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. In the European Union, for example, a clinical trial authorization ("CTA") must be submitted to each country's national health authority and an independent ethics committee, much like the FDA and the IRB, respectively. Once the CTA is approved in accordance with a country's requirements, clinical study development may proceed.

The requirements and process governing the conduct of clinical studies, product licensing, pricing and reimbursement vary from country to country. In all cases, the clinical studies are conducted in accordance with GCP and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

To obtain regulatory approval of an investigational biological product under European Union regulatory systems, we must submit a marketing authorization application. The application used to file the BLA in the United States is similar to that required in the European Union, with the exception of, among other things, country specific document requirements. The European Union also provides opportunities for market exclusivity. For example, in the European Union, upon receiving marketing authorization, new chemical entities generally receive eight years of data exclusivity and an additional two years of market exclusivity. If granted, data exclusivity prevents regulatory authorities in the European Union from referencing the innovator's data to assess a generic application. During the additional two year period of market exclusivity, a generic marketing authorization can be submitted, and the innovator's data may be referenced, but no generic product can be marketed until the expiration of the market exclusivity. However, there is no guarantee that a product will be considered by the European Union's regulatory authorities to be a new chemical entity, and products may not qualify for data exclusivity. Products receiving orphan designation in the European Union can receive ten years of market exclusivity, during which time no similar medicinal product for the same indication may be placed on the market. An orphan product can also obtain an additional two years of market exclusivity in the European Union for pediatric studies. No extension to any supplementary protection certificate can be granted on the basis of pediatric studies for orphan indications.

The criteria for designating an "orphan medicinal product" in the European Union are similar in principle to those in the United States. Under Article 3 of Regulation (EC) 141/2000, 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 European Union to justify investment; and (3) there exists no satisfactory method of diagnosis, prevention or treatment of such condition authorized for marketing in the European Union, or if such a method exists, the product

will be of significant benefit to those affected by the condition, as defined in Regulation (EC) 847/2000. Orphan medicinal products are eligible for financial incentives such as reduction of fees or fee waivers and are, upon grant of a marketing authorization, entitled to ten years of market exclusivity for the approved therapeutic indication. The application for orphan drug designation must be submitted before the application for marketing authorization. The

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applicant will receive a fee reduction for the marketing authorization application if the orphan drug designation has been granted, but not if the designation is still pending at the time the marketing authorization is submitted. 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. In addition, marketing authorization may be granted to a similar product for the same indication at any time if:

- the second applicant can establish that its product, although similar, is safer, more effective or otherwise clinically superior;
- the applicant consents to a second orphan medicinal product application; or
- the applicant cannot supply enough orphan medicinal product.

For other countries outside of the European Union, such as countries in Eastern Europe, Latin America or Asia, the requirements governing the conduct of clinical studies, product licensing, pricing and reimbursement vary from country to country. In all cases, again, the clinical studies 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.

Other Healthcare Laws

In addition to FDA restrictions on marketing of pharmaceutical and biological products, other U.S. federal and state healthcare regulatory laws restrict business practices in the pharmaceutical industry, which include, but are not limited to, state and federal anti kickback, false claims, data privacy and security and physician payment transparency laws. 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. 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 false claims and civil monetary penalties 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;

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- 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;
- 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 and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act ("HITECH"), and their respective implementing regulations, impose specified requirements relating to the privacy, security and transmission of individually identifiable health information held by covered entities and their business associates; 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

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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 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.

We expect that the current presidential administration and U.S. Congress will likely continue to seek to modify, repeal, or otherwise invalidate all, or certain provisions of, the Affordable Care Act.

For example, the Tax Cuts and Jobs Act was enacted, which, among other things, removes penalties for not complying with the Affordable Care Act'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 inseverable 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. While the Trump Administration and the Centers for Medicare & Medicaid Services have both stated that the ruling will have no immediate effect, it is unclear how this decision, subsequent appeals, if any, and other efforts to repeal and replace the ACA will impact the ACA. There may be additional challenges and amendments to the ACA in the future. We expect that the Affordable Care Act, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and lower reimbursement, and additional downward pressure on the price that we receive for any approved product. Any reduction in reimbursement from Medicare or other government funded programs may result in a similar reduction in payments from private payors. 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. 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.

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 up to 2% per fiscal year that will remain in effect through 2027 unless additional

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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.

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.

Research and Development Expenses

Our research and development expenses were $38.6 million, $46.3 million and $29.4 million for the years ended December 31, 2018, 2017, and 2016, 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.

Employees

As of December 31, 2018, we had 49 total employees, all of whom were full time and 40 of whom were primarily engaged in research and development activities.

Facilities

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

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Legal Proceedings

We are not currently a party to any material legal proceedings.

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://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 an emerging growth company as defined in the Jumpstart Our Business Startups Act of 2012 (JOBS Act). We will remain an emerging growth company until the earlier of (1) December 31, 2021, (2) the last day of the fiscal year in which we have total annual gross revenue of at least $1.07 billion, (3) the last day of the fiscal year in which we are deemed to be a "large accelerated filer" as defined in Rule 12b 2 under the Exchange Act, which would occur if the market value of our common stock held by non affiliates exceeded $700.0 million as of the last business day of the second fiscal quarter of such fiscal year, or (4) the date on which we have issued more than $1.0 billion in non convertible debt securities during the prior three year period. An emerging growth company may take advantage of specified reduced reporting requirements and is relieved of certain other significant requirements that are otherwise generally applicable to public companies. As an emerging growth company,

- We may present only two years of audited consolidated financial statements, plus unaudited condensed consolidated financial statements for any interim period, and related management's discussion and analysis of financial condition and results of operations;
- We may avail ourselves of the exemption from the requirement to obtain an attestation and report from our auditors on the assessment of our internal control over financial reporting pursuant to the Sarbanes Oxley Act of 2002 (Sarbanes Oxley);
- We may provide less extensive disclosure about our executive compensation arrangements; and
- We may not require stockholder non binding advisory votes on executive compensation or golden parachute arrangements.
- We have chosen to opt out of the extended transition periods available to emerging growth companies under the JOBS Act for complying with new or revised accounting standards. Section 107 of the JOBS Act provides that our decision to opt out of the extended transition periods for complying with new or revised accounting standards is irrevocable.

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://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

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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. 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, CPI-444 and CPI-006, and researching and developing additional product candidates, including CPI-818. 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 $46.9 million, $55.7 million and $36.4 million for the years ended December 31, 2018, 2017 and 2016, respectively. We had an accumulated deficit of $170.5 million as of December 31, 2018. 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 CPI-444 and CPI-006, and as we develop other product candidates, including the expected initiation of a Phase 1/1b clinical trial of CPI-818 in March 2019. 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 CPI-444, CPI-006 and CPI-818. 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 CPI-444, CPI-006, 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 CPI-444, CPI-006, CPI-818 or any other product candidates.

In March and April 2016, we completed our initial public offering ("IPO"), of our common stock pursuant to which we received proceeds of approximately $70.6 million, net of underwriting discounts and commission, and offering expenses, which included shares issued pursuant to the underwriters' exercise of their option in full to purchase additional shares of common stock. In March 2018, in a follow-on offering, we sold 8,117,647 shares of our common stock at a price of $8.50 per share, which included 1,058,823 shares issued pursuant to the underwriters' exercise of their

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option to purchase additional shares of common stock. We received aggregate net proceeds of approximately $64.9 million, after underwriting discounts, commissions and offering expenses.

As of December 31, 2018, we had capital resources consisting of cash, cash equivalents and marketable securities of $114.6 million. We do not expect our existing capital resources to be sufficient to enable us to fund the completion of our clinical trials and remaining development program of any of CPI-444, CPI-006 or CPI-818 through commercialization. In addition, 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 Sales Agreement we entered into with Cowen and Company, LLC in September 2017 in connection with our at-the-market offering (the "Sales Agreement"), 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 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 CPI-444, CPI-006 and CPI-818 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 need for, and the progress, costs and results of, any additional clinical trials of CPI-444, CPI-006, CPI-818 or any of our other product candidates we may initiate based on the results of our planned clinical trials or discussions with the FDA, 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 CPI-444, CPI-006, CPI-818 and our other product candidates, including commercial manufacturing if any product candidate is approved;

- the costs and timing of establishing sales and marketing capabilities;

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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;
- costs associated with any new product candidates that we may develop, in-license or acquire;
- 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.

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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 CPI-444, CPI-006, CPI-818 and our other product candidates, and we may be required to significantly curtail some or all of our activities.

Risks Related to the Discovery and Development of Our Product Candidates

Our product candidates are in early 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 are very early in our development efforts, with only two product candidates, CPI-444 and CPI-006, currently in early stage clinical development. In addition, we plan to advance CPI-818 into a multi-center Phase 1/1b clinical trial in patients with various malignant T-cell lymphomas in March 2019. 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 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;

- 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;

- delays in submitting 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 United States Food and Drug Administration (“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 or approval 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;

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- 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.

In addition, disruptions at the FDA and other regulatory agencies that are unrelated to our company or our products could also cause delays to the regulatory approval process for our products. For example, over the last several years, including in December 2018 and January 2019, the U.S. government has shut down several times and certain regulatory agencies, including the FDA, have had to furlough critical employees and stop critical activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions

We could find that the product candidates we or our collaborators pursue are not safe or efficacious. Furthermore, if one or more of our product candidates, particularly in relation to the adenosine pathway, 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 New Drug Application ("NDA") or Biologics License Application ("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 CPI-444, CPI-006 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 CPI-444, CPI-006 or CPI-818 will be successfully developed or commercialized. If we or any of our potential future collaborators are unable to develop, or obtain regulatory approval for, or, if approved, successfully commercialize CPI-444, CPI-006 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 potential future collaborators advance into clinical trials, including CPI-444, CPI-006 and CPI-818, 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. Prior to licensing our lead product candidate, CPI-444, it exhibited encouraging safety data in clinical studies performed by third parties. However, previous studies with CPI-444 had only been conducted in healthy volunteers and patients with attention deficit and hyperactivity disorder ("ADHD"). Since the initiation of our Phase 1/1b clinical trial in January 2016, CPI-444 been administered to more than 250 cancer patients and, while it has been well tolerated to date, 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 or amended Phase 1b/2 clinical trials for CPI-444 could respond in unexpected ways. Our Phase 1/1b clinical trial is 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 and Genentech's Phase 1b/2 clinical trial under our

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collaboration agreement, includes the administration of CPI-444 in combination with Genentech's cancer immunotherapy, Tecentriq, and we have recently been enrolling patients with various cancers to investigate higher doses of our drug as part of a protocol amendment, both of 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 CPI-444 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 or amended Phase 1b/2 clinical trials, Genentech's Phase 1b/2 clinical trial or any future clinical trial of CPI-444.

In March 2018, we began enrolling patients in our Phase 1/1b trial evaluating CPI-006. The protocol is designed to enroll successive cohorts of patients with advanced cancers who will receive increasing doses of CPI-006 both alone, or in combination with CPI-444 or an anti-PD-1. To date, a limited number of patients have been enrolled and, although no serious adverse events have been observed, the follow-up period has necessarily been short. However, CD73 is involved in several physiological systems and the administration of anti-CD73 antibodies such as CPI-006 could result in unforeseen safety issues. Similar to our Phase 1/1b clinical trial of CPI-444, it is possible that patients enrolled in our Phase 1/1b clinical trial for CPI-006 could respond in unexpected ways and that the administration of CPI-006 in combination with CPI-444 and pembrolizumab could exacerbate immune system related adverse events. As a result, there can be no assurance that we will be able to establish the safety and efficacy of CPI-006 or that we will be able to successfully complete our Phase 1/1b clinical trial.

We plan to advance CPI-818 into a multi-center Phase 1/1b clinical trial in patients with various malignant T-cell lymphomas in March 2019.

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.

