Calithera Biosciences, Inc.
Form 10-K
March 27, 2015

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

(Mark One)

x ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the fiscal year ended December 31, 2014

OR

¨TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934 FOR THE TRANSITION PERIOD FROM TO
Commission File Number 001-36644

CALITHERA BIOSCIENCES, INC.

(Exact name of Registrant as specified in its Charter)

Delaware (State or other jurisdiction of incorporation or organization)	27-2366329 (I.R.S. Employer Identification No.)
343 Oyster Point Blvd., Suite 200 South San Francisco, CA (Address of principal executive offices)	94080 (Zip Code)

Registrant's telephone number, including area code: (650) 870-1000

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

Common Stock, Par Value $0.0001 Per Share	Common stock traded on the NASDAQ stock market
(Title of Class)	(Name of Exchange on Which Registered)

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 x

Indicate by check mark if the Registrant is not required to file reports pursuant to Section 13 or 15(d) of the Act. YES ¨ NO x

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

Indicate by check mark whether the Registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the Registrant was required to submit and post such files). YES x 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. x

Indicate by check mark whether the Registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See the definition of "large accelerated filer", "accelerated filer", and "smaller reporting company" in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer	¨	Accelerated filer	¨
Non-accelerated filer	x (Do not check if a small reporting company)	Small reporting company	¨

Indicate by check mark whether the Registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). YES ¨ NO x

The registrant was not a public company as of the last business day of its most recently completed second fiscal quarter and, therefore, cannot calculate the aggregate market value of its voting and non-voting common equity held by non-affiliates as of such date.

The number of shares of Registrant's Common Stock outstanding as of March 20, 2015 was 17,946,393.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the Registrant's Definitive Proxy Statement relating to the 2015 Annual Meeting of Shareholders will be filed with the Commission within 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K and are incorporated by reference into Part III of this Annual Report on Form 10-K.

Table of Contents

CAUTIONARY INFORMATION REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K for the year ended December 31, 2014, or the Form 10-K, contains forward-looking statements concerning our business, operations, and financial performance and condition as well as our plans, objectives, and expectations for business operations and financial performance and condition. Any statements contained herein that are not of historical facts may be deemed to be forward-looking statements. You can identify these statements by words such as “anticipate,” “assume,” “believe,” “could,” “estimate,” “expect,” “intend,” “may,” “
“should,” “will,” “would,” and other similar expressions that are predictions of or indicate future events and future trends. These forward-looking statements are based on current expectations, estimates, forecasts, and projections about our business and the industry in which we operate and management's beliefs and assumptions and are not guarantees of future performance or development and involve known and unknown risks, uncertainties, and other factors that are in some cases beyond our control. As a result, any or all of our forward-looking statements in this Form 10-K may turn out to be inaccurate. Factors that could materially affect our business operations and financial performance and condition include, but are not limited to, those risks and uncertainties described herein under “Item 1A - Risk Factors.” You are urged to consider these factors carefully in evaluating the forward-looking statements and are cautioned not to place undue reliance on the forward-looking statements. The forward-looking statements are based on information available to us as of the filing date of this Form 10-K. Unless required by law, we do not intend to publicly update or revise any forward-looking statements to reflect new information or future events or otherwise. You should, however, review the factors and risks we describe in the reports we will file from time to time with the Securities and Exchange Commission, or the SEC, after the date of this Form 10-K.

PART I

Item 1. Business.

Overview

We are a clinical-stage pharmaceutical company focused on discovering and developing novel small molecule drugs directed against tumor metabolism and tumor immunology targets for the treatment of cancer. Tumor metabolism and tumor immunology have emerged as promising new fields for cancer drug discovery, and recent clinical successes with therapeutic agents in each field have demonstrated the potential to create fundamentally new therapies for cancer patients. Our lead product candidate, CB-839, is an internally discovered, first-in-class inhibitor of glutaminase, a critical enzyme in tumor metabolism. We are currently evaluating CB-839 in three Phase 1 clinical trials in solid and hematological tumors. Our lead preclinical program in tumor immunology is directed at developing inhibitors of the enzyme arginase and may provide a first-in-class therapeutic agent for this novel target. Our ongoing research efforts are focused on discovering additional product candidates against novel tumor metabolism and immunology targets.

The field of tumor metabolism seeks to exploit the unique ways in which cancer cells take up and utilize nutrients in order to grow and survive. It is now recognized that cancer cells rely on certain metabolic processes, or pathways, to a much greater extent than normal cells. The enhanced use of these pathways by cancer cells often results in a dependence on, or “addiction” to, these pathways that is not observed in normal cells. This creates an opportunity to selectively suppress the growth of cancer cells with therapeutic agents that specifically target these metabolic pathways.

Our lead product candidate in tumor metabolism, CB-839, takes advantage of the pronounced dependency many cancers have on the nutrient glutamine for growth and survival. CB-839 inhibits glutaminase, an enzyme required by cancer cells to utilize glutamine effectively. In preclinical studies, CB-839 demonstrated broad antitumor activity in

tumor cell lines, inhibited the growth of human tumors in animal models and was well tolerated in toxicity studies. CB-839 was also synergistic with several approved cancer therapeutics that are part of the current standard of care.

We are currently conducting three Phase 1 clinical trials of CB-839 in the United States in patients with solid tumors, leukemias, lymphomas and multiple myeloma. The purpose of these trials is to evaluate the safety of CB-839 both as a single agent and in combination with approved therapies and to seek preliminary evidence of efficacy. The dose escalation stage of these trials were conducted in 2014. Based on the dose identified during this stage, we are currently enrolling patient cohorts in select tumor types predicted to be sensitive to CB-839 based on results from our preclinical studies. CB-839 will be tested in these tumor types either as a single agent or in combination with approved therapies. We expect data to be available from our single agent trials in mid-2015 and from our combination trials in late 2015. Pending input from the U.S. Food and Drug Administration, or the FDA, on the results of our Phase 1 trials and our Phase 2 trial protocols, we plan to initiate one or more Phase 2 clinical trials in 2016 to study CB-839 as a single agent or in combination with approved therapies.

We believe CB-839 has the potential to be an important new therapeutic agent with a novel mechanism of action for the treatment of a broad range of cancers and is the only selective glutaminase inhibitor currently in clinical trials. Our clinical program seeks to identify cancers that will be most sensitive to CB-839 to allow the greatest benefit for patients and to pursue the most efficient

path to regulatory approval. We currently retain all commercial rights to CB-839 and have been granted a U.S. patent which includes composition of matter coverage for CB-839 through 2032.

Our second program in tumor metabolism is focused on the hexokinase II enzyme. A defining characteristic of most cancer cells is their increased uptake of glucose. Cancer cells use glucose in a different manner than normal cells, but an obligate first step in all glucose utilizing pathways is phosphorylation of glucose by the enzyme hexokinase. Due to their higher glucose needs, cancer cells frequently increase the level of this critical enzyme, specifically the isoform hexokinase II. We believe inhibitors of hexokinase II will significantly impede the ability of cancer cells to survive and proliferate may lead to new approaches in treating cancer. Our new program in hexokinase II inhibitors was in-licensed from TransTech Pharma and we seek to identify and advance a drug candidate into clinical development as quickly as possible. We will provide additional details on our development plans and timelines in the near future as we undertake pre-clinical studies to profile our portfolio of hexokinase II inhibitors.

The field of tumor immunology seeks to activate the body's own immune system to attack and kill cancer cells. Our preclinical program in tumor immunology is focused on developing selective inhibitors of the enzyme arginase. Arginase depletes arginine, a nutrient that is critical for the activation, growth and survival of the body's cancer-fighting immune cells, known as cytotoxic T cells. Secreted arginase is found in patients with certain cancers, including renal cancer, acute myeloid leukemia and other tumor types, and may play an immunosuppressive role by blocking T cell activation. We believe that inhibitors of arginase can promote an anti-tumor immune response by restoring arginine levels, thereby allowing activation of the body's cytotoxic T cells. In December of 2014 we entered into an exclusive global license agreement with Mars Symbioscience granting Calithera rights to research, develop and commercialize Symbioscience's portfolio of arginase inhibitors. Symbioscience's preclinical arginase inhibitor program will enhance Calithera's efforts to submit an Investigational New Drug application for an arginase inhibitor with the FDA for the treatment of cancer in early 2016.

Our Strategy

Our goal is to build a leading independent biopharmaceutical company. We intend to leverage our expertise to discover, develop and commercialize cancer therapies targeting tumor metabolism and tumor immunology pathways to treat patients with unmet medical needs. We intend to achieve our goal by:

Pursuing a broad clinical development program of CB-839 both as a single agent and in combination with approved therapies. CB-839 is an inhibitor of glutaminase, a tumor metabolism target that, based on our preclinical studies with cancer cell lines and animal tumor models, has been implicated in the growth and survival in multiple tumor types. Due to CB-839's novel mechanism of action, preclinical synergistic activity with existing cancer agents and favorable preclinical safety profile to date, we believe CB-839 has the potential to treat various cancers both as a single agent and in combination with approved therapies. We plan to pursue a broad development program for CB-839 focused on three distinct and significant opportunities:

- CB-839 as a single agent in cancers with large patient populations and significant unmet medical needs, such as triple-negative breast cancer, renal cell cancer, non-small cell lung cancer, and multiple myeloma.
- CB-839 in combination with standard of care drugs, including a cytotoxic agent for triple-negative breast cancer, an immunomodulatory agent for multiple myeloma, and signal transduction pathway inhibitors for renal cell cancer and non-small cell lung cancer.
- CB-839 as a single agent in rare tumors with identified driver mutations in metabolic enzymes where there is the potential for a rapid development pathway.

We will select potential indications for further clinical development of CB-839 based on the results of our Phase 1 trials with the goal of obtaining regulatory approvals in the United States and the European Union. We believe this broad product development program provides the best opportunity to maximize the commercial value of CB-839.

Identifying and pursuing efficient clinical development programs to enable rapid regulatory approval of CB-839.

We are currently conducting three Phase 1 trials of CB-839 in solid and hematological tumors. We are expanding these trials to evaluate CB-839 in specific tumor types that we believe may be most sensitive to CB-839 based on the results of our preclinical studies. We expect to initiate one or more Phase 2 trials of CB-839 in select tumor types, as a single agent or in combination with other therapies, in 2016. Some of these tumor types may offer the potential for rapid development pathways. In addition, we intend to utilize our expertise to identify relevant biomarkers for CB-839 that may predict which patients will be sensitive to treatment with CB-839.

Maximizing the commercial value of CB-839. We currently retain full global development, marketing and commercialization rights for CB-839 and we expect to maintain those rights in the near future. As we further develop CB-839, we may seek partners to maximize the commercial opportunity of CB-839 outside the United States.

Advancing our first-in-class arginase inhibitor into clinical development. We are leveraging our core expertise in tumor biology and medicinal chemistry to develop small molecule selective arginase inhibitors. Arginase is an enzyme that depletes arginine,

which is a naturally occurring amino acid that is critical for the activation, growth and survival of the body's cancer-fighting cytotoxic T cells. By inhibiting arginase, we can potentially restore the tumor killing activity of cytotoxic T cells by preventing the depletion of arginine. We are currently optimizing arginase inhibitors with the aim of submitting an IND application to the FDA in early 2016.

Advancing our first-in-class hexokinase II inhibitor into clinical development. We have expanded our portfolio of pre-clinical programs and further leveraged our expertise in tumor metabolism with the licensing of inhibitors of hexokinase II, which we believe is the first and rate-limiting enzyme in the pathway that enables cancer cells to convert glucose to energy and building blocks that feed cancer cell growth. We believe we can rapidly advance hexokinase II inhibitors into the clinic to become our third potential first-in-class therapy for cancer patients.