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 for our other product candidates, we must submit the results of preclinical testing to the FDA along with other information, including information about product candidate chemistry, manufacturing and controls and our proposed clinical trial protocol, as part of an investigational new drug ("IND") application. In addition, we may rely in part on preclinical, clinical and quality data generated by clinical research organizations ("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 may require us to conduct additional preclinical testing for any product candidate before it allows us to initiate clinical testing under any IND, 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 trial for CPI-444 in January 2016 and our Phase 1/1b trial for CPI-006 in March 2018, we do not know whether any of our other planned trials, including CPI-818, 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 failing to grant permission to proceed or placing the clinical trial on hold;

· subjects failing to enroll or remain in our trial at the rate we expect;

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- subjects choosing an alternative treatment for the indication for which we are developing CPI-444, CPI-006 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 CPI-444, CPI-006, CPI-818, 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") 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.

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 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

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trials are delayed, our competitors may be able to bring products to market before we do, and the commercial viability of CPI-444, CPI-006, CPI-818 or other product candidates could be significantly reduced. Any of these occurrences may harm our business, financial condition and prospects significantly.

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 has 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 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 potential future collaborators' clinical trials;

- we or any of our 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 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;

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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 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 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 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 potential future collaborators from commercializing our product candidates.

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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.

In our ongoing trial of CPI-444, we have enrolled over 250 patients with many different types of cancer and the disease-specific cohort for renal cell cancer is continuing to enroll. We have also been adding patients with various cancers to investigate higher doses of our drug as part of a protocol amendment. Lung cancer patients are also being enrolled in a Phase 1b/2 trial being conducted by Genentech under our collaboration agreement. We are also enrolling patients with many different types of cancer in our Phase 1/1b trial of CPI-006. 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 accounted for 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.

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 in patients receiving combination therapy with CPI-444 and Tecentriq include hemolytic anemia, encephalitis, hepatitis, pneumonitis, mucositis and dermatitis. Other toxicities observed during our Phase 1/1b 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 and various endocrine diseases. Such side effects could also be exacerbated when CPI-444 is administered in combination with Tecentriq which is provided for in a portion of our Phase 1/1b clinical trial as well as in Genentech's Phase 1b/2 clinical trial under our collaboration agreement, or when CPI-444 is administered in higher doses, which we have begun exploring as part of a protocol amendment. In addition, CPI-444 is known to bind to the A1

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adenosine receptor. This receptor is expressed in the heart, and although CPI-444 binds to the A1 receptor at a low affinity, it is possible that sufficient binding of the drug to the A1 receptor could occur, leading to adverse effects on the heart such as irregular heart rate or rapid heart rate.

In March 2018, we began enrolling patients in our Phase 1/1b trial evaluating CPI-006. We expect that successive cohorts of enrolled patients will receive increasing doses of CPI-006 alone, or in combination with CPI-444 or an anti-PD-1. To date, a limited number of patients have been enrolled and, although no serious adverse events have been observed, the follow-up period has necessarily been short.

We plan to advance CPI-818 into a multi-center Phase 1/1b clinical trial in patients with various malignant T-cell lymphomas in March 2019.

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 CPI-444, CPI-006 and CPI-818. Although CPI-444 and CPI-006 are currently in clinical development and we plan to advance CPI-818 into Phase 1/1b clinical trial in March 2019, 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.

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We are conducting clinical trials for CPI-444 and CPI-006, and may in the future, conduct clinical trials of other product candidates, at sites outside the United States, and the FDA may not accept data from trials conducted in foreign locations.

We are currently conducting our clinical trial for CPI-444 at leading medical centers in the U.S., Australia and Canada. In the future, we may add additional clinical sites outside of the United States in our clinical trials for CPI-444, CPI-006 or for our planned clinical trial for CPI-818. Although the FDA may accept data from clinical trials conducted outside the United States, acceptance of this data is subject to certain conditions imposed by the FDA. For example, the clinical trial must be well designed and conducted and performed by qualified investigators in accordance with ethical principles. The study population must also adequately represent the U.S. population, and the data must be applicable to the U.S. population and U.S. medical practice in ways that the FDA deems clinically meaningful. In general, the patient population for any clinical studies conducted outside of the United States must be representative of the population for whom we intend to label the product in the United States. In addition, while these clinical trials are subject to the applicable local laws, FDA acceptance of the data will be dependent upon its determination that the studies also complied with all applicable U.S. laws and regulations. There can be no assurance the FDA will accept data from trials conducted outside of the United States. If the FDA does not accept the data from our clinical trials for CPI-444, CPI-006, our planned clinical trial for 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 CPI-444, CPI-006, CPI-818 or any other product candidates.

Risks Related to Our Reliance on Third Parties

We rely, and expect to continue relying, 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 Phase 1/1b clinical trial and our amended Phase 1b/2 clinical trial for CPI-444, our Phase 1/1b clinical trial for CPI-006, and our planned Phase 1/1b trial for CPI-818, and expect to continue to be dependent on third parties to conduct any future clinical studies of CPI-444, CPI-006, CPI-818 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 Economic Area (“EEA”) 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, EMA 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 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.

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If any of our clinical trial sites terminates for any reason, 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 or BLA we submit by the FDA. Any such delay or rejection could prevent us from commercializing CPI-444, CPI-006, CPI-818 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 submissions and approval of our product candidates. 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 CPI-444 and CPI-818 molecules and rely on one manufacturer for CPI-006 drug substance.

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

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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, 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 trial for CPI-006 and as we commence any clinical trials for additional product candidates, including CPI-818.

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

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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. 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.

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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 our product candidates, the FDA 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 CPI-444, CPI-006, CPI-818 or any other product candidate, such candidate will also be subject to ongoing FDA 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 CPI-444, CPI-006, CPI-818 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.

In addition, if CPI-444, CPI-006, CPI-818 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 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 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.

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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 policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. For example, in December 2016, the 21st Century Cures Act, or Cures Act, was signed into law. The Cures Act, among other things, is intended to modernize the regulation of drugs and biologics and spur innovation. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained, which would adversely affect our business, prospects and ability to achieve or sustain profitability.

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

Changes in funding for the FDA and other government agencies could hinder their ability to hire and retain key

leadership and other personnel, or otherwise prevent new products and services from being developed or commercialized in a timely manner, which could negatively impact our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory, and policy changes. Average review times at the agency 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 may also slow the time necessary for new drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, including for 35 days beginning on December 22, 2018, 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. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

Even if we receive regulatory approval we still may not be able to successfully commercialize CPI-444, CPI-006, CPI-818 or any other product candidate, and the revenue that we generate from sales, if any, could be limited.

Even if CPI-444, CPI-006, CPI-818 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;

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- 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 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 CPI-444, CPI-006, CPI-818 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 Affordable Care Act, 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 Affordable Care Act, among other things, subjected biological products to potential competition by

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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 and Congressional challenges to certain aspects of the Affordable Care Act, and we expect there will be additional challenges and amendments to the Affordable Care Act in the future. The current Presidential Administration and U.S. Congress has sought and will likely continue to seek to modify, repeal, or otherwise invalidate all, or certain provisions of, the Affordable Care Act. For example, the Tax Cuts and Jobs Act was enacted, which, among other things, removes penalties for not complying with the Affordable Care Act'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 inseverable 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. While the Trump Administration and the Centers for Medicare & Medicaid Services have both stated that the ruling will have no immediate effect, it is unclear how this decision, subsequent appeals, if any, and other efforts to repeal and replace the ACA will impact the ACA. There may be additional challenges and amendments to the ACA in the future, and it is uncertain the extent to which any such changes may impact our business or financial condition.

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 2027 unless additional Congressional action is taken and additional specific reductions in 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 Affordable Care Act, 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 European Union, 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 European Union or member state level may result in significant additional requirements or obstacles that may increase our operating costs. The delivery of healthcare in the European Union, including the establishment and operation of health services and the pricing and reimbursement of medicines, is almost exclusively a matter for national, rather than European Union, 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 European Union member states have resulted in restrictions on the pricing and reimbursement of medicines by relevant health service providers. Coupled with ever-increasing European Union 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

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regulate post-approval activities and affect our ability to commercialize our product candidates, if approved. In markets outside of the United States and European Union, 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 European Union 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 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. 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. As a result, its ultimate impact, implementation and meaning are subject to uncertainty, and 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.

Though CPI-444 is a small molecule and will not be regulated as a biological product, CPI-006, which we have begun evaluating in a Phase 1/1b clinical trial, is a biological product. We believe that any of our future product candidates 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. 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 indication 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.

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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, if approved, could qualify for orphan drug designation. For instance, if CPI-444, CPI-006 or CPI-818 is approved for the treatment of certain solid tumors with small patient populations, such as melanoma, renal or triple-negative breast cancer, it is possible that it could qualify for orphan drug designation with respect to such indications. As a result, we may seek to obtain orphan drug designation for our product candidates for any qualifying indications they may be approved for 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 with different active moieties can be approved for the same condition. Even after an orphan product is approved, the FDA can subsequently approve the same drug with the same active moiety 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 CPI-444, CPI-006 and CPI-818. 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 CPI-444, 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 CPI-444 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, CPI-444

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 CPI-444 or Tecentriq is discontinued. If we fail to maintain these strategic collaborations with Genentech (1) the development of CPI-444 in combination with Tecentriq may be terminated or delayed; (2) our cash expenditures related to development of CPI-444 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 CPI-444 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.

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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 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.

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.

All of our product candidates, if approved, will compete with a range of therapeutic treatments that are either in development or currently marketed. We are aware of companies that have advanced adenosine A2A receptor antagonists into early- or late-stage clinical development for non-oncology indications, primarily Parkinson’s disease. These companies include Merck & Co., Inc. that has evaluated preladenant in Parkinson’s disease. In addition, Kyowa Hakko Kirin Pharma, Inc. has approval in Japan for an adenosine A2A receptor antagonist for use in Parkinson’s disease and is currently conducting a Phase 3 study in the United States for Parkinson’s disease. Within oncology, Novartis has announced an exclusive licensing agreement with Palobiofarma SL and is conducting a Phase 1 trial. AstraZeneca plc

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has licensed a preclinical A2A antagonist for use in cancer therapy from Heptares, Inc. 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 Squib, and Novartis in partnership with Surface Oncology, Inc. have initiated clinical trials with anti-CD73 antibodies in cancer patients. More generally, in the field of immuno-oncology, 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, Inc. and AbbVie Inc. are co-marketing Imbruvica (ibrutinib), which is a small molecule inhibitor of the kinase BTK that has also been reported to inhibit ITK.

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 CPI-444, CPI-006, CPI-818 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

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confirmation that CPI-444, CPI-006, CPI-818 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 CPI-444, CPI-006, CPI-818 or any other product candidates that we may develop, in-license or acquire; and

- our direct sales and marketing efforts may not be successful.

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.

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 European Union, 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.

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 34% 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.

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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.

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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 CPI-444, CPI-006, CPI-818 and our other product candidates. As we seek to advance CPI-444, CPI-006, CPI-818 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 approval for any of our product candidates and begin commercializing those products in the United States, our operations may be directly, or indirectly through our customers and third-party payors, subject to various U.S. federal and state 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; 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 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;

- 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;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act and its implementing regulations, which also imposes obligations, including mandatory contractual terms, with

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respect to safeguarding the privacy, security and transmission of individually identifiable health information;

- 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) 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 and payments or other "transfers of value" to such physician owners (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; 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; and state and foreign laws governing the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

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 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 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 CPI-444, CPI-006, CPI-818 or our other product candidates.