Further developing our pipeline by leveraging our expertise in tumor biology, drug discovery and clinical development. Our team has significant expertise in the discovery, development and approval of small molecule oncology drugs. In addition, we have accumulated significant experience and understanding of tumor metabolism and tumor immunology and are applying our medicinal chemistry capabilities to identify small molecules that exploit these pathways. We plan to continue to leverage our expertise to discover and develop additional product candidates, advance those product candidates through clinical testing, and, if approved, ultimately commercialize meaningful therapies for patients with cancer.

Our Research and Development Programs

The following table summarizes our ongoing and planned clinical trials through 2016 for our lead programs in tumor metabolism and tumor immunology. We also intend to develop additional product candidates from our research and discovery efforts in these fields. In December 2013, we submitted two INDs to the FDA for CB-839, one for solid tumors and one for hematological tumors, covering each of the indications set forth in the table below.

The Evolution of Cancer Therapeutic Agents

Cancer is characterized by the uncontrolled growth of aberrant cells in the body, leading to the invasion of essential organs and often death. Unlike normal cells, which grow only in response to carefully regulated signals from the body, cancer cells are able to proliferate largely without external signals. Cancer cells have gained this ability as the result of genetic alterations that change protein expression or function. Invasive tumors, also known as metastatic tumors, which are the greatest threat to patients, typically have multiple mutations, deletions or amplifications of genes encoding key proteins that regulate cell growth. These alterations allow the cancer cell to grow, invade other tissues, and avoid recognition and destruction by the body's immune system.

Initially, the pharmacological treatment of cancer utilized non-specific cytotoxic agents that targeted all rapidly dividing cells, including normal cells. These non-specific cytotoxic agents have anti-tumor effects but their use is often limited by severe toxicities. As the understanding of the proteins and pathways that enable cancer cells to thrive has evolved, newer more targeted agents have been developed that block specific proteins that are activated in cancer cells. Therapies such as imatinib (marketed as Gleevec) used to treat chronic myeloid leukemia are often highly effective for cancers that are driven by a single mutated protein, known as a driver mutation. However, use of targeted agents for tumors bearing multiple deleterious mutations has been less successful. Furthermore, certain proteins such as Ras and Myc, which are frequently mutated or activated in cancer and are clear driver mutations, are targets for which a drug has yet to be developed. This has created a need to identify additional fundamental differences between cancer cells and normal cells in order to find new drugs that broadly affect critical growth and survival mechanisms in cancer cells that have multiple mutations.

Tumor metabolism and tumor immunology represent two emerging fields for the development of therapeutics that can address the challenges presented in treating cancers with multiple mutations or with mutations that are difficult to inhibit. Certain fundamental changes in the metabolic pathways of cancer cells are observed in many cancer types with different mutational backgrounds. Therapeutic agents that can take advantage of these changes in metabolism have the potential to act broadly against many cancers. Similarly, genetically diverse tumor types have developed mechanisms to escape destruction by the body's immune system. Pharmacological activation of the immune system with agents such as ipilimumab (marketed as Yervoy) has resulted in favorable outcomes in melanoma, often with durable responses typically not observed with other chemotherapeutics. We believe additional opportunities exist to develop novel therapeutics that can further enhance the cancer-fighting ability of the immune system, either as single agents or in combination with approved therapeutics.

Rationale for Targeting Tumor Metabolism

Cancer cells acquire the ability to grow rapidly and spread to new sites in the body by accumulating genetic alterations in important genes that control growth and survival. These same genetic changes also result in altered metabolic pathways within the cancer cells that fuel the high demand for energy and the production of new proteins, lipids, RNA and DNA needed for rapid proliferation. We and others have observed that many types of cancer cells develop a unique dependence on specific metabolic pathways upon which normal cells are not reliant. Accordingly, when these metabolic pathways are blocked, cancer cells are essentially starved of critical nutrients and stop growing or die, whereas normal cells are largely unaffected.

Alterations in the fundamental metabolic pathways of tumors often cause a dramatic rise in the uptake of the nutrients glucose and glutamine. This has been directly demonstrated in cancer patients by the use of glucose and glutamine-related tumor imaging agents. Uptake of these agents is often significantly greater in tumor tissue than in surrounding normal tissue. We believe this enhanced uptake of glucose and glutamine by tumors occurs because of their greater need for these nutrients for growth and survival.

The primary goal of drugs targeting tumor metabolism pathways is to take advantage of cancer-specific nutrient dependencies to block cancer growth. Changes in cellular metabolism are remarkably consistent across many tumor types, yet fundamentally different from normal cells, providing the potential to develop broadly applicable agents that target these altered pathways, but have less toxicity than standard cytotoxic agents.

Glutaminase—A Key Tumor Metabolism Target

It has been understood for more than 50 years that most cancer cells require glutamine to thrive. Removal of glutamine leads to a substantial reduction in cell growth or induces cell death in glutamine-dependent cancer cells. Normal cells do not show this pronounced dependence on glutamine. This contrast has prompted significant interest in

discovering and developing novel anti-cancer agents that can inhibit glutamine utilization.

Our preclinical studies, as well as those conducted by other researchers, have identified the enzyme glutaminase as a critical choke point in the utilization of glutamine by cancer cells. We have shown in our preclinical studies that the cell lines most sensitive to glutamine withdrawal are also the most sensitive to glutaminase inhibitors. In glutamine-dependent cancer cells, the messenger RNA, or mRNA, that encodes glutaminase is often highly expressed. Furthermore, glutaminase mRNA levels are often increased in human tumors relative to the levels in corresponding normal tissue.

Glutaminase converts glutamine to glutamate, an amino acid required by cells for several essential functions. Many cancer cells, unlike normal cells, are dependent upon the enzyme glutaminase to make sufficient amounts of glutamate to grow and survive. This higher dependency upon the glutaminase pathway is likely due to an alternate use of the tricarboxylic acid, or TCA, cycle in cancer cells. The TCA cycle, which is sometimes referred to as the Krebs Cycle, is a set of chemicals and chemical reactions that cells use to generate energy and building blocks. As shown in the diagram below, normal cells primarily use glucose to feed the TCA cycle, which in turn is used primarily for energy production. In contrast, cancer cells divert many glucose-derived metabolites and several of the chemicals of the TCA cycle to make cellular building blocks to fuel their rapid growth. This depletes chemicals in the TCA cycle and requires the cancer cell to supply more glutamate into the TCA cycle, through a molecule called alpha-ketoglutarate, or -KG, to

replenish these chemicals. We believe that inhibitors of glutaminase may be able to selectively target tumor cells by virtue of their increased dependence on glutaminase to convert glutamine to glutamate to resupply the TCA cycle.

In addition, glutaminase inhibition may be effective in certain rare cancers that have mutations or deletions of TCA cycle enzymes including fumarate hydratase, or FH, succinate dehydrogenase, or SDH, and isocitrate dehydrogenase, or IDH. Glutamate feeds into the TCA cycle upstream of where these mutations or deletions occur, and inhibitors of glutaminase may block the effect of these mutations or deletions by limiting the availability of upstream starting materials.

Dysregulated growth factor receptors and associated downstream signaling pathways in tumor cells are known to act in part to increase glucose utilization. Since these pathways are the targets of a number of approved targeted cancer therapeutic agents, we believe it is possible to rationally combine such agents with a glutaminase inhibitor to block the two main nutrients that promote cancer cell growth, thereby providing an enhanced therapeutic benefit.

Hexokinase II- An essential pathway in the cellular utilization of glucose

A defining characteristic of most cancer cells is their increased uptake of glucose. As described above, cancer cells use glucose in a different manner than normal cells, but an obligate first step in all glucose utilizing pathways is phosphorylation of glucose by the enzyme hexokinase. Due to their higher glucose needs, cancer cells frequently increase the level of this critical enzyme, specifically the isoform hexokinase II. We believe inhibitors of hexokinase II will significantly impede the ability of cancer cells to survive and proliferate.

Our Programs

Our Lead Program in Tumor Metabolism: CB-839

CB-839 is a potent, selective, reversible and orally bioavailable inhibitor of human glutaminase. CB-839 binds to a unique site on glutaminase that is distinct from the site that binds glutamine, thereby reducing the potential for undesirable side effects due to inhibition of other enzymes and receptors that bind glutamine. In our preclinical studies, CB-839 has been shown to halt the growth of or kill cancer cells across a range of tumor types. The compound has demonstrated antitumor activity in several different tumor models in animals. In addition, CB-839 has shown strong synergy with immunomodulatory agents and several kinase inhibitors that target growth factor pathways. In preclinical toxicology studies, CB-839 was well tolerated in animals at doses above those shown to

inhibit tumor growth. In December 2013, we submitted an IND application to the FDA to enable the initiation of three Phase 1 trials in patients with both solid and hematological tumors. We initiated these trials in February 2014. We believe that CB-839 is the only selective glutaminase inhibitor currently in clinical trials.

Preclinical Activity of CB-839

In our preclinical studies, CB-839 demonstrated antiproliferative and cell killing activity across a panel of tumor cell lines. The figure below shows the extent of cell growth inhibition or induction of cell death across a panel of different cancer cell types treated with a concentration of CB-839 that inhibited glutaminase by more than 90%. The cell growth measurement reflects the ability of CB-839 to slow cell growth over 72 hours relative to cell growth observed in untreated cells. The cell death measurement reflects the loss of cells over 72 hours relative to the starting number of cells. Most of the triple-negative breast cancer, or TNBC, cell lines showed evidence of cell death in response to treatment with CB-839 or had growth reduced by more than 50% as compared to growth in untreated cells. In contrast, most hormone receptor-positive breast cancer cell lines were not severely affected by treatment with CB-839. Significant cell killing was seen in about half of non-small cell lung cancer, or NSCLC, cell lines, most lymphoma cell lines, about one-third of multiple myeloma cell lines and two of four acute lymphocytic leukemia cell lines tested. This same panel of cell lines was also tested for growth or cell death when glutamine was removed from the incubation medium. There was a strong correlation between the response to CB-839 and the effect of glutamine withdrawal. We believe that these results provide evidence for the critical role of glutaminase in the utilization of glutamine to drive tumor cell growth and survival.

We also evaluated the metabolic changes that resulted from inhibition of glutaminase in the same panel of cell lines shown above. In the glutamine-dependent cancer cells treated with CB-839, the conversion of glutamine to glutamate was blocked, leading to the accumulation of glutamine and the depletion of glutamate. As shown in a TNBC cell line in the figure below, the loss of cellular glutamate further results in a reduction in downstream metabolites that provide energy and building blocks for the cell, including TCA cycle intermediates, amino acids, and the antioxidant glutathione. We believe that the reduction of the level of these and other metabolites is responsible for the anti-tumor activity observed with CB-839.

In mice implanted with human tumors, CB-839 treatment caused glutamine to accumulate and glutamate to be depleted in the tumors, which was similar to the effects seen in the cell lines we tested. At plasma concentrations of CB-839 of 300 nM or above, maximal effects on glutamine and glutamate levels in tumors were observed. In contrast, normal tissues in the same animals showed only small changes in the levels of glutamine and glutamate, despite exposure to high levels of CB-839. We believe that normal cells and tissues can utilize other pathways to produce glutamate, whereas most tumor cells have been genetically re-wired to be highly reliant on glutaminase as their principal source of glutamate. This provides a potential explanation for why high doses of CB-839 are well-tolerated in animals.

In addition to showing single agent activity across a wide range of cells from different tumor types, CB-839 also acted synergistically when combined with drugs that target the Ras/Raf and PI3K/mTOR branches of growth factor signaling pathways. This means that these two agents acting together have a greater effect on the growth and survival of tumor cells than either agent used separately. CB-839 was synergistic with the epidermal growth factor receptor, or EGFR, inhibitor erlotinib (marketed as Tarceva) in NSCLC cells, with the multikinase inhibitors sunitinib (marketed as Sutent), sorafenib (marketed as Nexavar), trametinib (marketed as Mekinist), selumetinib (in development) and pazopanib (marketed as Votrient) and the mTOR inhibitors everolimus (marketed as Afinitor) and temsirolimus (marketed as Toricel) in renal cell carcinoma, or RCC, cells, and with the MEK inhibitor trametinib (marketed as Mekinist) and the AKT inhibitor MK-2206 (in development by Merck) in multiple cancer cell types. We believe these synergistic activities likely result from the fact that, as depicted in the diagram below, growth factor pathways control tumor metabolism and ultimately tumor cell dependence on glutamine and glucose.

When administered to animals at high doses in IND-enabling toxicity studies in rats and monkeys, CB-839 was well tolerated in both species, with no dose limiting toxicities observed in either study. The plasma concentration of CB-839 measured at the highest dose in rats in these studies was greater than ten-fold above the 300 nM concentration required in mice to achieve maximal effects on glutamine and glutamate levels in tumors and suppress tumor growth. In independent studies, CB-839 was shown to distribute broadly to all tissues except the brain, indicating that glutaminase could be strongly inhibited in normal tissues without causing any major toxicological effects.

Phase 1 Clinical Trials with CB-839

Trial Design

In February 2014, we initiated three Phase 1 clinical trials of CB-839 in patients with solid and hematological tumors. The favorable preclinical safety profile of CB-839 enabled a starting dose in these trials of 100 mg given orally three times daily, or TID. As shown in the table below, CX-839-001 is enrolling patients with solid tumors, CX-839-002 is enrolling patients with multiple myeloma or non-Hodgkin's lymphoma, and CX-839-003 is enrolling patients with acute myeloid or acute lymphocytic leukemia. The objectives of the Phase 1 clinical trials are to assess the safety and tolerability of CB-839. Each trial includes a dose escalation stage to identify the optimal dose for future clinical trials. This dose will be determined by the extent of glutaminase inhibition in blood and tumors, or by identifying a maximum tolerated dose. Each trial will also have an expansion stage in which additional patients with specific tumor types will be enrolled to further evaluate the safety of CB-839 and to seek preliminary evidence of efficacy. In addition to evaluating CB-839 as a single agent, we plan to enroll four Phase 1b combination cohorts, one in which CB-839 will be combined with paclitaxel in patients with triple-negative breast cancer, a second in which CB-839 will be combined with everolimus in renal cell cancer (RCC), a third in which CB-839 will be combined with dexamethasone in patients with multiple myeloma, and a fourth in which CB-839 will be combined with pomalidomide (marketed as Pomalyst) and dexamethasone in patients with multiple myeloma, to evaluate the safety and potential utility of CB-839 when used in combination with these drugs. We expect initial data to be available from our single agent trials in mid-2015 and from our combination trials in late 2015. In December 2013, we submitted two INDs to the FDA for CB-839, one for solid tumors and one for hematological tumors, covering each of the indications set forth in the table below.

The trial protocols are flexible and allow us to increase or decrease the number of patients enrolled during the dose expansion stage of each trial. We may decide to add additional cohorts testing CB-839 in combination with other agents.

Phase 1 Clinical Trials with CB-839

CX-839-001	Solid Tumors (including Triple-negative Breast Cancer (TNBC))	• Dose escalation in all solid tumors • Dose expansion cohorts in selected tumor types • Phase 1b in TNBC in combination with paclitaxel • Phase 1b in RCC in combination with everolimus
CX-839-002	Multiple Myeloma (MM) Non-Hodgkin's Lymphoma (NHL)	• Dose escalation in MM and NHL • Dose expansion cohorts in MM and selected subtypes of NHL • Phase 1b in MM in combination with dexamethasone • Phase 1b in MM in combination with pomalidomide and dexamethasone
CX-839-003	Acute Lymphocytic Leukemia (ALL) Acute Myeloid Leukemia (AML)	• Dose escalation in ALL and AML • Dose expansion cohorts in ALL and AML

Phase 1 Trial Status

We have completed enrolling patients in the dose escalation stage in all three trials. As of January 19, 2015, we enrolled a total of 61 patients across the three ongoing trials. All patients in these trials were relapsed and refractory to approved therapies. On average, patients had received five prior lines of drug treatment in the CX-839-001 and CX-839-002 trials and had received two prior lines of drug treatment in the CX-839-003 trial. During the dose escalation stage of these trials, we are monitoring the blood levels of CB-839 and the extent of glutaminase inhibition in platelets isolated from blood using an assay we have developed. Patients at the starting dose of 100 mg TID had measurable drug concentration of CB-839 in blood, and the drug concentration generally has increased with dose. The half-life of CB-839 in blood is approximately four hours. The majority of patients during dose escalation received CB-839 three times daily. Based upon the successful evaluation of twice-daily dosing in the solid tumor trial, this regimen is now being tested in all three studies. In the patients evaluated to date, increasing concentrations of CB-839 in blood are correlated with increasing inhibition of glutaminase in blood platelets. Our goal is to achieve a plasma concentration of CB-839 that maintains inhibition of glutaminase at greater than 90% continuously in tumors, which was the inhibition level required for maximal inhibition of tumor growth in animal models. Inhibition of glutaminase activity in tumor biopsy samples from patients in early dose cohorts during dose escalation has demonstrated >75% glutaminase inhibition in tumors.

CB-839 has been generally well tolerated across all three studies using doses up to 1000 mg TID and 800 mg BID. As of January 19, 2015, the date of our most recent data safety cutoff, and based on 57 patients treated with CB-839, the majority of treatment-emergent adverse events have been mild to moderate (Grade 1/2). Treatment-emergent Grade ≥ 3 adverse events occurring in >5% of patients included febrile neutropenia, thrombocytopenia, hyponatremia, and increases in liver enzymes aspartate aminotransferase (AST), alanine aminotransferase (ALT) and alkaline phosphatase. The only dose limiting toxicity event that has been reported to date was an instance of elevated creatinine (at the 250mg TID dose), however renal dysfunction has not been a significant toxicity signal for the program, even at doses up to 1000mg TID. A maximum tolerated dose has not been defined to date.

Indications to be Evaluated in our Phase 1b Dose Expansion Trials

We believe several specific tumor types will be sensitive to glutaminase inhibition and benefit from treatment with CB-839. These tumor types include triple-negative breast cancer, non-small cell lung cancer, multiple myeloma, renal cell carcinoma, and several rare cancers with metabolic enzyme mutations or deletions. These tumor types represent areas with significant unmet medical needs, and we believe that they may be particularly attractive indications for further development of CB-839.

Triple-Negative Breast Cancer

According to the American Cancer Society, over 230,000 new cases of invasive breast cancer will be diagnosed in the United States and approximately 40,000 women will die from the disease in 2015. It is estimated that between 10% to 20% of newly diagnosed cases of breast cancer are classified as triple-negative breast cancer. TNBC is a subset of breast cancer that lacks the estrogen receptor, or ER, the progesterone receptor, or PR, and the human epidermal growth factor receptor known as HER2. In comparison with other breast cancers, TNBC tends to grow faster and has a higher rate of metastasis. Furthermore, TNBC tends to recur more often and sooner following first line treatment than other subtypes of breast cancer. Patients with TNBC generally have a poorer prognosis and a lower overall survival rate than patients with breast cancers that express ER, PR and HER2. In addition, TNBC patients have relatively few treatment options since they lack expression of the targets for hormone- and HER2-based therapeutics.

Our preclinical data support the development of CB-839 in TNBC either as a single agent or in combination with standard of care therapies. The majority of TNBC tumor cell lines we have tested to date were sensitive to CB-839 and underwent cell death in

response to exposure to CB-839. In contrast, ER and HER2 positive breast cancer cell lines were relatively resistant to CB-839. Sensitivity to CB-839 in TNBC cells was directly correlated with the level of glutaminase expression, making glutaminase expression a potential companion diagnostic for identifying tumors sensitive to CB-839 for further clinical study. CB-839 had single agent anti-tumor activity in mice bearing a patient-derived TNBC tumor as shown in the figure below. When CB-839 was used to treat a breast cancer cell line implanted in animals, it showed activity both as a single agent and in combination with paclitaxel, a standard drug used in the treatment of TNBC. In the combination arm of the study, CB-839 prevented the re-growth of the tumor following discontinuation of paclitaxel dosing.

In the Phase 1 trial CX-839-001, we plan to include an expansion cohort of refractory TNBC patients treated with CB-839 as a single agent and a Phase 1b cohort of earlier stage TNBC patients who will receive CB-839 in combination with paclitaxel.

Multiple Myeloma

Multiple myeloma, or myeloma, is a hematological malignancy characterized by the proliferation of monoclonal plasma cells in the bone marrow, the presence of monoclonal immunoglobulin, or M protein, in the blood and/or urine, as well as bone disease, kidney disease, and immunodeficiency. It is more common in elderly patients, with a median age at diagnosis of 65 to 74 years. The American Cancer Society estimates that there will be approximately 26,850 new cases of myeloma diagnosed in the United States in 2015.

Our preclinical data support the development of CB-839 in myeloma either as a single agent or in combination with standard of care therapies. CB-839 had anti-tumor activity and induced cell death in a subset of myeloma cell lines. We have identified a biomarker that correlates with CB-839 sensitivity and that we believe can be used to identify myeloma patients whose tumors may have enhanced sensitivity to CB-839 treatment. CB-839 demonstrated single agent anti-tumor activity in mice bearing myeloma tumors. In myeloma cells in culture, CB-839 was synergistic with lenalidomide (marketed as Revlimid) and pomalidomide, two approved immunomodulatory drugs used to treat myeloma. In addition, treatment of myeloma tumors in animals with

B-839 in combination with either lenalidomide or pomalidomide led to long-lasting and complete suppression of tumor growth. The results of the pomalidomide study are shown in the figure below.

Patients with myeloma are being evaluated in the dose escalation stage of CX-839-002. In the expansion stage of this trial, we are evaluating two cohorts of myeloma patients treated with CB-839, one in combination with dexamethasone and a second in combination with pomalidomide and dexamethasone.

Non-Small Cell Lung Cancer (NSCLC)

According to the American Cancer Society, an estimated 221,200 new cases of lung cancer will be diagnosed in the United States in 2015. Lung cancer typically presents relatively late in its clinical course, when locally directed therapy, such as surgery and radiation, is not curative. The treatment of locally advanced and metastatic lung cancer is a significant unmet medical need.

Most primary NSCLC tumors have been shown to have elevated glutaminase expression and the majority of NSCLC cell lines that we have evaluated were sensitive to the antiproliferative or cell-killing effects of CB-839. We also observed marked synergistic activity with erlotinib in NSCLC cell lines. We plan to evaluate single agent CB-839 in an NSCLC cohort in the dose expansion stage of our solid tumor Phase 1 clinical trial. We may also evaluate CB-839 in combination with approved tyrosine kinase inhibitors in NSCLC patients in future clinical trials.

Renal Cell Carcinoma (RCC)

According to the National Cancer Institute, renal cell carcinoma is diagnosed in approximately 61,560 people each year in the United States. Approximately 50% of renal cell carcinoma patients will require chemotherapy at some point to treat their metastatic disease.