We face an inherent risk of product liability as a result of the clinical testing of CPI-444, CPI-006, the planned clinical testing of CPI-818 and our other product candidates and will face an even greater risk if we commercialize our product candidates. For example, we may be sued if CPI-444, CPI-006, CPI-818 or our other product candidates

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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 CPI-444, CPI-006, CPI-818 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 CPI-444, CPI-006, CPI-818 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 CPI-444, CPI-006, CPI-818 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 potential future collaborators will be required to report to regulatory authorities if any of our approved products 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 potential future collaborators are successful in commercializing our products, the FDA and foreign regulatory authorities would require that we and any of our 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 potential future collaborators or CROs may fail to report adverse events within the prescribed timeframe. If we or any of our 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.

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Our internal computer systems, or those of any of our 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.

Despite the implementation of security measures, our internal computer systems and those of our current and any future CROs and other contractors, consultants and collaborators are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. 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, the media or individuals pursuant to various federal and state privacy and security laws, if applicable, including the Health Insurance Portability and Accountability Act of 1996, or HIPAA, as amended by the Health Information Technology for Clinical Health Act of 2009, or HITECH, and its implementing rules and regulations, as well as regulations promulgated by the Federal Trade Commission and state breach notification 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, 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.

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

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

Cybersecurity breaches could expose us to liability, damage our reputation, compromise our confidential information or otherwise adversely affect our business.

We maintain sensitive company data on our computer networks, 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 our security measures, our infrastructure may be vulnerable to attacks by hackers or other disruptive problems. 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. A cybersecurity breach could adversely affect our reputation and could result in other negative

consequences, including disruption of our internal operations, increased cyber security protection costs, lost revenues or litigation.

Business disruptions could seriously harm our future revenue and financial condition and increase our costs and expenses.

Our operations could be subject to earthquakes, power shortages, telecommunications failures, water shortages, floods, hurricanes, typhoons, fires, extreme weather conditions, medical epidemics 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 CPI-444 molecule and CPI-818 molecule, on one manufacturer for CPI-006 drug substance and other third-party manufacturers to produce our other product candidates. Our ability to obtain clinical supplies of CPI-444, CPI-006, CPI-818 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.

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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 CPI-444 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, CPI-006. 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.

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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 CPI-444, 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 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;

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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

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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 CPI-444 in that country. That Australian patent is expected to expire in 2022. Our ability to commercialize CPI-444 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 CPI-444, 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

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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 CPI-444, CPI-006, CPI-818 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 CPI-444, CPI-006, CPI-818 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 CPI-444, CPI-006, CPI-818 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 CPI-444, CPI-006, CPI-818 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 CPI-444, CPI-006, CPI-818 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 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

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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.

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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 CPI-444 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;

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- 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 FDA marketing approval of CPI-444, CPI-006 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

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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 CPI-444 in the United States and certain foreign territories, and pending patent applications directed at CPI-444, CPI-006, CPI-818 and other product candidates in the United States and other countries, filing, prosecuting and defending patents on CPI-444, CPI-006, CPI-818 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.

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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 maintained.

Prior to our IPO in March 2016, there had been no public market for our common stock. Although our common stock is listed on The Nasdaq Global Market ("Nasdaq"), an active trading market for our common stock may never 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 maintained, 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.

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

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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 CPI-444, CPI-006, CPI-818 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;
- regulatory developments in the United States and foreign countries;
- 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 expected 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;
- 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;

- 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,

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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, 2018, our executive officers, directors and greater than 5% stockholders, in the aggregate, owned approximately 66% 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.

Raising additional funds by issuing securities may cause dilution to our existing stockholders.

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. On September 20, 2017, we filed a prospectus supplement and entered into the Sales Agreement with Cowen and Company, LLC ("Cowen") to sell shares of our common stock, from time to time, with aggregate gross sales proceeds of up to $125,000,000, through an at-the-market equity offering program under which Cowen will act as our sales agent. As of December 31, 2018, we have sold 52,569 shares of common stock for gross proceeds of approximately $894,000 pursuant to the Sales Agreement. 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).

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

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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 an emerging growth company, and the reduced reporting requirements applicable to emerging growth companies may make our common stock less attractive to investors.

We are an "emerging growth company," as defined in the JOBS Act. For as long as we continue to be an emerging growth company, we may take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies, including, but not limited to, not being required to comply with the auditor attestation requirements of Section 404 of Sarbanes-Oxley, reduced disclosure obligations regarding executive compensation in our Annual Report on Form 10-K and our periodic reports and proxy statements and exemptions from the requirements of holding nonbinding advisory votes on executive compensation and stockholder approval of any golden parachute payments not previously approved. We will remain an emerging growth company until the earlier of (1) December 31, 2021, (2) the last day of the fiscal year in which we have total annual gross revenue of at least $1.07 billion, (3) the last day of the fiscal year in which we are deemed to be a "large accelerated filer" as defined in Rule 12b-2 under the Exchange Act, which would occur if the market value of our common stock held by non-affiliates exceeded $700.0 million as of the last business day of the second fiscal quarter of such fiscal year, or (4) the date on which we have issued more than $1.0 billion in non-convertible debt securities during the prior three-year period. If 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.

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.

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, when we lose our status as an “emerging growth company” and 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

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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

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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. For a description of our capital stock, see the section titled “Description of Capital Stock.”

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.

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, 2018, we had federal net operating loss (“NOL”) carryforwards of approximately $105.3 million and state NOL carryforwards of approximately $134.8 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, 2018, we also had $4.4 million of federal and $3.7 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 three year period in excess of 50 percentage points. Similar provisions under state tax law may also apply. We may have experienced an ownership change in the past, including in connection with our IPO and/or our March 2018 follow-on offering, and 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.

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. Our lease expires in 2023. We frequently explore alternatives that would provide us with additional space to accommodate our anticipated growth.

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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.

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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
2018		
First Quarter	$ 11.64	$ 7.42
Second Quarter	$ 13.91	$ 9.05
Third Quarter	$ 11.53	$ 8.50
Fourth Quarter	$ 9.19	$ 3.22
2017		
First Quarter	$ 22.14	$ 13.06
Second Quarter	$ 21.30	$ 8.27
Third Quarter	$ 17.64	$ 11.13
Fourth Quarter	$ 17.30	$ 9.11

Holders of Record

As of March 7, 2019, there were approximately 26 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.

Stock Performance Graph

The following graph shows the total stockholder's return on an investment of $100 in cash at market close on March 23, 2016 (the first day of trading of our common stock), through December 31, 2018 for (i) our common stock, (ii) the Nasdaq Composite Index and (iii) the Nasdaq Biotechnology Index.

Pursuant to applicable Securities and Exchange Commission rules, all values assume reinvestment of the full amount of all dividends, however, no dividends have been declared on our common stock to date. The stockholder return shown on the graph below is not necessarily indicative of future performance, and we do not make or endorse any predictions as to future stockholder return. This graph and the table below it shall not be deemed "soliciting material" or be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934 as amended (the "Exchange Act"), or otherwise subject to the liabilities under that Section, and shall not be deemed to be incorporated by reference into any

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of our filings under the Securities Act of 1933, as amended (the "Securities Act"), whether made before or after the date hereof and irrespective of any general incorporation language in any such filing.

$100 investment in stock or index	March 23, 2016	December 31, 2016	December 31, 2017	December 31, 2018
Corvus (CRVS)	$ 100.00	$ 100.35	$ 72.70	$ 25.75
NASDAQ Composite Index (IXIC)	$ 100.00	$ 112.88	$ 144.76	$ 139.14
NASDAQ Biotech Index (^NBI)	$ 100.00	$ 104.36	$ 126.33	$ 114.55

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

None.

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, 2018, 2017 and 2016 and the consolidated balance sheet data as of December 31, 2018 and 2017 are derived from our audited consolidated financial

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statements included elsewhere in this Annual Report on Form 10 K. The consolidated statement of operations data for the year ended December 31, 2015 and the period from January 27, 2014 (inception) to December 31, 2014 and the consolidated balance sheet data as of December 31, 2016, 2015 and 2014 are derived from our consolidated audited 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.

ted Statements of Operations and Comprehensive Loss Data:	Year Ended December 31, 2018	2017	2016	2015	P J 2 (t D 2
	(In thousands, except share and per share amounts)				
expenses:					
nd development	$ 38,586	$ 46,305	$ 29,356	$ 11,352	$
d administrative	10,636	10,219	7,620	2,418	
ating expenses	49,222	56,524	36,976	13,770	
operations	(49,222)	(56,524)	(36,976)	(13,770)	
fair value of convertible preferred stock liability	—	—	—	(17,600)	
come and other expense, net.	2,283	861	601	35	
	$ (46,939)	$ (55,663)	$ (36,375)	$ (31,335)	$
r share, basic and diluted	$ (1.71)	$ (2.72)	$ (2.36)	$ (83.86)	$
d to compute net loss per share, basic and diluted	27,509,960	20,488,506	15,422,041	373,643	
prehensive income (loss):					
l gain (loss) on marketable securities	7	(2)	6	(45)	
nsive loss	$ (46,932)	$ (55,665)	$ (36,369)	$ (31,380)	$

Consolidated Balance Sheet Data:	Year Ended December 31, 2018	2017	2016	2015	Period from January 27, 2014 (inception) to December 31, 2014
	(In thousands)				
Cash, cash equivalents and marketable securities	$ 114,597	$ 90,055	$ 134,896	$ 94,386	$ 12,517
Working capital	108,562	82,265	130,089	92,593	9,855
Total assets	118,232	94,775	140,150	98,459	12,529
Convertible preferred stock	—	—	—	125,780	10,011
Total stockholders' equity (deficit)	$ 110,336	$ 84,835	$ 132,801	$ (31,101)	$ (159)

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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 focused on the development and commercialization of precisely targeted oncology therapies. Since we began operations in November 2014, we have built a pipeline of five oncology programs, three of which focus on the adenosine cancer axis to modulate an immune response. Our lead product candidate, CPI 444, is an oral, small molecule antagonist of the A2A receptor for adenosine, an immune checkpoint. In January 2016, we began enrolling patients in a large expansion cohort trial for CPI 444. This Phase 1/1b clinical trial is designed to examine safety, tolerability, biomarkers and preliminary efficacy of CPI 444 in several solid tumor types, both as a single agent and in combination with Genentech, Inc.'s cancer immunotherapy, Tecentriq® (atezolizumab), a fully humanized monoclonal antibody targeting PD L1. In November 2016, we completed enrollment of 48 patients in the first step of the Phase 1/1b clinical trial, which was designed to determine the optimal dose of CPI 444 as both a single agent therapy and in combination with Tecentriq for use in the cohort expansion stage of the trial. The expansion cohort portion of the trial enrolled patients with non small cell lung cancer ("NSCLC"), renal cell cancer ("RCC"), melanoma ("MEL"), triple negative breast cancer ("TNBC") and other cancers including colorectal cancer, prostate cancer, head and neck cancer and bladder cancer at leading medical centers in the U.S., Australia and Canada. We have enrolled over 250 patients in this clinical trial to date. In 2017, both the single agent and combination arms of the NSCLC and RCC cohorts met the protocol defined criteria for expansion from 14 to 26 patients, and both arms of the RCC cohort further met the protocol defined criteria for expansion to 48 patients In December 2017, Genentech began enrolling patients in a Phase 1b/2 trial that is evaluating CPI 444 in combination with Tecentriq in patients with NSCLC under an umbrella protocol known as Morpheus. In 2018, we amended our Phase 1/1b protocol to enroll up to 50 patients with RCC who have failed therapies with both anti-PD-(L)1 antibodies and tyrosine kinase inhibitors (TKI).

The other product and development candidates in our pipeline also continue to advance. In February 2018, we began enrollment in a Phase 1/1b trial of our second program, an anti CD73 monoclonal antibody ("CPI 006") that inhibits the production of adenosine. In addition, we plan to advance CPI-818 into a multi-center Phase 1/1b clinical trial in patients with various malignant T-cell lymphomas in March 2019. In addition, we expect to begin IND enabling studies in 2019 for the development candidate we selected for our third adenosine program, a small molecule antagonist of the A2B receptor, as well as a monoclonal antibody to a novel target in immuno oncology that we in-licensed in 2017. We believe the breadth and status of our pipeline demonstrates our management team's expertise in understanding and developing oncology 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.