Most patients with RCC lack the tumor suppressor gene VHL. In preclinical studies by academic researchers, VHL-deficient cell lines have been shown to have an increased requirement for glutamine due to a loss of ability to make fatty acids from glucose. Accordingly, we believe that most patients with RCC tumors will have increased susceptibility to inhibition of glutaminase with CB-839. In RCC cell lines, we have demonstrated both single agent activity of CB-839 and synergistic activity in combination with approved multi-kinase inhibitors and mTOR inhibitors. We have also observed suppression of the mTOR pathway in cells treated with CB-839, likely due to a reduction in cellular amino acids and/or other nutrients. We are currently evaluating single agent CB-839 in an RCC cohort in the dose expansion stage of our solid tumor Phase 1 clinical trial. We also plan to evaluate CB-839 in a separate cohort of patients who will receive CB-839 in combination with the mTOR inhibitor everolimus.

Tumors with TCA Cycle Driver Mutations

There are rare tumors with driver mutations in two different TCA cycle enzymes, fumarate hydratase and succinate dehydrogenase, in which the enzymes are inactive, leading to abnormally high levels of fumarate and succinate and driving tumor formation. Published third-party studies indicate that glutamine metabolism is important in the synthesis of fumarate and succinate. In addition to FH and SDH, there is evidence that glutamine contributes to the production of 2-hydroxyglutarate, another driver of tumor formation that accumulates in patients with tumors harboring mutations in the enzyme isocitrate dehydrogenase. Therefore, we believe that CB-839 has the potential to be efficacious in treating tumors in these well-defined patient populations.

Fumarate hydratase: Rare mutations in FH lead to the development of hereditary leiomyomatosis and renal cell cancer, or HLRCC, where patients can develop tumors of the skin, uterus and kidneys. This is a hereditary disease with early onset and limited treatment options for patients.

Succinate dehydrogenase: Approximately 15% of gastrointestinal stromal tumors, or GIST, are resistant to imatinib (marketed as Gleevec), the current standard of care. This form of GIST is often hereditary and the tumor arises from the lack of expression of SDH. Other SDH loss-of-function mutations are found in patients harboring a rare head and neck cancer, known as paraganglioma, a rare adrenal or extra-adrenal cancer, known as pheochromocytoma, and a rare subset of renal cell carcinoma. These patients also have early disease onset and limited treatment options.

Isocitrate dehydrogenase: Some patients with glioma, a form of brain cancer, chondrosarcoma, a rare bone cancer, cholangiocarcinoma, a rare bile duct tumor, AML, high-risk myelodysplasia/myeloproliferative disorders, a group of blood disorders, have IDH1 or IDH2 driver mutations.

We are currently evaluating CB-839 in patients with FH, SDH or IDH mutations in our ongoing Phase 1 clinical trials.

Our Lead Program in Tumor Immunology: Arginase Inhibitors

Tumors have developed several strategies to avoid recognition and destruction by the immune system. One key mechanism is through suppression of cytotoxic T cells that would otherwise attack and kill the cancer cells. Arginine is an amino acid that is fundamental to the function of cytotoxic T cells. Without arginine, tumor specific cytotoxic T cells fail to express a functional T cell receptor on their surface and as a result are unable to activate, proliferate, or mount an effective anti-tumor response.

In response to tumor-secreted factors, myeloid-derived suppressor cells, or MDSCs, accumulate around the tumor and secrete the enzyme arginase, resulting in depletion of arginine from the tumor microenvironment. Depletion of arginine due to elevated levels of arginase has been observed in renal cell carcinoma and acute myeloid leukemia. In addition, significant MDSC infiltrates have been observed in pancreatic, breast and other tumor types. We believe that inhibitors of arginase can promote an anti-tumor immune response by restoring arginine levels, thereby allowing activation of the body’s cytotoxic T cells.

A similar process exists whereby cytotoxic T cells are blocked from activation through depletion of the amino acid tryptophan. Indoleamine 2, 3-dioxygenase, or IDO, a tryptophan metabolizing enzyme, depletes tryptophan from the tumor microenvironment resulting in suppression of T cell function. Both Incyte Corporation and NewLink Genetics Corporation have commenced clinical trials of IDO inhibitors and Incyte has announced early clinical results demonstrating combination activity of their IDO inhibitor with ipilimumab in metastatic melanoma.

Arginase License Agreement

In December 2014, we entered into an exclusive license agreement, or the Arginase License Agreement, with Mars, Inc., by and through its Mars Symbioscience division, or Symbioscience, under which we have been granted the exclusive, worldwide license rights to develop and commercialize Symbioscience's portfolio of arginase inhibitors for use in human healthcare. Under the terms of the Arginase License Agreement, we paid Symbioscience an upfront license fee of $0.3 million and may pay potential development and regulatory milestone payments totaling up to $24.4 million for the first licensed product. Symbioscience is eligible for an additional $95.0 million in potential sales-based milestones, as well as royalty payments, at a mid-single digit royalty rate, based on sales of the first commercialized licensed product. If we develop additional licensed products, after achieving regulatory approval of the first licensed product, we would owe additional regulatory milestone payments and additional royalty payments based on sales of such additional licensed products. The Arginase License Agreement does not alter our ability to fund operating expenses and capital expenditure requirements for at least the next twelve months.

Under the Arginase License Agreement, we are responsible for the worldwide development and commercialization of the licensed products at our cost, are required to use commercially reasonable efforts with respect to such development and commercialization activities, and must meet certain general diligence obligations. We hold the first right to prosecute and to enforce all licensed rights under the Arginase Licenses Agreement throughout the world, and Symbioscience will retain certain step-in enforcement rights. Under the exclusivity provisions of the Arginase License Agreement, each party agrees not to develop any other arginase inhibitors for use in human healthcare outside of the scope of the Arginase License Agreement.

The Arginase License Agreement, unless terminated earlier, will continue until expiration upon the last to expire of all royalty obligations Calithera owes to Symbioscience. Upon expiration of the Arginase License Agreement, we will retain non-exclusive, royalty-free license rights to the relevant licensed Symbioscience intellectual property for use in human healthcare. Symbioscience may terminate the Arginase License Agreement early if we materially breach the agreement and do not cure such breach in a specified notice period. We may terminate the Arginase License Agreement for Symbioscience's uncured material breach, or at will for any or no reason.

We are developing small molecule selective inhibitors of arginase and are in the process of optimizing these compounds with the aim to submit an IND to the FDA in early 2016.

Our Second Program in Tumor Metabolism: Hexokinase II

Most cancer cells have increased uptake of the sugar glucose relative to surrounding normal cells. This phenomenon forms the basis for the widely used tumor imaging procedure known as ^{18}F-2-deoxyglucose (FDG)/PET. Tumors take up more FDG, a radioactive glucose analog, than the surrounding normal tissue and this differential can be visualized with PET imaging. Not only do tumors take up more glucose, but they also utilize the nutrient in a unique way. Tumors convert glucose into lactic acid in a process known as aerobic glycolysis, or the "Warburg effect", a route rarely utilized in normal cells. This unique uptake and processing of

14

glucose by tumors relative to normal tissue creates an opportunity to selectively target tumors by cutting off their ability to use this fuel.

Hexokinase is the first enzyme in the pathway that enables cancer cells to convert glucose to energy and building blocks that feed cancer cell growth. In many cancers, the isoform hexokinase II is over expressed and has been linked to more aggressive and invasive tumors. Pre-clinical studies in mice have confirmed that the reduction of hexokinase II activity through genetic deactivation (siRNA knockdown studies) results in a significant reduction of tumor growth. The hexokinase II inhibitors in-licensed from TransTech may provide an opportunity to inhibit the unique way cancer cells utilize glucose, and the overall Warburg effect, which could result in new treatments for cancer.

Hexokinase License Agreement

In March 2015, we entered into a License and Research agreement, or the Hexokinase License Agreement, with High Point Pharmaceuticals, LLC and TransTech Pharma LLC, or collectively, TransTech, under which we obtained an exclusive, worldwide license to develop and commercialize TransTech's hexokinase II inhibitors.

Under the terms of the Hexokinase License Agreement, we paid TransTech an initial license fee of $0.6 million, and will pay potential development and regulatory milestone payments totaling up to $30.5 million for the first licensed product. TransTech is eligible for an additional $77.0 million in potential sales-based milestones, as well as royalty payments, at mid-single digit royalty rates, based on tiered sales of the first commercialized licensed product. In addition, we will fund up to $1.1 million during the first 12 months of the Hexokinase License Agreement for the costs associated with up to four full-time employees for TransTech to develop additional hexokinase inhibitors. If we develop additional licensed products, after achieving regulatory approval of the first licensed product, we would owe additional regulatory milestone payments and additional royalty payments based on sales of such additional licensed products. The Hexokinase License Agreement will not impact our ability to fund operating expenses and capital expenditure requirements for at least the next twelve months.

Except for the research program funded by us at TransTech, we are responsible for the worldwide development and commercialization of the licensed products at our cost, are required to use commercially reasonable efforts with respect to such development and commercialization activities, and must meet certain specified diligence obligations. We hold the first right to prosecute and to enforce all licensed patents under the Hexokinase License Agreement throughout the world, and TransTech will retain certain step-in enforcement rights.

The Hexokinase License Agreement, unless terminated earlier, will continue on a product-by-product and country-by-country basis until expiration of the royalty obligations we owe to TransTech on such product in such country. TransTech may terminate the Hexokinase License Agreement early if we materially breach the agreement and do not cure such breach in a specified notice period or upon our insolvency. We may terminate the Hexokinase License Agreement for TransTech's uncured material breach or insolvency, or at will for any or no reason.

Intellectual Property

Our commercial success depends in large part on our ability to obtain and maintain intellectual property protection for our product candidates, including CB-839 and our preclinical compounds, and our core technologies. Our policy is to seek to protect our intellectual property position by, among other methods, filing U.S. and foreign patent applications related to the technology, inventions and improvements that are important to the development and implementation of our business strategy. We also rely on trade secrets, know-how and continuing technological innovation to develop and maintain our proprietary position.

We file patent applications directed to our product candidates, preclinical compounds and related technologies to establish intellectual property positions on these compounds and their uses in disease. We are seeking patent protection for the use of biomarkers to identify patients most likely to benefit from treatment with our product candidates. As of December 31, 2014, we own two issued U.S. patents and approximately 26 pending U.S. and foreign patent applications in the following foreign jurisdictions: Argentina, Australia, Brazil, Canada, China, the Eurasian Patent Organization, Europe, India, Israel, Japan, Mexico, New Zealand, Singapore, South Africa, South Korea and Taiwan.

As of December 31, 2014, the intellectual property portfolio for our glutaminase inhibitor program, which includes CB-839, consisted of two issued U.S. patents directed to compositions of matter and methods of treating cancer with for CB-839, both of which expire in 2032. We also have seven pending U.S. patent applications and 19 corresponding pending PCT and foreign patent applications directed to compositions of matter for CB-839 and related chemical compounds, as well as methods of using these compounds. These pending patent applications also include one pending U.S. patent application relating to methods for measuring various biomarkers in cancer patients to identify patients suitable for treatment with glutaminase inhibitors.

The intellectual property portfolio for our arginase inhibitor program, which we have exclusively licensed from Symbioscience, includes both issued patents and pending patent applications. This portfolio includes 5 pending U.S. patent

applications, 43 corresponding pending foreign patent applications, and one issued foreign patent directed to various arginase inhibitors and therapeutic methods of using the compounds.

In March 2015, we exclusively licensed from TransTech the intellectual property portfolio for our hexokinase II inhibitor program. This portfolio comprises four pending PCT patent applications directed to compositions of matter for hexokinase II inhibitors, potential combination therapy and assay methods, and three pending U.S. Provisional patent applications directed to additional compositions of matter.

The term of individual patents depends upon the legal term of the patents in the countries in which they are obtained. In most countries, including the United States, the patent term is 20 years from the earliest filing date of a non-provisional patent application. In the United States, a patent's term may be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the U.S. Patent and Trademark Office, or the USPTO, in examining and granting a patent, or may be shortened if a patent is terminally disclaimed over an earlier filed patent. The term of a U.S. patent that covers a drug or biological product may also be eligible for patent term extension when FDA approval is granted, provided statutory and regulatory requirements are met. In the future, if and when our product candidates receive approval from the FDA or foreign regulatory authorities, we expect to apply for patent term extensions on issued patents covering those products, depending upon the length of the clinical trials for each drug and other factors. There can be no assurance that any of our pending patent applications will issue or that we will benefit from any patent term extension or other favorable adjustment to the term of any of our patents.

As with other biotechnology and pharmaceutical companies, our ability to maintain and solidify our proprietary and intellectual property position for our product candidates, including CB-839 and our preclinical compounds, and our core technologies will depend on our success in obtaining effective patent claims and enforcing those claims if granted. However, patent applications that we may file or license from third parties may not result in the issuance of patents. We also cannot predict the breadth of claims that may be allowed or enforced in our patents. Any issued patents that we may receive in the future may be challenged, invalidated or circumvented. For example, prior to March 16, 2013, in the United States, patent applications were subject to a "first to invent" rule of law. Applications filed subsequent to March 16, 2013 (with the exception of certain applications claiming the benefit of earlier-filed applications) are subject to a "first to file" rule of law.

Discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. We cannot be certain that any existing or future application will be subject to the "first to file" or "first to invent" rule of law, that we were the first to make the inventions claimed in our existing patents or pending patent applications subject to the prior laws, or that we were the first to file for patent protection of such inventions subject to the new laws. If third parties prepare and file patent applications in the United States that also claim technology we have claimed in our patents or patent applications, we may have to participate in interference proceedings in the USPTO to determine priority of invention, which could result in substantial costs to us, even if the eventual outcome is favorable to us. In addition, because of the extensive time required for clinical development and regulatory review of a product candidate we may develop, it is possible that, before any of our product candidates can be commercialized, any related patent may expire or remain in force for only a short period following commercialization, thereby reducing any advantage of any such patent.

In addition to patents, we rely upon unpatented trade secrets, know-how, and continuing technological innovation to develop and maintain our competitive position. We seek to protect our proprietary information, in part, by using confidentiality agreements with our collaborators, scientific advisors, employees and consultants, and invention assignment agreements with our employees. We also have agreements requiring assignment of inventions with selected consultants, scientific advisors and collaborators. The confidentiality agreements are designed to protect our proprietary information and, in the case of agreements or clauses requiring invention assignment, to grant us

ownership of technologies that are developed under those agreements.

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 to manufacture clinical supplies of CB-839. CB-839 is an organic compound of low molecular weight. Our third-party contract manufacturers are currently producing CB-839 for use in our clinical trials utilizing reliable and reproducible synthetic processes and common manufacturing techniques. We obtain our supplies from manufacturers on a purchase order basis and do not have any long-term arrangements. In addition, we do not currently have arrangements in place for bulk drug substance or drug product services of CB-839. We intend to identify and qualify additional manufacturers to provide bulk drug substance and drug product services prior to submission of a new drug application to the FDA if necessary to ensure sufficient commercial quantities of CB-839. We also intend to rely upon third-party contract manufacturers to provide us with clinical supplies for our arginase and hexokinase II inhibitor programs and for our other research and discovery programs.

Research and Development

We have and will continue to make substantial investments in research and development. Our research and development expenses totaled $16.4 million, $9.9 million and $6.6 million in 2014, 2013 and 2012, respectively.

In the ordinary course of business, we enter into agreements with third parties, such as contract research organizations, medical institutions, clinical investigators and contract laboratories, to conduct our clinical trials and aspects of our research and preclinical testing. These third parties provide project management and monitoring services and regulatory consulting and investigative services.

Competition

The pharmaceutical and biotechnology industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. While we believe that our technology, development experience and scientific knowledge provide us with competitive advantages, we face potential competition from many different sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions and governmental agencies and public and private research institutions. Any product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future.

Our principal competitors in the field of tumor metabolism include Advanced Cancer Therapeutics, LLC, Agios Pharmaceuticals, Inc., AstraZeneca plc, Bayer Pharma AG, Celgene Pharmaceuticals, Cornerstone Pharmaceuticals, Inc., Eli Lilly and Company, Forma Therapeutics Holdings, LLC, GlaxoSmithKline plc, Novartis International AG, Pfizer Inc., Quantum Pharmaceuticals, 3-V Biosciences, Inc., Roche Holdings, and its subsidiary Genentech Inc. and Takeda Pharmaceutical Co. Ltd. Our principal competitors in the field of tumor immunology include AstraZeneca plc, Boehringer Ingelheim GmbH, Bristol-Myers Squibb Company, Coronado Biosciences, CureTech Ltd., EMD Serono, Inc., Flexus Biosciences, Incyte Corporation, iTeos Therapeutics, Merck & Co., NewLink Genetics Corporation, Ono Pharmaceuticals, Co., Ltd, Pfizer Inc., Roche Holdings and TG Therapeutics, Inc.

The most common methods of treating patients with cancer are surgery, radiation and drug therapy, including chemotherapy, hormone therapy and targeted drug therapy. There are a variety of available drug therapies marketed for cancer. In many cases, these drugs are administered in combination to enhance efficacy. Any product candidates we develop will compete with many existing drug and other therapies. To the extent they are ultimately used in combination with or as an adjunct to these therapies, our product candidates will not be competitive with them. Some of the currently approved drug therapies are branded and subject to patent protection, and others are available on a generic basis. Many of these approved drugs are well established therapies and are widely accepted by physicians, patients and third-party payors. In general, although there has been considerable progress over the past few decades in the treatment of cancer and the currently marketed therapies provide benefits to many patients, these therapies all are limited to some extent in their efficacy and frequency of adverse events, and none are successful in treating all patients. As a result, the level of morbidity and mortality from cancer remains high.

In addition to currently marketed therapies, there are also a number of therapeutics in late stage clinical development to treat cancer. These therapeutics in development may provide efficacy, safety, convenience and other benefits that are not provided by currently marketed therapies. As a result, they may provide significant competition for any product candidate for which we may obtain market approval.

Many of our competitors may have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved therapeutics than we do. Mergers and acquisitions in the pharmaceutical, biotechnology and diagnostic industries may result in even more resources being concentrated among a smaller number of our competitors. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Smaller or early stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies.

The key competitive factors affecting the success of CB-839 and any future product candidates we develop, if approved, are likely to be their efficacy, safety, synergy with other approved therapies, convenience, price and the availability of reimbursement from government and other third-party payors.

Our competitors may develop and commercialize therapeutics that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any therapeutics that we may develop. Our competitors also may obtain FDA or other regulatory approval for their therapeutics more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. In addition, our ability to compete may be affected in many cases by insurers or other third-party and government programs seeking to control healthcare costs.

Government Regulation

Government authorities in the United States, at the federal, state and local level, and in other countries extensively regulate, among other things, the research, development, testing, manufacture, including any manufacturing changes, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, post-approval monitoring and reporting, import and export of pharmaceutical products, such as those we are developing.

United States Drug Approval Process

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and implementing regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations requires the expenditure of substantial time and financial resources. Failure to comply with the applicable United States requirements at any time during the product development process, approval process or after approval, may subject an applicant to a variety of administrative or judicial sanctions, such as the FDA's refusal to approve pending applications, withdrawal of an approval, imposition of a clinical hold, issuance of warning letters and untitled letters, product recalls, product seizures, total or partial suspension of production or distribution injunctions, fines, refusals of government contracts, restitution, disgorgement of profits or civil or criminal penalties.

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

- contract manufacturing expenses, primarily for the production of clinical supplies;
- completion of preclinical laboratory tests, animal studies and formulation studies in compliance with the FDA's good laboratory practice, or GLP, regulations;
- submission to the FDA of an IND, which must become effective before human clinical trials may begin;
- approval by an independent institutional review board, or IRB, at each clinical site before each trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with good clinical practices, or GCP, to establish the safety and efficacy of the proposed drug for each indication;
- submission to the FDA of a new drug application, or NDA;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the product is produced to assess compliance with current good manufacturing practices, or cGMP, requirements and 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.

Preclinical Studies and IND

Preclinical studies include laboratory evaluation of product chemistry and formulation, as well as in vitro and animal studies to assess the potential for adverse events, and in some cases, to establish a rationale for therapeutic use. The conduct of preclinical studies is subject to federal regulations and requirements, including GLP regulations for safety/toxicology studies. An IND sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical trials, among other things, to the FDA as part of an IND. Some long-term preclinical testing, such as animal tests of reproductive adverse events and carcinogenicity, may continue after the IND is submitted. An IND automatically becomes effective 30 days after receipt by the FDA, unless before that time, the FDA raises concerns or questions related to one or more proposed clinical trials and places the trial on clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. As a result, submission of an IND may not result in the FDA allowing clinical trials to commence.

Clinical Trials

Clinical trials involve the administration of the investigational new drug to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include, among other things, the requirement that all research subjects provide their informed consent in writing before their participation in any clinical trial. Clinical trials are conducted under written study protocols detailing, among other things, the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. In addition, an IRB

at each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution, and the IRB must conduct continuing review. The IRB must review and approve, among other things, the study protocol and informed consent information to be provided to study subjects. An IRB must operate in compliance with FDA regulations. Information about certain clinical trials must be submitted within specific timeframes to the National Institutes of Health for public dissemination at www.clinicaltrials.gov. Human clinical trials are typically conducted in three sequential phases, which may overlap or be combined:

- Phase 1: The drug is initially introduced into healthy human subjects or patients with the target disease or condition and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an early indication of its effectiveness.

- Phase 2: The drug is administered to 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 optimal dosage.
- Phase 3: The drug is administered to an expanded patient population in adequate and well-controlled clinical trials to generate sufficient data to statistically confirm the efficacy and safety of the product for approval, to establish the overall risk-benefit profile of the product and to provide adequate information for the labeling of the product.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and, more frequently, if serious adverse events occur. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, or at all. Furthermore, the FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects 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.

Marketing Approval

Assuming successful completion of the required clinical testing, the results of the preclinical studies and clinical trials, together with detailed information relating to the product's chemistry, manufacture, controls and proposed labeling, among other things, are submitted to the FDA as part of an NDA requesting approval to market the product for one or more indications. Under federal law, the submission of most NDAs is additionally subject to a substantial application user fee, and the sponsor of an approved NDA is also subject to annual product and establishment user fees, which fees are typically increased annually.

The FDA conducts a preliminary review of all NDAs within the first 60 days after submission before accepting them for filing to determine whether they are sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also 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 has agreed to specified performance goals in the review of NDAs. Under these goals, the FDA has committed to review most such applications for non-priority products within 10 months, and most applications for priority review products, that is, drugs that the FDA determines represent a significant improvement over existing therapy, within six months. The review process may be extended by the FDA for three additional months to consider certain information or clarification regarding information already provided in the submission. The FDA may also refer applications for novel drugs or products that present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Before approving an NDA, the FDA typically will inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. In addition, before approving an NDA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP and integrity of the clinical data submitted.