To date, the majority of our efforts have been focused on the research, development and advancement of CPI 444 and CPI-006, 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, 2018 and 2017 was $46.9 million and $55.7 million, respectively. As of December 31, 2018, we had an accumulated deficit of $170.5 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 CPI 444 and CPI-006, and as we develop other product candidates, including our expected initiation of a Phase 1/1b clinical trial of CPI 818 in March 2019. Even if we achieve profitability in the future, we may not be able to sustain profitability in subsequent periods.

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Since our inception and through December 31, 2018, we have funded our operations primarily through the sale and issuance of stock. On March 22, 2016, our registration statement on Form S 1 (File No. 333 208850) relating to our initial public offering ("IPO") of our common stock was declared effective by the SEC. Shares of our common stock began trading on the Nasdaq Global Market on March 23, 2016. The IPO closed on March 29, 2016, pursuant to which we sold 4,700,000 shares of our common stock at a public offering price of $15.00 per share. In April 2016, we sold an additional 502,618 shares of our common stock to the underwriters upon partial exercise of their over allotment option, at the initial offering price of $15.00 per share. We 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 of our outstanding shares of convertible preferred stock were converted into 14.3 million shares of our common stock. In March 2018, in a follow-on offering, we sold 8,117,647 shares of our 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. We received aggregate net proceeds of approximately $64.9 million, after underwriting discounts, commissions and offering expenses

In September 2017, we entered into a sales agreement (the "Sales Agreement") with Cowen and Company, LLC ("Cowen") to sell shares of the Company's common stock, from time to time, with aggregate gross sales proceeds of up to $125,000,000, through an at the market equity offering program under which Cowen will act as our sales agent. The issuance and sale of shares of common stock by us pursuant to the Sales Agreement are deemed an "at the market" offering under the Securities Act of 1933, as amended. Cowen 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 Cowen under the Sales Agreement.

As of December 31, 2018, we had capital resources consisting of cash, cash equivalents and marketable securities of approximately $114.6 million. We do not expect our existing capital resources to be sufficient to enable us to fund the completion of our clinical trials and remaining development program of any of CPI-444, CPI-006 or CPI-818 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.

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.

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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 of our product candidates. Our current planned research and development activities include the following:

- enrollment and completion of our Phase 1/1b and amended Phase 1b/2 clinical trials of CPI-444;
- enrollment of our ongoing Phase 1/1b clinical trial of CPI-006;
- we plan to advance CPI-818 into a multi-center Phase 1/1b clinical trial in patients with various malignant T-cell lymphomas in March 2019;
- process development and manufacturing of drug supply of CPI-444, CPI-006 and CPI-818; 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 1, 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.

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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 2017 to 2018	Change 2016 to 2017
	2018	2017	2016		
Operating expenses:					
Research and development	$ 38,586	$ 46,305	$ 29,356	$ (7,719)	$ 16,949
General and administrative	10,636	10,219	7,620	417	2,599
Total operating expenses	49,222	56,524	36,976	(7,302)	19,548
Loss from operations	(49,222)	(56,524)	(36,976)	7,302	(19,548)
Interest income and other expense, net	2,283	861	601	1,422	260
Net loss	$ (46,939)	$ (55,663)	$ (36,375)	$ 8,724	$ (19,288)

Research and Development Expenses

Research and development expense for the years ended December 31, 2018 and 2017, consisted of the following costs by program (specific program costs consist solely of external costs):

	Year ended December 31,			Change 2017 to 2018	Change 2016 to 2017
	2018	2017	2016		
CPI 444	$ 10,378	$ 23,156	$ 12,150	$ (12,778)	$ 11,006
CPI 006	6,108	6,008	2,823	100	3,185
CPI-818	4,707	1,791	1,655	2,916	136
Other Programs	877	581	591	296	(10)
Unallocated employee and overhead costs	16,516	14,769	12,137	1,747	2,632
	$ 38,586	$ 46,305	$ 29,356	$ (7,719)	$ 16,949

For the year ended December 31, 2018, the decrease in CPI 444 costs of $12.8 million as compared to the year ended December 31, 2017, primarily consisted of a $3.0 million milestone payment to Vernalis in 2017, a decrease of $7.4 million in clinical trial expenses associated with lower enrollment in accordance with our protocol amendment focusing on RCC patients, a decrease of $1.8 million in contracted research costs, and a decrease of $0.6 million in

drug manufacturing costs.

For the year ended December 31, 2018, the increase in CPI-006 costs of $0.1 million as compared to the year ended December 31, 2017, primarily consisted of a $2.5 million increase in clinical trial expenses, partially offset by a $1.6 million decrease in drug manufacturing costs and a $0.8 million decrease in IND-enabling study costs.

For the year ended December 31, 2018, the increase in CPI-818 costs of $2.9 million as compared to the year ended December 31, 2017, primarily consisted of a $1.9 million increase in drug manufacturing costs and a $1.0 million increase in IND-enabling study costs.

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For the year ended December 31, 2018, the increase in costs related to other programs of $0.3 million as compared to the year ended December 31, 2017, primarily consisted of outside chemical synthesis and testing of research compounds.

For the year ended December 31, 2018, the increase in unallocated costs of $1.7 million as compared to the year ended December 31, 2018, primarily consisted of an increase of $1.2 million in personnel and related costs (including an increase in stock compensation expense of $0.2 million) and an increase of $0.5 million in contracted research costs.

For the year ended December 31, 2017, the increase in CPI 444 costs of $11.0 million as compared to the year ended December 31, 2016, primarily consisted of an increase of $4.2 million in clinical trial costs related to our Phase 1/1b clinical trial, an increase of $1.6 million in drug manufacturing costs to support our clinical trial, an increase of $2.2 million in contracted research costs, and a $3.0 million license payment to Vernalis in 2017.

For the year ended December 31, 2017, the increase in CPI 006 costs of $3.2 million as compared to the year ended December 31, 2016, primarily consisted of an increase of $2.3 million in drug manufacturing costs and increase of $0.8 million in IND enabling study costs.

For the year ended December 31, 2017, the increase in CPI-818 costs of $0.1 million as compared to the year ended December 31, 2016, primarily consisted of pre clinical costs.

For the year ended December 31, 2017, costs related to other programs of $0.6 million were comparable to the year ended December 31, 2016, and primarily consisted of outside chemical synthesis and testing of research compounds.

For the year ended December 31, 2017, the increase in unallocated costs of $2.6 million as compared to the year ended December 31, 2016, primarily consisted of a $2.1 million increase in personnel and related costs due to an increase in headcount (including an increase in stock compensation expense of $1.0 million).

General and Administrative Expenses

For the year ended December 31, 2018, the increase in general and administrative expenses of $0.4 million as compared to the year ended December 31, 2017, primarily consisted of an increase of $0.7 million in stock compensation expense, partially offset by a decrease of $0.3 million in professional services costs.

For the year ended December 31, 2017, the increase in general and administrative expenses of $2.6 million as compared to the year ended December 31, 2016, primarily consisted of an increase of $1.8 million in personnel and related costs associated with an increase in headcount (including an increase in stock compensation expense of $1.4 million), an increase of $0.7 million in costs associated with being a public company and an increase of $0.1 million in facility related expenses.

Interest Income and Other Expense, net

For the year ended December 31, 2018, the increase in interest income and other expense, net of $1.4 million as compared to the year ended December 31, 2017, primarily consisted of additional interest income earned due to a higher rate of return on investments.

For the year ended December 31, 2017, the increase in interest income and other expense, net of $0.3 million as compared to the year ended December 31, 2016, primarily consisted of additional interest income earned due to a higher rate of return on investments.

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Liquidity and Capital Resources

Sources of Liquidity

As of December 31, 2018, we had cash, cash equivalents and marketable securities of $114.6 million and an accumulated deficit of $170.5 million, compared to cash, cash equivalents and marketable securities of $90.1 million and an accumulated deficit of $123.5 million as of December 31, 2017. We have financed our operations primarily through sales of our common stock and convertible preferred stock.

In March 2016, we consummated our IPO and sold 4,700,000 shares of our common stock at a price of $15.00 per share, and in April 2016, sold 502,618 shares at a price of $15.00 per share pursuant to the partial exercise of the underwriters' option to purchase additional shares of common stock. We received net proceeds of approximately $70.6 million, after deducting underwriting discounts, commissions and estimated offering expenses. Immediately prior to the consummation of our IPO, all outstanding shares of the convertible preferred stock were converted into common stock on a one for one basis.

In March 2018, in a follow-on offering, we sold 8,117,647 shares of our 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. We received aggregate net proceeds of approximately $64.9 million, after underwriting discounts, commissions and offering expenses

In September 2017, we entered into the Sales Agreement pursuant to which we may sell shares of our common stock from time to time with aggregate gross proceeds of up to $125,000,000, through an at-the-market equity offering program under the Sales Agreement. During the year ended December 31, 2018, the Company received no proceeds from the sale of shares of common stock pursuant to the 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 the year ended December 31, 2018. The amounts and timing of our actual expenditures depend on numerous factors, including:

- the initiation, progress, timing, costs and results of clinical trials for CPI 444, CPI-006 and CPI-818;
- 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

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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	Change 2016 to
	2018	2017	2016	2017 to 2018	2017
Net cash provided by (used in)					
Operating activities	$ (40,988)	$ (46,212)	$ (27,857)	$ 5,224	$ (18,355)
Investing activities	(30,192)	84,826	(42,556)	(115,018)	127,382
Financing activities	65,270	1,442	71,358	63,828	(69,916)
Net increase (decrease) in cash and cash equivalents	$ (5,910)	$ 40,056	$ 945	$ (45,966)	$ 39,111

Cash Flows from Operating Activities

Cash used in operating activities during the year ended December 31, 2018 was $41.0 million, which primarily consisted of a net loss of $46.9 million, adjusted by non cash charges of $7.4 million, primarily consisting of $7.1 million of stock compensation expense, a decrease of $2.0 million in accounts payable and accrued and other liabilities and an decrease of $0.6 million in current and other assets, primarily associated with the timing of payments to vendors.

Cash used in operating activities during the year ended December 31, 2017 was $46.2 million, which primarily consisted of a net loss of $55.7 million, adjusted by non cash charges of $6.9 million, primarily consisting of $6.2 million of stock compensation expense and $0.8 million of depreciation expense, an increase of $3.1 million in accounts payable and accrued and other liabilities, primarily associated with our increased research and development activities.

Cash used in operating activities during the year ended December 31, 2016 was $27.9 million, which primarily consisted of a net loss of $36.4 million, adjusted by non cash charges of $5.1 million and a net change of $3.4 million in our net operating assets. The non cash charges were primarily associated with stock based compensation expense of $3.8 million. The change in our net operating assets and liabilities was primarily attributable to an increase in accounts payable and accrued and other liabilities of $3.4 million, which was primarily due to the timing of payments to vendors.

Cash Flows from Investing Activities

Cash used in investing activities during the year ended December 31, 2018 was $30.2 million, which consisted of purchases of marketable securities of $161.9 million and purchases of property and equipment of $0.4 million, which were partially offset by proceeds from maturities of marketable securities of $132.0 million.

Cash provided by investing activities during the year ended December 31, 2017 was $84.8 million, which consisted of proceeds from maturities of marketable securities of $173.4 million, which was partially offset by purchases of marketable securities of $88.3 million and purchases of property and equipment of $0.3 million.

Cash used in investing activities during the year ended December 31, 2016 was $42.6 million, which consisted of purchases of marketable securities of $258.3 million and purchases of property and equipment of $2.2 million, which were partially offset by proceeds from maturities and sales of marketable securities of $217.9 million.