The testing and approval process requires substantial time, effort and financial resources, and each may take many years to complete. Data obtained from clinical activities are not always conclusive and may be susceptible to varying interpretations, which could delay, limit or prevent regulatory approval. The FDA may not grant approval on a timely basis, or at all. We may encounter difficulties or unanticipated costs in our efforts to develop our product candidates and secure necessary governmental approvals, which could delay or preclude us from marketing our products.

After the FDA's evaluation of the NDA and inspection of the manufacturing facilities, the FDA may issue an approval letter or a complete response letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. If and when those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the NDA, the FDA will issue an approval letter. The FDA has committed to reviewing such resubmissions in two or six months depending on the type of information included. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval and refuse to approve the NDA. Even if the FDA approves a product, it may limit the approved indications for use for the product, require that contraindications, warnings or precautions be included in the product labeling, require that post-approval studies, including phase 4 clinical trials, be conducted to further assess a drug's safety after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution restrictions or other risk management mechanisms, including Risk Evaluation and Mitigation Strategies, or REMs, which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-market studies or surveillance

programs. After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Fast Track Designation

The FDA is required to facilitate the development and expedite the review of drugs that are intended for the treatment of a serious or life-threatening condition for which there is no effective treatment and which demonstrate the potential to address unmet medical needs for the condition. Under the fast track program, the sponsor of a new product candidate may request the FDA to designate the product for a specific indication as a fast track product concurrent with or after the submission of the IND for the product candidate. The FDA must determine if the product candidate qualifies for fast track designation within 60 days after receipt of the sponsor's request.

In addition to other benefits, such as the ability of the sponsor to use surrogate endpoints in the evaluation of the pivotal clinical trials and have more frequent interactions with the FDA, the FDA may initiate review of sections of a fast track product's NDA before the application is complete. This rolling review is available if the applicant provides and the FDA approves a schedule for the submission of the remaining information and the applicant pays applicable user fees. However, the FDA's time period goal for reviewing a fast track application does not begin until the last section of the NDA is submitted. In addition, the fast track designation may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

Priority Review

Under FDA policies, a product candidate may be eligible for priority review, or review generally within a six-month time frame from the time a complete application is received. Products regulated by the FDA's Center for Drug Evaluation and Research, or CDER, are eligible for priority review if they provide a significant improvement compared to marketed products in the treatment, diagnosis or prevention of a disease. A fast track designated product candidate would ordinarily meet the FDA's criteria for priority review.

Accelerated Approval

Under the FDA's accelerated approval regulations, the FDA may approve a drug for a serious or life-threatening illness that provides meaningful therapeutic benefit to patients over existing treatments based upon a surrogate endpoint that is reasonably likely to predict clinical benefit. In clinical trials, a surrogate endpoint is a measurement of laboratory or clinical signs of a disease or condition that substitutes for a direct measurement of how a patient feels, functions or survives. Surrogate endpoints can often be measured more easily or more rapidly than clinical endpoints. A product candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of Phase 4 or post-approval clinical trials to confirm the effect on the clinical endpoint. Failure to conduct required post-approval trials, or confirm a clinical benefit during post-marketing studies, would allow the FDA to withdraw the drug from the market on an expedited basis. All promotional materials for drug candidates approved under accelerated regulations are subject to prior review by the FDA.

Breakthrough Therapy Designation

Under the provisions of the Food and Drug Administration Safety and Innovation Act, or FDASIA, enacted in 2012, a sponsor can request designation of a product candidate as a "breakthrough therapy." A breakthrough therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the product candidate may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial

treatment effects observed early in clinical development. Drugs designated as breakthrough therapies are also eligible for accelerated approval. The FDA must take certain actions, such as holding timely meetings and providing advice, intended to expedite the development and review of an application for approval of a breakthrough therapy. Even if a product candidate qualifies for one or more of these programs, the FDA may later decide that the product candidate no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

Orphan Drugs

Under the Orphan Drug Act, the FDA may grant orphan drug designation to drugs intended to treat a rare disease or condition, which is generally defined as a disease or condition that affects fewer than 200,000 individuals in the United States. Orphan drug designation must be requested before submitting an NDA. After the FDA grants orphan drug designation, the generic identity of the drug and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in,

or shorten the duration of, the regulatory review and approval process. The first NDA applicant to receive FDA approval for a particular active ingredient to treat a particular disease with FDA orphan drug designation is entitled to a seven-year exclusive marketing period in the United States for that product, for that indication. During the seven-year exclusivity period, the FDA may not approve any other applications to market the same drug for the same orphan indication, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity in that it is shown to be safer, more effective or makes a major contribution to patient care. Orphan drug exclusivity does not prevent the FDA from approving a different drug for the same disease or condition, or the same drug for a different disease or condition. Among the other benefits of orphan drug designation are tax credits for certain research and a waiver of the NDA application user fee.

Pediatric Exclusivity and Pediatric Use

Under the Best Pharmaceuticals for Children Act (BPCA) certain drugs may obtain an additional six months of exclusivity, if the sponsor submits information requested in writing by the FDA (a Written Request) relating to the use of the active moiety of the drug in children. The FDA may not issue a Written Request for studies on unapproved or approved indications or where it determines that information relating to the use of a drug in a pediatric population, or part of the pediatric population, may not produce health benefits in that population.

In addition, the Pediatric Research Equity Act (PREA) requires a sponsor to conduct pediatric studies 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, biologics license application and supplements thereto, must contain a pediatric assessment unless the sponsor has received a deferral or waiver. Unless otherwise required by regulation, PREA does not apply to any drug for an indication where orphan designation has been granted. The required assessment must assess 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 studies for some or all of the pediatric subpopulations. A deferral may be granted for several reasons, including a finding that the drug or biologic is ready for approval for use in adults before pediatric studies are complete or that additional safety or effectiveness data needs to be collected before the pediatric studies begin. After April 2013, 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.

As part of the FDASIA, the U.S. Congress made a few revisions to BPCA and PREA, which were slated to expire on September 30, 2012, and made both laws permanent.

Overview of FDA Regulation of Companion Diagnostics

We may seek to develop in vitro companion diagnostics for use in selecting the patients that we believe will respond to our therapeutics. In July 2011, the FDA issued a draft guidance that states that if safe and effective use of a therapeutic product depends on an in vitro diagnostic, then the FDA generally will require approval or clearance of the diagnostic at the same time that the FDA approves the therapeutic product. When finalized, the guidance would address issues critical to developing and obtaining approval or clearance for companion diagnostics and provide guidance as to when the FDA will require that the in vitro diagnostic, which is regulated as a medical device, and the drug be approved simultaneously. The FDA has yet to issue further guidance, and it is unclear whether it will do so, or what the scope would be. Nevertheless, although the draft guidance is not finalized, the FDA has already required in vitro companion diagnostics intended to select the patients who will respond to cancer treatment to obtain approval simultaneously with approval of the drug.

Other Regulatory Requirements

Any drug manufactured or distributed by us pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims are subject to prior FDA review and approval.

The FDA may impose a number of post-approval requirements, including REMs, as a condition of approval of an NDA. For example, the FDA may require post-marketing testing, including phase four clinical trials, and surveillance to further assess and monitor the product's safety and effectiveness after commercialization. Regulatory approval of oncology products often requires that patients in clinical trials be followed for long periods to determine the overall survival benefit of the drug.

In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and state agencies, and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with cGMP requirements. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon us and any third-party manufacturers that we may

decide to use. Accordingly, manufacturers must continue to expend time, money and effort in the areas of production and quality control to maintain cGMP compliance.

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information, imposition of post-market studies or clinical trials to assess new safety risks or imposition of distribution or other restrictions under a Risk Evaluation and

Mitigation Strategy program. Other potential consequences include, among other things:

• restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;

• fines, warning letters or holds on post-approval clinical trials;

• refusal of the FDA to approve pending applications or supplements to approved applications, or

suspension or revocation of product license approvals;

• product seizure or detention, or refusal to permit the import or export of products; or

• consent decrees, injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Drugs may be promoted only for the approved indications and in accordance with the provisions of the approved label. 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 liability.

Additional Provisions

In addition to FDA restrictions on marketing of pharmaceutical products, several other types of state and federal laws have been applied to restrict certain marketing practices in the pharmaceutical industry in recent years. These laws include anti-kickback statutes and false claims statutes. The federal healthcare program anti-kickback statute prohibits, among other things, knowingly and willfully offering, paying, soliciting or receiving remuneration to induce or in return for purchasing, leasing, ordering or arranging for the purchase, lease or order of any healthcare item or service reimbursable under Medicare, Medicaid or other federally financed healthcare programs. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers and formulary managers on the other. Violations of the anti-kickback statute are punishable by imprisonment, criminal fines, civil monetary penalties and exclusion from participation in federal healthcare programs. Although there are a number of statutory exemptions and regulatory safe harbors protecting certain common activities from prosecution or other regulatory sanctions, the exemptions and safe harbors are drawn narrowly, and practices that involve remuneration intended to induce prescribing, purchases or recommendations may be subject to scrutiny if they do not qualify for an exemption or safe harbor.

Federal false claims laws prohibit any person from knowingly presenting, or causing to be presented, a false claim for payment to the federal government, or knowingly making, or causing to be made, a false statement to have a false claim paid. Recently, several pharmaceutical and other healthcare companies have been prosecuted under these laws

for allegedly inflating drug prices they report to pricing services, which in turn were used by the government to set Medicare and Medicaid reimbursement rates, and for allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. In addition, certain marketing practices, including off-label promotion, may also violate false claims laws. The majority of states also have statutes or regulations similar to the federal anti-kickback law and false claims laws, which apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor.

Foreign Regulation

In order to market any product outside of the United States, we would need to comply with numerous and varying regulatory requirements of other countries regarding safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of our products. Whether or not we obtain FDA approval for a product, we would need to obtain the necessary approvals by the comparable regulatory authorities of foreign countries before we can commence clinical trials or marketing of the product in those countries. The approval process varies from country to country and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries might differ from and be longer than that required to obtain FDA approval. Regulatory approval in one country does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country may negatively impact the regulatory process in others.

New Legislation and Regulations

From time to time, legislation is drafted, introduced and passed in Congress that could significantly change the statutory provisions governing the testing, approval, manufacturing and marketing of products regulated by the FDA. In addition to new legislation, FDA regulations and policies are often revised or interpreted by the agency in ways that may significantly affect our business and our products. It is impossible to predict whether further legislative changes will be enacted or whether FDA regulations, guidance, policies or interpretations changed or what the effect of such changes, if any, may be.

Employees

As of December 31, 2014, we had 37 full-time employees, including 16 employees with Ph.D. or M.D. degrees. Of these full-time employees, 28 employees are engaged in research and development activities. None of our employees is represented by a labor union or covered by a collective bargaining agreement.

Facilities

We occupy approximately 29,000 square feet of office and laboratory space in South San Francisco, California under a lease that expires in November 2017 with an option to extend another two years to November 2019. Approximately 4,500 square feet of laboratory space have been leased to another biotechnology company under a two-year sublease agreement. We believe that our facility is sufficient to meet our current needs and that suitable additional space will be available as and when needed.

Legal Proceedings

From time to time, we may become involved in litigation relating to claims arising from the ordinary course of business. Our management believes that there are currently no claims or actions pending against us, the ultimate disposition of which could have a material adverse effect on our results of operations, financial condition or cash flows.

Item 1A. Risk Factors.