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Cash Flows from Financing Activities

Cash provided by financing activities during the year ended December 31, 2018 was $65.3 million, consisting of $64.9 million of net proceeds from our follow-on offering and $0.4 million of proceeds from the exercise of stock options.

Cash provided by financing activities during the year ended December 31, 2017 was $1.4 million, consisting of $0.7 million of stock sales and $0.7 million of proceeds from the exercise of stock options.

Cash provided by financing activities during the year ended December 31, 2016 was $71.4 million, consisting of the net proceeds from our IPO.

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

We lease our facilities under a non cancelable operating lease that expires in 2023. As of December 31, 2018, contractual obligations were as follows (in thousands):

	Payment Due by Period				
	Total	Less than 1 year	2 - 3 years	4 - 5 years	More than 5 years
Contractual obligations:					
Operating lease obligations	$ 4,908	$ 1,110	$ 2,393	$ 1,405	$ —
Total contractual obligations	$ 4,908	$ 1,110	$ 2,393	$ 1,405	$ —

In August 2015 we entered into an agreement for a line of credit of $0.1 million for the purpose of issuing our landlord a letter of credit of $0.1 million as a security deposit under our facility lease. We pledged money market funds and marketable securities as collateral for the line of credit. Pursuant to our license agreements with each of Vernalis and Scripps, we have obligations to make future milestone and royalty payments to these parties. However, because these amounts are contingent, they have not been included on our balance sheet.

Critical Accounting Policies

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. Our estimates are based 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 that the accounting policies discussed below are critical to understanding our historical and future performance, as these policies relate to the more

significant areas involving management's judgments and estimates. 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.

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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, 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.

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JOBS Act Accounting Election

We are an emerging growth company, as defined in the JOBS Act. Under the JOBS Act, emerging growth companies can delay adopting new or revised accounting standards issued subsequent to the enactment of the JOBS Act until such time as those standards apply to private companies. We have irrevocably elected not to avail ourselves of this exemption from new or revised accounting standards and, therefore, will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies. We also intend to rely on other exemptions provided by the JOBS Act, including, without limitation, providing an auditor's attestation report on our system of internal controls over financial reporting pursuant to Section 404(b) of the Sarbanes Oxley Act. We will remain an emerging growth company until the earlier of (1) December 31, 2021, (2) the last day of the fiscal year in which we have total annual gross revenue of at least $1.07 billion, (3) the last day of the fiscal year in which we are deemed to be a "large accelerated filer" as defined in Rule 12b 2 under the Exchange Act, which would occur if the market value of our common stock held by non affiliates exceeded $700.0 million as of the last business day of the second fiscal quarter of such fiscal year, or (4) the date on which we have issued more than $1.0 billion in non convertible debt securities during the prior three year period.

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 $114.6 million as of December 31, 2018, which consisted of U.S. government agency securities and corporate debt obligations. 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.

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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, 2018 and 2017, and the related consolidated statements of operations and comprehensive loss, changes in convertible preferred stock and stockholders' equity (deficit), and cash flows for each of the three years in the period ended December 31, 2018, 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, 2018 and 2017, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2018 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.

/s/ PricewaterhouseCoopers LLP

San Jose, California

March 7, 2019

We have served as the Company’s auditor since 2015

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CORVUS PHARMACEUTICALS, INC.

CONSOLIDATED BALANCE SHEETS

(in thousands, except share and per share data)

	December 31, 2018	2017
Assets		
Current assets:		
Cash and cash equivalents	$ 39,196	$ 45,106
Marketable securities	75,401	44,949
Prepaid and other current assets	992	1,179
Total current assets	115,589	91,234
Property and equipment, net	2,180	2,672
Other assets	463	869
Total assets	$ 118,232	$ 94,775
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 1,998	$ 3,454
Accrued and other liabilities	5,029	5,515
Total current liabilities	7,027	8,969
Other liabilities	869	971
Total liabilities	7,896	9,940
Commitments and contingencies (Note 11)		
Stockholders' equity:		
Preferred stock: $0.0001 par value; 10,000,000 shares authorized at December 31, 2018 and December 31, 2017; 0 shares issued and outstanding at December 31, 2018 and December 31, 2017	—	—
Common stock: $0.0001 par value; 290,000,000 shares authorized at December 31, 2018 and December 31, 2017; 29,323,930 and 21,041,250 shares issued and outstanding at December 31, 2018 and December 31, 2017, respectively	3	2
Additional paid-in capital	280,840	208,408
Accumulated other comprehensive loss	(34)	(41)
Accumulated deficit	(170,473)	(123,534)
Total stockholders' equity	110,336	84,835
Total liabilities and stockholders' equity	$ 118,232	$ 94,775

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

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CORVUS PHARMACEUTICALS, INC.

CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS

(in thousands, except share and per share data)

	Year Ended December 31,		
	2018	2017	2016
Operating expenses:			
Research and development	$ 38,586	$ 46,305	$ 29,356
General and administrative	10,636	10,219	7,620
Total operating expenses	49,222	56,524	36,976
Loss from operations	(49,222)	(56,524)	(36,976)
Interest income and other expense, net	2,283	861	601
Net loss	$ (46,939)	$ (55,663)	$ (36,375)
Net loss per share, basic and diluted	$ (1.71)	$ (2.72)	$ (2.36)
Shares used to compute net loss per share, basic and diluted	27,509,960	20,488,506	15,422,041
Other comprehensive income (loss):			
Unrealized gain (loss) on marketable securities	7	(2)	6
Comprehensive loss	$ (46,932)	$ (55,665)	$ (36,369)

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

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CORVUS PHARMACEUTICALS, INC.

CONSOLIDATED STATEMENTS OF CHANGES IN CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT)

(in thousands, except share and per share data)

	Convertible Preferred Stock		Common Stock		Aditional Paid-in	Accumlated Other Comprehensive	Accumelated	Total Stockhold Equity
	Shares	Amount	Shares	Amount	Capital	Income	Deficit	(Deficit)
alance at ecember 31, 2015	14,274,741	$ 125,780	1,431,615	$ —	$ 440	$ (45)	$ (31,496)	$ (31,101
onversion of eries A and B onvertible referred stock into ommon stock	(14,274,741)	(125,780)	14,274,741	1	125,779	—	—	125,780
suance of ommon stock upon itial public ffering, net	—	—	5,202,618	1	70,624	—	—	70,625
ommon stock sued on exercise f stock options	—	—	13,454	—	4	—	—	4
esting of restricted ock issued upon arly exercise of ock options	—	—	—	—	34	—	—	34
tock-based ompensation xpense	—	—	—	—	3,828	—	—	3,828
nrealized gain on arketable ecurities	—	—	—	—	—	6	—	6
et loss	—	—	—	—	—	—	(36,375)	(36,375
alance at ecember 31, 2016	—	$ —	20,922,428	$ 2	$ 200,709	$ (39)	$ (67,871)	$ 132,801
suance of ommon stock in onjunction with e Sales greement, net	—	—	52,569	—	711	—	—	711
ommon stock sued on exercise f stock options	—	—	66,253	—	731	—	—	731
	—	—	—	—	28	—	—	28

esting of restricted ock issued upon arly exercise of ock options tock-based ompensation xpense	—	—	—	—	6,229	—	—	6,229
nrealized loss on arketable ecurities	—	—	—	—	—	(2)	—	(2)
et loss	—	—	—	—	—	—	(55,663)	(55,663
alance at ecember 31, 2017	—	$ —	21,041,250	$ 2	$ 208,408	$ (41)	$ (123,534)	$ 84,835
suance of ommon stock upon llow-on public ffering, net	—	—	8,117,647	1	64,876	—	—	64,877
ommon stock ssued on exercise f stock options	—	—	165,033	—	393	—	—	393
esting of restricted ock issued upon arly exercise of ock options	—	—	—	—	28	—	—	28
tock-based ompensation xpense	—	—	—	—	7,135	—	—	7,135
nrealized gain on arketable ecurities	—	—	—	—	—	7	—	7
et loss	—	—	—	—	—	—	(46,939)	(46,939
alance at ecember 31, 2018	—	$ —	29,323,930	$ 3	$ 280,840	$ (34)	$ (170,473)	$ 110,336

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

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CORVUS PHARMACEUTICALS, INC.

CONSOLIDATED STATEMENTS OF CASH FLOWS

(in thousands)

	Year Ended December 31,		
	2018	2017	2016
Cash flows from operating activities			
Net loss	$ (46,939)	$ (55,663)	$ (36,375)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	847	842	594
Accretion related to marketable securities	(608)	(195)	648
Stock-based compensation	7,135	6,229	3,828
Changes in operating assets and liabilities:			
Prepaid and other current assets	187	(44)	290
Other assets	406	–	(869)
Accounts payable	(1,456)	1,554	518
Accrued and other liabilities	(458)	1,499	2,814
Other long-term liabilities	(102)	(434)	695
Net cash used in operating activities	(40,988)	(46,212)	(27,857)
Cash flows from investing activities			
Purchases of marketable securities	(161,861)	(88,309)	(258,281)
Sales of marketable securities	—	–	4,199
Maturities of marketable securities	132,024	173,401	213,725
Purchase of property and equipment	(355)	(266)	(2,199)
Net cash provided by (used) in investing activities	(30,192)	84,826	(42,556)
Cash flows from financing activities			
Proceeds from issuance of common stock, net (includes $30,850 and $34,000 in aggregate gross proceeds from related parties for the years ended December 31, 2018 and 2016, respectively)	64,877	711	71,354
Proceeds from exercise of common stock options	393	731	4
Net cash provided by financing activities	65,270	1,442	71,358
Net increase (decrease) in cash and cash equivalents	(5,910)	40,056	945
Cash and cash equivalents at beginning of the period	45,106	5,050	4,105
Cash and cash equivalents at end of the period	$ 39,196	$ 45,106	$ 5,050
Supplemental disclosures of cash flow information			
Purchases of property and equipment incurred but not paid	$ 84	$ –	$ 84

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

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CORVUS PHARMACEUTICALS, INC.

NOTE 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 focused on the development and commercialization of precisely targeted oncology therapies. The Company's operations are located in Burlingame, California. The Company has four insignificant subsidiaries.

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. 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, 2018, the Company had an accumulated deficit of $170.5 million and cash, cash equivalents and marketable securities of $114.6 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.

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.

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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. government agency securities and corporate debt obligations, 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 (deficit). 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.

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

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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.

Consolidation

The consolidated financial statements include the accounts of the Company and its wholly owned subsidiaries. Intercompany balances and transactions have been eliminated in consolidation.

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, 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.

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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 expense for options granted to non-employees is periodically re-measured as the underlying options vest. 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.

On December 22, 2017, the 2017 Tax Cuts and Jobs Act (the "Tax Act") was enacted into law and the new legislation contains several key tax provisions that affected the Comapny, including a one-time mandatory transition tax on accumulated foreign earnings and a reduction of the corporate income tax rate to 21% effective January 1, 2018. The Company is required to recognize the effect of the tax law changes in the period of enactment, such as determining the transition tax, remeasuring the Company's U.S. deferred tax assets and liabilities as well as reassessing the net realizability of deferred tax assets and liabilities. In December 2017, the SEC staff issued Staff Accounting Bulletin

No. 118, Income Tax Accounting Implications of the Tax Cuts and Jobs Act (SAB 118), which allowed the Company to record provisional amounts during a measurement period not to extend beyond one year of the enactment date. In accordance with this guidance, the Company recorded a decrease related to the net deferred tax asset balance of $4.9 million with a corresponding net adjustment to the Company's valuation allowance. During the year ending December 31, 2018, the Company did not record any measurement period adjustments to this amount as the Company's accounting

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for the Tax Act related to deferred remeasurement was complete during the period ending December 31, 2017. The Company's overall accounting for the impact of the 2017 Tax Act is complete as of the period ending December 31, 2018. Refer to Note 10 in these notes to the consolidated financial statements for additional information.

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 during the period, without consideration of potentially dilutive securities. Diluted net loss per share is computed by dividing the net loss by the weighted average number of common shares and potentially dilutive securities outstanding for the period. For purposes of the diluted net loss per share calculation, common stock subject to repurchase and stock options are considered to be potentially dilutive securities. Because the Company has reported a net loss for all periods presented, diluted net loss per common share is the same as basic net loss per common share for those periods.

Recent Accounting Pronouncements

In May 2014, the Financial Accounting Standards Board ("FASB") issued Accounting Standards Update ("ASU") No. 2014-09, Revenue from Contracts with Customers, which required an entity to recognize the amount of revenue to which it expects to be entitled for the transfer of promised goods or services to customers. ASU No. 2014-09 will replace most existing revenue recognition guidance in U.S. GAAP when it becomes effective. The new standard is effective January 1, 2018 for public companies. Early application is permitted as of January 1, 2017. The standard permits the use of either the retrospective or cumulative effect transition method. In March 2016, the FASB issued ASU No. 2016-08, Revenue from Contracts with Customers (Topic 606): Principal versus Agent Considerations (Reporting Revenue Gross versus Net), which clarifies the implementation guidance on principal versus agent considerations in ASU No. 2014-09. In April 2016, the FASB issued ASU No. 2016-10, Revenue from Contracts with Customers (Topic 606): Identifying Performance Obligations and Licensing, which clarifies certain aspects of identifying performance obligations and licensing implementation guidance. In May 2016, the FASB issued ASU No. 2016-12, Revenue from Contracts with Customers (Topic 606): Narrow-Scope Improvements and Practical Expedients, which relates to disclosures of remaining performance obligations, as well as other amendments to guidance on collectability, non-cash consideration and the presentation of sales and other similar taxes collected from customers. These standards have the same effective date and transition date of January 1, 2018. The Company adopted this guidance on January 1, 2018. The adoption of this guidance did not have a material impact on its condensed consolidated financial statements as the Company is not yet generating revenues.

In February 2016, the FASB, issued "ASU 2016-02, Leases." The standard requires entities to recognizew in the consolidated balance sheet a liability to make lease payments and a right-of-use asset representing its right to use the underlying asset for the lease term. We will adopt the standard on January 1, 2019 using the modified retrospective method in the year of adoption, and electing certain transition practical expedients. We are in the process of evaluating the impact of this standard and expect it to primarily relate to our operating leases for office and laboratory space noted in "Part I. Item 2. Properties" of this Annual Report on Form 10-K, for which we will record a lease liability and corresponding right-of-use asset upon adoption. We do not expect the adoption of this standard to impact accumulated deficit on January 1, 2019.

In May 2017, the FASB issued ASU No 2017-09, Compensation—Stock Compensation (Topic 718) — Scope of Modification Accounting, to clarify when to account for a change to the terms or conditions of a share-based payment award as a modification. Under the new standard, modification is required only if the fair value, the vesting conditions, or the classification of an award as equity or liability changes as a result of the change in terms or conditions. ASU 2017-09 was effective for the Company beginning January 1, 2018 and is applied prospectively. Early adoption is permitted. The Company adopted this guidance on January 1, 2018. The adoption of this guidance did not have a material impact

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on its consolidated financial statements as the Company has not made any changes to the terms or conditions of its share-based payment awards.

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,		
	2018	2017	2016
Numerator:			
Net loss - basic and diluted	$ (46,939)	$ (55,663)	$ (36,375)
Denominator:			
Weighted average common shares outstanding	27,686,909	20,958,557	16,188,980
Less: weighted average common shares subject to repurchase	(176,949)	(470,051)	(766,939)
Weighted average common shares outstanding used to compute basic and diluted net loss per share	27,509,960	20,488,506	15,422,041
Net loss per share, basic and diluted	$ (1.71)	$ (2.72)	$ (2.36)

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,		
	2018	2017	2016
Common stock subject to repurchase	43,076	319,203	611,698
Outstanding options	3,778,259	3,013,394	2,350,582
Total shares of common stock equivalents	3,821,335	3,332,597	2,962,280

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.

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The following tables present information as of December 31, 2018 and 2017 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, 2018			
	Fair Value Measured Using			Total
	(Level 1)	(Level 2)	(Level 3)	Balance
Assets				
Cash equivalents	$ 38,698	$ —	$ —	$ 38,698
Marketable securities	—	75,401	—	75,401
	$ 38,698	$ 75,401	$ —	$ 114,099

	December 31, 2017			
	Fair Value Measured Using			Total
	(Level 1)	(Level 2)	(Level 3)	Balance
Assets				
Cash equivalents	$ 44,555	$ —	$ —	$ 44,555
Marketable securities	—	44,949	—	44,949
	$ 44,555	$ 44,949	$ —	$ 89,504

As of December 31, 2018, marketable securities had a maximum remaining maturity of ten months.

As of December 31, 2018 and 2017, the fair value of available for sale marketable securities by type of security were as follows (in thousands):

	December 31, 2018			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
U.S. Government agency securities	$ 49,124	$ —	$ (27)	$ 49,097
Corporate debt obligations	26,311	—	(7)	26,304
	$ 75,435	$ —	$ (34)	$ 75,401

	December 31, 2017			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
U.S. Government agency securities	$ 32,311	$ —	$ (39)	$ 32,272
Corporate debt obligations	12,679	—	(2)	12,677
	$ 44,990	$ —	$ (41)	$ 44,949

5. 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.

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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. The first minimum annual fee payment is due on the first anniversary of effective date of the agreement and will be due on each subsequent anniversary of the effective date 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 $2.6 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 CPI-444. 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 CPI-444 in the Company's Phase 1/1b clinical trial. The aggregate potential milestone payments are approximately $220 million for all indications.

The Company has also agreed to pay Vernalis tiered incremental royalties based on the annual net sales of licensed products containing CPI-444 on a product-by-product and country-by-country basis, subject to certain offsets and reductions. The tiered royalty rates for products containing CPI-444 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 CPI-444 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 uncured 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.

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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 CPI-444 combined with Genentech's investigational cancer immunotherapy, Tecentriq, a fully humanized monoclonal antibody targeting protein programmed cell death ligand 1("PD-L1"), in a variety of solid tumors in a 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 representatives of the Company and representatives of Genentech. Genentech will supply Tecentriq. 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 CPI-444 in combination with an anti-PD-1 or anti-PD-L1 antibody. If the Company and Genentech 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 it decide to license development and commercialization rights to CPI-444. Should the Company and Genentech not reach agreement on the terms of such a license within a specified time period, it retains the right to enter into a license with another third party.

The Company and Genentech each have the right to terminate the agreement for material breach by the other party. In addition, the agreement may be terminated by either party due to safety considerations, if directed by a regulatory authority or if development of CPI-444 or Tecentriq is discontinued. Further, the agreement will expire after a set period of time following the provision by the Company of the final clinical study report to Genentech.

In May 2017, the Company signed a second clinical trial collaboration agreement with Genentech. Under the new agreement, CPI-444 administered in combination with Tecentriq will be 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. It is anticipated that the study will enroll up to 65 patients in the treatment arm. Genentech will be responsible for the conduct of the study and the parties 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 CPI-444 and retains global development and commercialization rights to CPI-444. The Company and Genentech each have the right to terminate the agreement for material breach by the other party. In addition, the agreement may be terminated by either party due to safety considerations, if directed by a regulatory authority or if development of CPI-444 or Tecentriq is discontinued.

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6. Balance Sheet Components (in thousands):

	December 31, 2018	2017
Prepaid and Other Current Assets		
Interest receivable	$ 337	$ 132
Prepaid research and development manufacturing expenses	75	327
Prepaid facility expenses	149	144
Prepaid insurance	166	164
Other	265	412
	$ 992	$ 1,179
Property and Equipment		
Laboratory equipment	$ 2,371	$ 2,034
Computer equipment and purchased software	142	130
Leasehold improvements	2,084	2,078
	4,597	4,242
Less: accumulated depreciation and amortization	(2,417)	(1,570)
	$ 2,180	$ 2,672
Accrued and Other Liabilities		
Accrued clinical trial related	$ 2,718	$ 2,870
Accrued manufacturing expense	1,077	1,056
Personnel related	649	572
Deferred rent	160	410
Accrued legal and accounting	77	224
Other accrued expenses	348	383
	$ 5,029	$ 5,515
Other Liabilities		
Deferred rent	$ 869	$ 960
Shares subject to vesting	—	11
	$ 869	$ 971

7. Common Stock

As of December 31, 2018, 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, 2018, no dividends on common stock had been declared.

On September 20, 2017, the Company entered into a sales agreement (the "Sales Agreement") with Cowen and Company, LLC ("Cowen") to sell shares of the Company's common stock, from time to time, with aggregate gross sales proceeds of up to $125,000,000, through an at-the-market equity offering program under which Cowen will act as its sales agent. The issuance and sale of shares of common stock by the Company pursuant to the Sales Agreement are deemed an "at-the-market" offering under the Securities Act of 1933, as amended. Cowen 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 Cowen under the Sales Agreement. During the year ended December 31, 2018 and 2017, the Company received no proceeds and approximately $0.7 million, respectively, from the sale of shares of common stock pursuant to the Sales Agreement.

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

	December 31,		
	2018	2017	2016
Shares available for future option grants	2,486,637	2,576,535	2,475,600
Outstanding options	3,778,259	3,013,394	2,350,582
Unvested restricted common stock (founders and early exercise of stock options)	43,076	319,203	611,698
Shares reserved for employee stock purchase plan	400,000	400,000	200,000
Total	6,707,972	6,309,132	5,637,880

8. 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 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:

		Options Outstanding	
	Shares Available for Grant	Number of Options	Weighted Average Exercise Price
Balance at December 31, 2017	2,576,535	3,013,394	$ 11.78
Additional shares authorized	840,000	—	—
Options granted	(1,449,250)	1,449,250	7.30
Options exercised	—	(165,033)	2.38
Options forfeited	519,352	(519,352)	12.85

Balance at December 31, 2018	2,486,637	3,778,259	$ 10.32

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The following table summarizes information about stock options outstanding at December 31, 2018 and 2017:

	Options Outstanding at December 31, 2018			Options Vested at December 31, 2018		
Exercise Price	Number	Weighted Average Remaining Contractual Life (in Years)	Weighted Average Exercise Price	Number	Weighted Average Remaining Contractual Life (in Years)	Weighted Average Exercise Price
$0.28 - $4.65	301,803	6.44	$ 0.72	261,373	6.42	$ 0.68
$5.94 - $9.52	1,101,750	9.92	$ 6.10	3,585	8.69	$ 8.92
$9.60 - $14.43	1,026,180	8.97	$ 10.89	269,731	8.70	$ 10.56
$15.00 - $16.70	1,348,526	7.50	$ 15.49	834,456	7.38	$ 15.37
	3,778,259	8.52	$ 10.32	1,369,145	7.46	$ 11.60

	Options Outstanding at December 31, 2017			Options Vested at December 31, 2017		
Exercise Price	Number	Weighted Average Remaining Contractual Life (in Years)	Weighted Average Exercise Price	Number	Weighted Average Remaining Contractual Life (in Years)	Weighted Average Exercise Price
$0.28 - $4.65	535,136	7.55	$ 1.46	325,397	7.53	$ 1.34
$6.75 - $10.60	701,600	9.86	$ 10.44	2,688	7.87	$ 6.75
$11.21 - $16.70	1,776,658	8.57	$ 15.41	596,727	8.28	$ 15.23
	3,013,394	8.69	$ 11.78	924,812	8.02	$ 11.40

The weighted average grant date fair value of options granted for the years ended December 31, 2018, 2017 and 2016, was $5.23, $8.93 and $10.78, respectively.