Our business involves significant risks, some of which are described below. You should carefully consider these risks, as well as other information in this Annual Report on Form 10-K, including our financial statements and the related notes and "Management's Discussion and Analysis of Financial Condition and Results of Operations." The occurrence of any of the events or developments described below could harm our business, financial condition, results of operations, cash flows, the trading price of our common stock and our growth prospects. 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 Financial Position and Need For Additional Capital

We have incurred significant operating losses since our inception and anticipate that we will continue to incur substantial operating losses for the foreseeable future. We may never achieve or maintain profitability.

Since our inception, we have incurred significant operating losses. Our net loss was $21.7 million, $12.4 million and $8.0 million for 2014, 2013 and 2012, respectively. As of December 31, 2014, we had an accumulated deficit of $51.9 million. To date, we have financed our operations primarily through private placements of our preferred stock and our initial public offering in October 2014. We have devoted substantially all of our financial resources and efforts to research and development. We began Phase 1 clinical trials on our lead product candidate, CB-839, in early 2014 and expect that it will be many years, if ever, before we receive regulatory approval and have a product candidate ready for commercialization. We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. Our net losses may fluctuate significantly from quarter to quarter and year to year. We anticipate that our expenses will increase substantially if and as we:

- advance further into clinical trials our existing clinical product candidate, CB-839, a glutaminase inhibitor for the treatment of solid and hematological tumors;
- continue the preclinical development of our arginase and hexokinase II inhibitor programs and advance candidates into clinical trials;
- identify additional product candidates and advance them into preclinical development;
- seek marketing approvals for our product candidates that successfully complete clinical trials;
- establish a sales, marketing and distribution infrastructure to commercialize any product candidates for which we obtain marketing approval;
- maintain, expand and protect our intellectual property portfolio;
- hire additional clinical, regulatory and scientific personnel;
- add operational, financial and management information systems and personnel, including personnel to support product development; and
- acquire or in-license other product candidates and technologies.

To become and remain profitable, we must develop and eventually commercialize one or more products with significant market potential. This will require us to be successful in a range of challenging activities, including completing preclinical studies and clinical trials of our product candidates, obtaining marketing approval for these product candidates, manufacturing, marketing and selling those product candidates for which we may obtain marketing approval, and satisfying any post-marketing requirements. We may never succeed in these activities and, even if we do, may never generate revenue that are significant or large enough to achieve profitability. We are currently only in Phase 1 clinical trials for CB-839 and in preclinical studies for our arginase and hexokinase II inhibitor programs. Our failure to become and remain profitable would decrease the value of the company and could impair our ability to raise capital, maintain our research and development efforts, expand our business or continue our operations. A decline in the value of our company could also cause you to lose all or part of your investment.

We will need substantial additional funding. If we are unable to raise capital when needed, we would be forced to delay, reduce or eliminate our product development programs or commercialization efforts.

We expect our expenses to increase in connection with our ongoing activities, particularly as we continue the research and development of, continue and initiate clinical trials of and seek marketing approval for our product candidates, specifically CB-839 and as we become obligated to make milestone payments pursuant to our outstanding license agreements. In addition, if we obtain marketing approval for any of our product candidates, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution of the approved product.

Our future capital requirements will depend on many factors, including:

- the scope, progress, results and costs of drug discovery, preclinical development, laboratory testing and clinical trials for our product candidates, in particular CB-839;
- the costs, timing and outcome of any regulatory review of our product candidate, CB-839;
- the cost of our arginase and hexokinase II inhibitor programs, and any other product programs we pursue;
- the costs and timing of commercialization activities, including manufacturing, marketing, sales and distribution, for any product candidates that receive marketing approval;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;
- our ability to establish and maintain collaborations on favorable terms, if at all; and
- the extent to which we acquire or in-license other product candidates and technologies.

Identifying potential product candidates and conducting preclinical studies and clinical trials are time consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve product sales for any of our current or future product candidates. In addition, our product candidates, if approved, may not achieve commercial success. Our commercial revenue, if any, will be derived from sales of products that we do not expect to be commercially available for many years, if at all.

Accordingly, we will need substantial additional funding in connection with our continuing operations and to achieve our goals. As of December 31, 2014, we had cash and cash equivalents of $102.0 million. We expect that our existing cash and cash equivalents will be sufficient to enable us to meet our current operating plan for at least the next 12 months. However, our existing cash and cash equivalents may prove to be insufficient for these activities. If we are unable to raise capital when needed or on attractive terms, we would be forced to delay, reduce or eliminate our research and development programs or future commercialization efforts. Adequate additional financing may not be available to us on acceptable terms, or at all. In addition, we may seek additional financing due to favorable market conditions or strategic considerations, even if we believe we have sufficient funds for our operating plans.

Raising additional capital may cause dilution to our stockholders restrict our operations or require us to relinquish rights to our technologies or product candidates.

Until such time, if ever, as we can generate substantial product revenue, we expect to finance our cash needs through a combination of equity and debt financings, as well as entering into collaborations, strategic alliances and licensing arrangements. We do not currently have any committed external source of funds. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a common stockholder. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends, and may be secured by all or a portion of our assets. If we raise funds by entering into collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or to grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings or through collaborations, strategic alliances or licensing arrangements when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Our short operating history may make it difficult for you to evaluate the success of our business to date and to assess our future viability.

We were founded in March 2010 and our operations to date have been limited to organizing and staffing our company, business planning, raising capital, developing our technology, identifying potential product candidates, undertaking preclinical studies and commencing Phase 1 clinical trials of our product candidate. We have one product candidate in Phase 1 clinical trials, and all of our other programs are in research and preclinical development. We have not yet demonstrated our ability to successfully complete any clinical trials, including large-scale, pivotal clinical trials required for regulatory approval of our product candidates, obtain marketing approvals, manufacture a commercial scale product, or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful commercialization. Typically, it takes many years to develop one new product from the time it is discovered to when it is commercially available. Consequently, any predictions made about our future success or viability may not be as accurate as they could be if we had a longer operating history or if we had product candidates in advanced clinical trials.

In addition, as a new business, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors that may alter or delay our plans. We will need to transition from a company with a research focus to a company capable of supporting development activities and, if a product candidate is approved, a company with commercial activities. We may not be successful in any step in such a transition.

Risks Related to Drug Discovery, Development and Commercialization

Our approach to the discovery and development of product candidates that target tumor metabolism and tumor immunology is unproven and may never lead to marketable products.

Our scientific approach focuses on using our understanding of cellular metabolic pathways and the role of glutaminase and hexokinase in these pathways, as well as the role of arginase in the anti-tumor immune response, to identify molecules that are potentially promising as therapies for cancer indications. Any product candidates we develop may not effectively modulate metabolic or immunology pathways. The scientific evidence to support the feasibility of developing product candidates based on inhibiting tumor metabolism or impacting the anti-tumor immune response are both preliminary and limited. Although preclinical studies suggest that inhibiting glutaminase and hexokinase can suppress the growth of certain cancer cells, to date no company has translated this mechanism into a drug that has received marketing approval. Even if we are able to develop a product candidate in preclinical studies, we may not succeed in demonstrating the safety and efficacy of the product candidate in human clinical trials. Our expertise in cellular metabolic pathways, the role of glutaminase and hexokinase in these pathways, and the role of arginase in the anti-tumor immune response may not result in the discovery and development of commercially viable products to treat cancer.

We are very early in our development efforts, which may not be successful.

We have invested a significant portion of our efforts and financial resources in the identification of our most advanced product candidate, CB-839, which is being evaluated in three Phase 1 clinical trials. Our arginase inhibitor and hexokinase II inhibitor programs are in preclinical development. Because of the early stage of our development efforts and our unproven and novel approach to discovery and development of product candidates, we do not have a clearly defined clinical development path. It is also too early in our development efforts to determine whether our product candidates will demonstrate single-agent activity or will be developed for use in combination with other approved therapies, or both. As a result, the timing and costs of the regulatory paths we will follow and marketing approvals remain uncertain. Our ability to generate product revenue, which we do not expect will occur for many years, if ever, will depend heavily on the successful development and eventual commercialization of CB-839. The success of CB-839, our arginase and hexokinase II inhibitor programs and any other product candidates we may develop will depend on many factors, including the following:

- successful enrollment in, and completion of, clinical trials;
- demonstrating safety and efficacy;
- receipt of marketing approvals from applicable regulatory authorities;
- establishing commercial manufacturing capabilities or making arrangements with third-party manufacturers;
- obtaining and maintaining patent and trade secret protection and non-patent exclusivity for our product candidates;
- launching commercial sales of the product candidates, if and when approved, whether alone or selectively in collaboration with others;
- acceptance of the product candidates, if and when approved, by patients, the medical community and third-party payors;
- effectively competing with other therapies;
- a continued acceptable safety profile of the products following approval; and
- enforcing and defending intellectual property rights and claims.

If we do not accomplish one or more of these goals in a timely manner, or at all, we could experience significant delays or an inability to successfully commercialize our product candidates, which would harm our business.

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

Our drug discovery efforts may not be successful in identifying compounds that are useful in treating cancer. Our research programs may initially show promise in identifying potential product candidates, yet fail to yield product candidates for clinical development for a number of reasons. In particular, our research methodology used may not be successful in identifying compounds

with sufficient potency or bioavailability to be potential product candidates. In addition, our potential product candidates may, on further study, be shown to have harmful side effects or other negative characteristics.

Research programs to identify new product candidates require substantial technical, financial and human resources. We may choose to focus our efforts and resources on potential product candidates that ultimately prove to be unsuccessful. If we are unable to identify suitable compounds for preclinical and clinical development, we will not be able to generate product revenue, which would harm our financial position and adversely impact our stock price.

If clinical trials of our product candidates fail to demonstrate safety and efficacy to the satisfaction of regulatory authorities or do not otherwise produce positive results, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates.

Before obtaining marketing approval from regulatory authorities for the sale of our product candidates, we must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates in humans. Clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to outcome. A failure of one or more clinical trials could occur at any stage of testing. The outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and interim results of a particular clinical trial do not necessarily predict final results of that trial.

Moreover, preclinical and clinical data are often susceptible to multiple interpretations and analyses. Many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their products.

We may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent our ability to receive marketing approval or commercialize our product candidates, including that:

- regulators or institutional review boards may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we may have delays in reaching or fail to reach agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites;
- clinical trials of our product candidates may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon product development programs;
- the number of patients required for clinical trials of our product candidates may be larger than we anticipate; enrollment in these clinical trials may be slower than we anticipate, or participants may drop out of these clinical trials at a higher rate than we anticipate;
- our third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- regulators or institutional review boards may require that we or our investigators suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks;
- the cost of clinical trials of our product candidates may be greater than we anticipate; and
- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate.

If we are required to conduct additional clinical trials or other testing of our product candidates beyond those that we currently contemplate, if we are unable to successfully complete clinical trials of our product candidates or other testing, if the results of these trials or tests are not positive or are only modestly positive or if there are safety concerns, we may:

- be delayed in obtaining marketing approval for our product candidates;

- not obtain marketing approval at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or safety warnings, including boxed warnings;

·be subject to additional post-marketing testing requirements; or
·have the product removed from the market after obtaining marketing approval.
Product development costs will also increase if we experience delays in testing or in receiving marketing approvals. We do not know whether any clinical trials will begin as planned, will need to be restructured or will be completed on schedule, or at all. Significant clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates, could allow our competitors to bring products to market before we do, and could impair our ability to successfully commercialize our product candidates, any of which may harm our business and results of operations.

If we experience delays or difficulties in enrolling patients in clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented.