Options outstanding and exercisable that had vested or were expected to vest at December 31, 2018 were as follows:

	Number of shares	Weighted Average Exercise Price	Weighted Average Remaining Contractual Life (years)	Aggregate Intrinsic Value (in thousands)
Vested	1,369,145	$ 11.60	7.46	$ 804,162
Expected to vest	2,409,114	$ 9.60	6.83	$ 115,555

In the table above, aggregate intrinsic value represents the difference between the exercise price of the options to purchase common stock and the estimated fair value of the Company’s common stock of $3.67.

The aggregate intrinsic value of stock options exercised in the years ended December 31, 2018, 2017 and 2016, was $1.1 million, $0.3 million and $0.2 million, respectively.

The total fair value of options that vested in the year ended December 31, 2018, 2017 and 2016, was $7.1 million, $5.8 million, and $3.2 million, respectively.

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9. Stock Based Compensation

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

	Year Ended December 31,		
	2018	2017	2016
Research and development	$ 2,919	$ 2,692	$ 1,685
General and administrative	4,216	3,537	2,143
Total	$ 7,135	$ 6,229	$ 3,828

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, 2018, 2017 and 2016:

	Year Ended December 31,		
	2018	2017	2016
Risk-free interest rate	2.8 %	2.1 %	1.6 %
Expected volatility	82.7 %	91.4 %	84.6 %
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 used an average historical stock price volatility of comparable public companies within the biotechnology and pharmaceutical industry that have been indentified as the Company's industry peers.

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, 2018, 2017 and 2016, the unrecognized compensation expense associated with respect to options granted to employees was $15.8 million, $18.6 million and $18.5 million, respectively, and is expected to be recognized on a straight line basis over 2.72, 2.85, and 3.28 years, respectively.

Stock-based compensation expense related to awards to non-employees is recognized based on the then-current fair value at each measurement date over the associated service period of the award, which is generally the vesting term, on a straight line basis. The Company used the Black-Scholes valuation model to assist it in determining the fair value

of stock-based awards. Stock-based compensation expense for non-employees was $52,000, $74,000 and $142,500 for the years ended December 31, 2018, 2017 and 2016, respectively.

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The following assumptions were used in valuation of non-employee stock options:

	Year Ended December 31,		
	2018	2017	2016
Risk-free interest rate	2.55 % - 3.05 %	2.17 % - 2.33 %	1.90 % - 1.94 %
Expected volatility	83.2 % - 95.2 %	80.3 % - 83.0 %	92.1 % - 92.7 %
Expected term (in years)	6.1 - 10.0	7.1 - 7.6	8.1 - 8.6
Expected dividend yield	0 %	0 %	0 %

10. Income Taxes

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

	December 31,		
	2018	2017	2016
Domestic	$ (47,096)	$ (28,253)	$ (11,375)
Foreign	157	(27,410)	(25,000)
	$ (46,939)	$ (55,663)	$ (36,375)

During the years ended December 31, 2018, 2017 and 2016, 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,		
	2018	2017	2016
Federal tax benefit at statutory rate	21 %	34 %	34 %
State tax, net of Federal benefit	9 %	7 %	8 %
Foreign rate differential	—	(17) %	(23) %
Federal rate change impact	—	(9) %	—
Change in valuation allowance	(41) %	(16) %	(19) %
Research and development tax credits	2 %	2 %	2 %
Prior year federal true-up	10 %	(3) %	— %
Other	(1) %	2 %	(2)
Effective income tax rate	0 %	0 %	0 %

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

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

	December 31, 2018	2017	2016
Net operating loss carryforwards	$ 31,533	$ 15,438	$ 9,339
Tax credit carryforwards	6,441	4,351	1,960
Capitalized tax assets	138	131	241
Accruals	188	183	230
Stock compensation	2,879	1,730	954
Other	58	52	67
Total deferred tax assets	41,237	21,885	12,791
Valuation allowance	(41,237)	(21,885)	(12,791)
Net deferred tax assets	$ —	$ —	$ —

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The Company recorded a valuation allowance against its deferred tax assets at December 31, 2018 and 2017 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 $19.4 million and $9.1 million for the years ended December 31, 2018 and 2017, 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, 2018, the Company had federal NOL carryforwards of approximately $105.3 million and state NOL carryforwards of approximately $134.8 million which are available to reduce future taxable income. The NOLs will begin to expire in 2034, if not utilized.

As of December 31, 2018, the Company also had $4.4 million of federal and $3.7 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.

In general, if the Company experiences a greater than 50 percentage point aggregate change in ownership over a three-year period (a Section 382 ownership change), utilization of its pre-change NOL carryforwards are subject to an annual limitation under Section 382 of the Internal Revenue Code (California has similar laws). The annual limitation generally is determined by multiplying the value of the Company's stock at the time of such ownership change (subject to certain adjustments) by the applicable long-term tax-exempt rate. Such limitations may result in expiration of a portion of the NOL carryforwards before utilization. The Company has not utilized any NOL carryovers through December 31, 2018. In addition, the Company's deferred tax assets are subject to full valuation allowance, and thus no benefit for deferred tax assets have been recorded. The Company's ability to use the remaining NOL carryforwards may be further limited if the Company experiences a Section 382 ownership change as a result of changes in stock ownership. The Company is currently performing an analysis to determine whether any of its NOL carryforwards are limited due to a change in ownership.

On December 22, 2017, the U.S. government enacted comprehensive tax legislation commonly referred to as the Tax Cuts and Jobs Act (the "Tax Act"). The Tax Act makes broad and complex changes to the U.S. tax code, including, but not limited to, (1) reducing the U.S. federal corporate tax rate from 35% to 21%; (2) requiring companies to pay a one-time transition tax on certain unrepatriated earnings of foreign subsidiaries; (3) generally eliminating U.S. federal income taxes on dividends from foreign subsidiaries; (4) requiring a current inclusion in U.S. federal taxable income of certain earnings of controlled foreign corporations; (5) eliminating the corporate alternative minimum tax (AMT) and changing how existing AMT credits can be realized; (6) creating the base erosion anti-abuse tax (BEAT), a new minimum tax; (7) creating a new limitation on deductible interest expense; and (8) changing rules related to uses and limitations of net operating loss carryforwards created in tax years beginning after December 31, 2017.

The SEC staff issued SAB 118, which provides guidance on accounting for the tax effects of the Tax Act. SAB 118 provides a measurement period that should not extend beyond one year from the Tax Act enactment date for companies to complete the accounting under ASC 740. In accordance with SAB 118, a company must reflect the income tax effects of those aspects of the Tax Act for which the accounting under ASC 740 is complete. To the extent that a company's accounting for certain income tax effects of the Tax Act is incomplete but it is able to determine a reasonable estimate, it must record a provisional estimate in the financial statements. If a company cannot determine a provisional estimate to be included in the financial statements, it should continue to apply ASC 740 on the basis of the provisions of the tax laws that were in effect immediately before the enactment of the Tax Act. As of December 31, 2018, no provisional estimate has been recorded as the Company has completed its accounting under the Tax Act.

The Company's accounting for the following elements of the Tax Act is complete:

Reduction of US federal Corporate Tax Rate: The Tax Act reduces the corporate tax rate to 21%, effective January 1, 2018. Accordingly, the Company has re-measured all deferred taxes at 21% as of December 31, 2017. Consequently, the Company has recorded a decrease related to the net deferred tax asset balance of $4.9 million, with a corresponding net adjustment to the Company's valuation allowance.

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Deemed Repatriation Transition Tax: The Deemed Repatriation Transition Tax ("Transition Tax") is a tax on previously untaxed accumulated and current earnings and profits (E&P) of certain of our foreign subsidiaries. To determine the amount of the Transition Tax, the Company must determine, in addition to other factors, the amount of post-1986 E&P of the relevant subsidiaries, as well as the amount of non-U.S. income taxes paid on such earnings. The Company has a cumulative foreign E&P deficit as of December 31, 2017. As such, the Company does not have a transition tax liability in the 2017 tax year.

Global Intangible Low Taxed Income ("GILTI"): The Tax Act creates a new requirement that certain income (i.e., GILTI) earned by a controlled foreign corporations ("CFCs") must be included currently in the gross income of the CFCs' U.S. shareholder. GILTI is the excess of the shareholder's "net CFC tested income" over the net deemed tangible income return, which is currently defined as the excess of (1) 10 % of the aggregate of the U.S. shareholder's pro rata share of the qualified business asset investment of each CFC with respect to which it is a U.S. shareholder over (2) the amount of certain interest expense taken into account in the determination of net CFC-tested income. The Company is allowed to make an accounting policy election of either recognizing deferred taxes for temporary differences expected to reverse as GILTI in future years or recognizing such taxes as a current period expense when incurred. GILTI does not have a material impact on our 2018 financial statements

As of December 31, 2018, the Company had unrecognized tax benefits ("UTBs") of approximately $1.8 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,		
	2018	2017	2016
Unrecognized tax benefits beginning of the period	$ 1,219	$ 604	$ 135
Decrease related to the prior year	—	(51)	—
Increase related to the prior year	—	–	6
Increased related to the current year	585	666	463
Unrecognized tax benefits, end of the period	$ 1,804	$ 1,219	$ 604

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. The Company will recognize both accrued interest and penalties related to unrecognized benefits in income tax expense. The Company currently has no federal or state tax examinations in progress nor has it had any federal or state tax examinations since its inception. As a result of the Company's net operating loss carryforwards, all of its tax years are subject to federal and state tax examination.

11. Commitments and Contingencies

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 October 2018, 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 2023. 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. The lease requires the Company to pay additional amounts for operating and maintenance expenses. Rent expense related to the facilities lease for the years ended years ended December 31, 2018, 2017 and 2016 was approximately $748,000, $734,000 and $584,000, respectively. As of December 31, 2018, future minimum lease payments under the facility lease were as follows (in thousands):

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Year Ended December 31 (in thousands)	
2019	$ 1,110
2020	1,142
2021	1,251
2022	1,296
2023	109
Total	$ 4,908

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. 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 5.

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.

12. Related Party Transactions

In 2017, the Company purchased $461,000 of research services from a vendor during the normal course of business, where a Corvus director is also a member of the vendor's board of directors.

In March 2016, the Company completed its initial public offering of its common stock pursuant to which the Company sold 4,700,000 shares of its common stock. In April 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.

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.

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The following aggregate number of shares of common stock were sold to our owners of more than 5% of our common stock, directors, or executive officers during the 2018 and 2016 underwritten public offerings:

	2018 Public Offering		2016 Initial Public Offering	
	Number of Shares of Common Stock	Aggregate Purchase Price	Number of Shares of Common Stock	Aggregate Purchase Price
Owners of More Than 5% of Our Common Stock				
FMR LLC	1,176,470	$ 9,999,995	850,000	$ 12,750,000
Orbimed Advisors LLC (1)	588,235	4,999,998	550,000	8,250,000
Novo Holdings A/S (2)	1,176,470	9,999,995	666,666	9,999,990
Adams Street Partners (3)	588,235	4,999,998	200,000	3,000,000
Board of Directors				
Richard A. Miller, M.D.	100,000	850,000	—	—

(1) Peter Thompson, M.D., a member of our Board of Directors since November 2014, is a Private Equity Partner for OrbiMed Advisors, LLC.
(2) Peter Moldt, Ph.D., a Partner at Novo Ventures (US) Inc., which provide certain consultancy services to Novo Holdings A/S, served as a member of our Board of Directors from January 2015 to January 2019.
(3) Elisha P. (Terry) Gould III, a member of our Board of Directors since November 2014, is a Partner at Adams Street Partners, LLC.

13. Quarterly Selected Financial Data (unaudited)

	Quarter Ended			
(in thousands, except per share amounts)	December 31, 2018	September 30, 2018	June 30, 2018	March 31, 2018
Operating expenses	$ 11,171	$ 11,149	$ 12,258	$ 14,644
Net loss	(10,509)	(10,498)	(11,631)	(14,301)
Net loss per share, basic and diluted	$ (0.36)	$ (0.36)	$ (0.40)	$ (0.63)

	Quarter Ended			
(in thousands, except per share amounts)	December 31, 2017	September 30, 2017	June 30, 2017	March 31, 2017
Operating expenses	$ 12,189	$ 12,944	$ 15,174	$ 16,217
Net loss	(11,929)	(12,717)	(14,981)	(16,036)
Net loss per share, basic and diluted	$ (0.58)	$ (0.62)	$ (0.73)	$ (0.79)

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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, 2018, 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 adverse 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, 2018 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, 2018.

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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.

Attestation Report of the Registered Public Accounting Firm

This Annual Report on Form 10 K does not include an attestation report of our registered public accounting firm due to an exemption established by the JOBS Act for “emerging growth companies.”

Changes in Internal Control Over Financial Reporting

There were no changes in our internal control over financial reporting that occurred during the fiscal year ended December 31, 2018 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting

Item 9B. Other Information

Not applicable.

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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 Securities and Exchange Commission 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 Securities and Exchange Commission within 120 days after the Company's fiscal year end and is incorporated herein by reference.

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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.

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EXHIBIT INDEX

Exhibit Number	Exhibit Description	Incorporated by Reference Form	Date	Number	Filed Herewith
3.1	Amended and Restated Certificate of Incorporation.	8 K	3/29/2016	3.1	
3.2	Amended and Restated Bylaws.	8 K	3/29/2016	3.2	
4.1	Reference is made to Exhibits 3.1 through 3.2.				
4.2	Form of Common Stock Certificate.	S 1	1/4/2016	4.2	
4.3	Amended and Restated Investors' Rights Agreement, dated September 16, 2015, by and among Corvus Pharmaceuticals, Inc. and the investors listed therein.	S 1/A	2/8/2016	4.3	
10.1(a)	Office Lease, dated as of January 27, 2015, by and between Corvus Pharmaceuticals, Inc. and ARE 819/863 Mitten Road, LLC.	S 1	1/4/2016	10.2(a)	
10.1(b)	First Amendment to Office Lease, dated as of March 19, 2015, by and between Corvus Pharmaceuticals, Inc. and ARE 819/863 Mitten Road, LLC.	S 1	1/4/2016	10.2(b)	
10.1(c)	Second Amendment to Office Lease, dated as of August 20, 2015, by and between Corvus Pharmaceuticals, Inc. and ARE 819/863 Mitten Road, LLC	S 1	1/4/2016	10.2(c)	
10.1(d)	Third Amendment to Office Lease, dated as of June 27, 2016, by and between Corvus Pharmaceuticals, Inc. and ARE 819/863 Mitten Road, LLC.	10 Q	8/4/2016	10.1(d)	
10.1(e)	Fourth Amendment to Office Lease, dated as of August 15, 2016, by and between Corvus Pharmaceuticals, Inc. and ARE 819/863 Mitten Road, LLC.	10 Q	11/3/2016	10.1(e)	
10.1(f)	Fifth Amendment to Office Lease, dated as of March 2, 2018, by and between Corvus Pharmaceuticals, Inc. and ARE 819/863 Mitten Road, LLC.	10 Q	5/3/2018	10.3	
10.1(g)	Sixth Amendment to Office Lease, dated as of April 5, 2018, by and between Corvus Pharmaceuticals, Inc. and ARE 819/863 Mitten Road, LLC.	10 Q	8/2/2018	10.2	
10.1(h)	Seventh Amendment to Office Lease, dated as of October 11, 2018, by and between Corvus Pharmaceuticals, Inc. and ARE 819/863 Mitten Road, LLC.				X
10.2(a)#	2014 Equity Inventive Plan.	S 1	1/4/2016	10.4(a)	
10.2(b)#	Amendment to the 2014 Equity Incentive Plan, dated November 26, 2014.	S 1	1/4/2016	10.4(b)	
10.2(c)#	Amendment to the 2014 Equity Incentive Plan, dated July 24, 2015.	S 1	1/4/2016	10.4(c)	
10.2(d)#		S 1	1/4/2016	10.4(d)	

	Amendment to the 2014 Equity Incentive Plan, dated September 14, 2015.				
10.2(e)#	Form of Stock Option Grant Notice and Stock Option Agreement under the 2014 Equity Incentive Award Plan.	S	1	1/4/2016	10.4(e)
10.2(f)#	Form of Restricted Stock Purchase Right Grant Notice and Restricted Stock Purchase Agreement under the 2014 Equity Incentive Plan.	S	1	1/4/2016	10.4(f)
10.3(a)#	2016 Equity Incentive Award Plan.	S	8	3/29/2016	99.2(a)
10.3(b)#	Form of Stock Option Grant Notice and Stock Option Agreement under the 2016 Equity Incentive Award Plan.	S	1	1/4/2016	10.5(b)
10.3(c)#	Form of Restricted Stock Award Agreement and Restricted Stock Award Grant Notice under the 2016 Equity Incentive Award Plan.	S	1	1/4/2016	10.5(c)

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Exhibit Number	Exhibit Description	Incorporated by Reference Form	Date	Number	Filed Herewith
10.3(d)#	Form of Restricted Stock Unit Award Agreement and Restricted Stock Unit Award Grant Notice under the 2016 Equity Incentive Award Plan.	S 1	1/4/2016	10.5(d)	
10.4#	Form of Indemnification Agreement for directors and officers.	S 1	1/4/2016	10.6	
10.5#	Amended and Restated Employment Agreement, dated as of December 22, 2015, by and between Corvus Pharmaceuticals, Inc. and Richard A. Miller.	S 1	1/4/2016	10.7	
10.6#	Amended and Restated Employment Agreement, dated as of December 22, 2015, by and between Corvus Pharmaceuticals, Inc. and Leiv Lea.	S 1	1/4/2016	10.8	
10.7(a)#	Offer Letter, dated as of November 27, 2014, by and between Corvus Pharmaceuticals, Inc. and William B. Jones.	S 1	1/4/2016	10.9(a)	
10.7(b)#	Change in Control and Severance Agreement, dated December 23, 2015, by and between Corvus Pharmaceuticals, Inc. and William B. Jones.	S 1	1/4/2016	10.9(b)	
10.8(a)#	Offer Letter, dated as of December 28, 2014, by and between Corvus Pharmaceuticals, Inc. and Erik J. Verner.	S 1	1/4/2016	10.10(a)	
10.8(b)#	Change in Control and Severance Agreement, dated December 23, 2015, by and between Corvus Pharmaceuticals, Inc. and Erik J. Verner.	S 1	1/4/2016	10.10(b)	
10.9(a)#	Offer Letter, dated as of November 22, 2017 by and between Corvus Pharmaceuticals, Inc. and Daniel Hunt.	10-K	3/1/2018	10.9(a)	
10.9(b)#	Change in Control and Severance Agreement dated December 13, 2017, by and between Corvus Pharmaceuticals, Inc. and Daniel Hunt.	10-K	3/1/2018	10.9(b)	
10.10#	Employment Agreement, dated as of November 26, 2014 by and between Corvus Pharmaceuticals, Inc. and Joseph J. Buggy.	10-Q	5/3/2018	10.2	
10.11(a)#	Offer Letter, dated as of January 7, 2019 by and between Corvus Pharmaceuticals, Inc. and Mehrdad Mobasher.				X
10.11(b)#	Change in Control and Severance Agreement, dated January 28, 2019, by and between Corvus Pharmaceuticals, Inc. and Mehrdad Mobasher.				X
10.12#	Corvus Pharmaceuticals, Inc. 2016 Employee Stock Purchase Plan.	S 8	3/29/2016	99.3	
10.13#	Non Employee Director Compensation Program.	S 1	1/4/2016	10.12	
10.14(a)†	License Agreement, dated February 25, 2015, by and between Corvus Pharmaceuticals, Inc. and Vernalis (R&D) Limited.	S 1/A	3/10/2016	10.13(a)	
10.14(b)†	Amendment to License Agreement dated November 5, 2015, by and between Corvus	S 1	1/4/2016	10.13(b)	

	Pharmaceuticals, Inc. and Vernalis (R&D) Limited.					
10.15†	License Agreement, dated December 20, 2014, by and between Corvus Pharmaceuticals, Inc. and The Scripps Research Institute	S	1	1/4/2016	10.14	
10.16†	Collaboration Agreement, dated October 5, 2015, by and between Corvus Pharmaceuticals, Inc. and Genentech, Inc	S	1/A	2/8/2016	10.15	
10.17	Phase 1b/II Combination Study Agreement dated May 1, 2017, by and between Corvus Pharmaceuticals, Inc. and Genentech, Inc.	10	Q	8/3/2017	10.1	
10.18	Sales Agreement dated September 20, 2017, by and between Corvus Pharmaceuticals, Inc. and Cowen and Company, LLC.	8	K	9/20/2017	1.1	
21.1	List of Subsidiaries					X

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Exhibit Number	Exhibit Description	Incorporated by Reference Form	Date	Number	Filed Herewith
23.1	Consent of Independent Registered Public Accounting Firm.				X
24.1	Power of Attorney (included on signature page)				X
31.1	Certification by Chief Executive Officer pursuant to Section 302 of the Sarbanes Oxley Act of 2002.				X
31.2	Certification by Chief Financial Officer pursuant to Section 302 of the Sarbanes Oxley Act of 2002.				X
32.1**	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.				X
101.INS	XBRL Instance Document.				X
101.SCH	XBRL Taxonomy Extension Schema Document.				X
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document.				X
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document.				X
101.LAB	XBRL Taxonomy Extension Label Linkbase Document.				X
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document.				X

† Confidential treatment has been granted for a portion of this exhibit

# 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.

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SIGNATURES

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

CORVUS PHARMACEUTICALS, INC.

Date: March 7, 2019 By: /s/ RICHARD. A. MILLER
Richard A. Miller, M.D.
President, Chief Executive Officer and Director
(Principal Executive Officer)

Date: March 7, 2019 By: /s/ LEIV LEA
Leiv Lea
Chief Financial Officer
(Principal Financial and Accounting Officer)

POWER OF ATTORNEY

Each person whose individual signature appears below hereby authorizes and appoints Richard A. Miller, M.D. and Leiv Lea and each of them, with full power of substitution and resubstitution, as his or her true and lawful attorney in fact and agent to act in his or her name, place and stead and to execute in the name and on behalf of each person, individually and in each capacity stated below, and to file any and all amendments to this Annual Report on Form 10 K and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorney in fact and agents full power and authority to do and perform each and every act and thing, ratifying and confirming all that said attorney in fact and agents or his substitute or substitutes may lawfully do or cause to be done by virtue thereof. Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

/s/ RICHARD A. MILLER, M.D. Richard A. Miller, M.D.	President, Chief Executive Officer and Director (Principal Executive Officer)	March 7, 2019
/s/ LEIV LEA Leiv Lea	Chief Financial Officer (Principal Financial and Accounting Officer)	March 7, 2019
/s/ IAN T. CLARK Ian T. Clark	Director	March 7, 2019
/s/ TERRY GOULD Elisha P. (Terry) Gould III	Director	March 7, 2019
/s/ LINDA S. GRAIS, M.D., J.D. Linda S. Grais, M.D., J.D.	Director	March 7, 2019
/s/ STEVE E. KROGNES Steve E. Krognes	Director	March 7, 2019

/s/ SCOTT W. MORRISON Scott W. Morrison	Director	March 7, 2019
/s/ PETER THOMPSON, M.D. Peter Thompson, M.D.	Director	March 7, 2019