We may not be able to initiate or continue clinical trials for our product candidates if we are unable to identify and enroll a sufficient number of eligible patients to participate in these trials as required by the U.S. Food and Drug Administration, or FDA, or analogous regulatory authorities outside the United States. In addition, some of our competitors may have ongoing clinical trials for product candidates that would treat the same indications as our product candidates, and patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors' product candidates. Patient enrollment is also affected by other factors, including:

·severity of the disease under investigation;
·availability and efficacy of approved medications for the disease under investigation;
·eligibility criteria for the trial in question;
·perceived risks and benefits of the product candidate under study;
·efforts to facilitate timely enrollment in clinical trials;
·patient referral practices of physicians;
·the ability to monitor patients adequately during and after treatment; and
·proximity and availability of clinical trial sites for prospective patients.
Our inability to enroll a sufficient number of patients for our clinical trials would result in significant delays or may require us to abandon one or more clinical trials altogether. Enrollment delays in our clinical trials may result in increased development costs for our product candidates, which would cause the value of our company to decline and limit our ability to obtain additional financing.

If serious adverse effects or unexpected characteristics of our product candidates are identified during development, we may need to abandon or limit our development of some or all of our product candidates.

CB-839 is our only product candidate in Phase 1 clinical trials, all our other programs are in preclinical development and their risk of failure is high. It is impossible to predict when or if any of our product candidates will prove effective or safe in humans or will receive marketing approval. If our product candidates are associated with undesirable side effects or have characteristics that are unexpected, we may need to abandon their development or limit development to certain uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. Many agents that initially showed promise in early stage testing for treating cancer or other diseases have later been found to cause side effects that prevented further development of the agent.

We are in early clinical trials with CB-839 and we have seen several adverse events deemed possibly or probably related to CB-839. As of January 19, 2015, a variety of adverse events, or AEs, have been reported. Treatment-emergent Grade ≥ 3 AEs occurring in >5% of patients included febrile neutropenia, thrombocytopenia , hyponatremia, and increases in liver enzymes aspartate aminotransferase (AST), alanine aminotransferase (ALT) and alkaline phosphatase. We have treated an insufficient number of patients to assess the safety of CB-839 and, as our

trials progress, we may experience more frequent or more severe adverse events. Our ongoing trials for CB-839 may fail due to safety issues, and we may need to abandon development of CB-839. Our arginase and hexokinase II inhibitor programs may also fail due to preclinical safety issues, causing us to abandon or delay the development of a product candidate from this program.

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

We have limited financial and managerial resources. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications 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 products. 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.

Even if any of our product candidates receive marketing approval, they may fail to achieve the degree of market acceptance by physicians, patients, third party payors and others in the medical community necessary for commercial success.

If any of our product candidates receive marketing approval, they may nonetheless fail to gain sufficient market acceptance by physicians, patients, third party payors and others in the medical community for us to achieve commercial success. For example, current cancer treatments like chemotherapy and radiation therapy for certain diseases and conditions are well established in the medical community, and doctors may continue to rely on these treatments. If our product candidates do not achieve an adequate level of acceptance, we may not generate significant product revenue to become profitable. The degree of market acceptance of our product candidates, if approved for commercial sale, will depend on a number of factors, including:

- the efficacy and potential advantages compared to alternative treatments;
- our ability to offer any approved products for sale at competitive prices;
- convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the strength of marketing and distribution support;
- sufficient third-party coverage or reimbursement; and
- the prevalence and severity of any side effects.

If, in the future, we are unable to establish sales and marketing capabilities or to selectively enter into agreements with third parties to sell and market our product candidates, we may not be successful in commercializing our product candidates if and when they are approved.

We do not have a sales or marketing infrastructure and have no experience in the sale, marketing or distribution of pharmaceutical products. To achieve commercial success for any approved product for which we retain sales and marketing responsibilities, we must either develop a sales and marketing organization or outsource these functions to other third parties. In the future, we may choose to build a focused sales and marketing infrastructure to sell some of our product candidates if and when they are approved.

There are risks involved both with establishing our own sales and marketing capabilities and with entering into arrangements with third parties to perform these services. For example, recruiting and training a sales force is expensive and time consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

Factors that may inhibit our efforts to commercialize our product candidates on our own include:

- our inability to recruit and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe any future products; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

If we enter into arrangements with third parties to perform sales, marketing and distribution services, our product revenue or the profitability of these product revenue to us may be lower than if we were to market and sell any products that we develop ourselves. In

addition, we may not be successful in entering into arrangements with third parties to sell and market our product candidates or may be unable to do so on terms that are favorable to us. We may have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively. If we do not establish sales and marketing capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates.

We face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than we do.

The development and commercialization of new drug products is highly competitive. We face competition with respect to our current product candidates, and will face competition with respect to any product candidates that we may seek to develop or commercialize in the future, from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide. There are a number of large pharmaceutical and biotechnology companies that currently market and sell products or are pursuing the development of products for the treatment of the cancer indications for which we are focusing our product development efforts. Some of these competitive products and therapies are based on scientific approaches that are the same as or similar to our approach and others are based on entirely different approaches. Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization.

We are developing our product candidates for the treatment of various cancers. There are a variety of available drug therapies marketed for cancer. In many cases, these drugs are administered in combination to enhance efficacy. Some of the currently approved drug therapies are branded and subject to patent protection, and others are available on a generic basis. Many of these approved drugs are well-established therapies and are widely accepted by physicians, patients and third-party payors. Insurers and other third-party payors may also encourage the use of generic products. We expect that if our product candidates are approved, they will be priced at a significant premium over competitive generic products. This may make it difficult for us to achieve our business strategy of using our product candidates in combination with existing therapies or replacing existing therapies with our product candidates.

There are also a number of product candidates in preclinical and clinical development by third parties to treat cancer by targeting cellular metabolism. Our principal competitors in the field of tumor metabolism include Advanced Cancer Therapeutics, LLC, Agios Pharmaceuticals, Inc., AstraZeneca plc, Bayer Pharma AG, Celgene Pharmaceuticals, Cornerstone Pharmaceuticals, Inc., Eli Lilly and Company, Forma Therapeutics Holdings, LLC, GlaxoSmithKline plc, Novartis International AG, Pfizer Inc., Quantum Pharmaceuticals, 3-V Biosciences, Inc., Roche Holdings, and its subsidiary Genentech Inc and Takeda Pharmaceutical Co. Ltd. Our principal competitors in the field of tumor immunology include AstraZeneca plc, Boehringer Ingelheim GmbH, Bristol-Myers Squibb Company, Coronado Biosciences, CureTech Ltd., EMD Serono, Inc., Flexus Biosciences, Incyte Corporation, iTeos Therapeutics, Merck & Co., NewLink Genetics Corporation, Ono Pharmaceuticals, Co., Ltd, Pfizer Inc., Roche Holdings and TG Therapeutics, Inc.

Our competitors may develop products that are more effective, safer, more convenient or less costly than any that we are developing or that would render our product candidates obsolete or non-competitive. In addition, our competitors may discover biomarkers that more efficiently measure metabolic pathways than our methods, which may give them a competitive advantage in developing potential products. Our competitors may also obtain marketing approval from the FDA or other regulatory authorities for their products sooner than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. Many of our competitors have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources

being concentrated among a smaller number of our competitors. Smaller and other early stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties may compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

Even if we are able to commercialize any product candidates, these products may become subject to unfavorable pricing regulations, third-party reimbursement practices or healthcare reform initiatives, which would harm our business.

The regulations that govern marketing approvals, pricing and reimbursement for new drugs vary widely from country to country. In the United States, new and future legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product-licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial marketing approval is granted. As a result, we might obtain marketing approval for a drug in a particular country, but then be subject to price regulations that delay its commercial launch, possibly for lengthy time periods, and negatively impact the revenue we are able to

generate from the sale of the drug in that country. Adverse pricing limitations may hinder our ability to commercialize and generate revenue from one or more product candidates, even if our product candidates obtain marketing approval.

Our ability to commercialize any product candidates successfully also will depend in part on the extent to which reimbursement for these products and related treatments will be available from government health programs, private health insurers and other organizations. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. A significant trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and third-party payors have attempted to control costs by limiting coverage and the amount of payment 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 medical products. Reimbursement may not be available for any product that we commercialize and, if reimbursement is available, the level of reimbursement may not be sufficient. Reimbursement may impact the demand for, or the price of, any product candidate for which we obtain marketing approval. If reimbursement is not available or is available only to limited levels, we may not be able to successfully commercialize any product candidate for which we obtain marketing approval.

There may be significant delays in obtaining reimbursement for newly approved products, and coverage may be more limited than the purposes for which the product is approved by the FDA or similar regulatory authorities outside the United States. Moreover, eligibility for reimbursement does not imply that any product will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the drug and the medical circumstances under which it is used, may be based on reimbursement levels already set for lower cost products or procedures or may be incorporated into existing payments for other services. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Third-party payors often rely upon Medicare coverage policies and payment limitations in setting their own reimbursement policies. Our inability to promptly obtain coverage and profitable payment rates from both government-funded programs and private payors for any approved products that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize our approved products and our overall financial condition.

Product liability lawsuits against us could cause us to incur substantial liabilities and could limit the commercialization of any product candidates we may develop.

We face an inherent risk of product liability exposure related to the testing of our product candidates in human clinical trials and will face an even greater risk if we commercially sell any products that we may develop after approval. If we cannot successfully defend ourselves against claims that our product candidates caused injuries, we could incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for any product candidates that we may develop;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- significant costs to defend any related litigation;
- substantial monetary awards to trial participants or patients;
- loss of revenue; and
- the inability to commercialize any products we may develop.

Although we maintain product liability insurance coverage in the amount of up to $10.0 million per claim and in the aggregate, it may not be adequate to cover all liabilities that we may incur. We anticipate that we will need to increase

our insurance coverage as we continue clinical trials and if we successfully commercialize any products. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could harm our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological and radioactive materials. Our operations also produce

hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties.

Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees in our workplace, including those resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, chemical, hazardous or radioactive materials.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Risks Related to Our Dependence on Third Parties

We rely on third parties to conduct our clinical trials and some aspects of our research and preclinical testing, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials, research or testing.

We currently rely and expect to continue to rely on third parties, such as contract research organizations, clinical data management organizations, medical institutions and clinical investigators, to conduct our clinical trials and to conduct some aspects of our research and preclinical testing. Any of these third parties may terminate their engagements with us at any time. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we will not be able to obtain, or may be delayed in obtaining, marketing approvals for our product candidates and will not be able to, or may be delayed in our efforts to, successfully commercialize our product candidates. Furthermore, these third parties may also have relationships with other entities, some of which may be our competitors. If we need to enter into alternative arrangements, it would delay our product development activities.

Our reliance on these third parties for research and development activities will reduce our control over these activities but will not relieve us of our responsibilities. For example, we will remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA requires us to comply with standards, commonly referred to as Good Clinical Practices, for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. We also are required to register ongoing clinical trials and post the results of completed clinical trials on a government sponsored database, available at www.clinicaltrials.gov, within certain timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

We also rely on other third parties to store and distribute drug supplies for our clinical trials. Any performance failure on the part of our distributors could delay clinical development or marketing approval of our product candidates or commercialization of our product candidates, producing additional losses and depriving us of potential product revenue.

We do not have any manufacturing facilities. We currently rely, and expect to continue to rely, on third party manufacturers for the manufacture of our product candidates for preclinical studies and clinical trials and for

commercial supply of any of these product candidates for which we obtain marketing approval. To date, we have obtained materials for CB-839 for our Phase 1 trial from third-party manufacturers. We have engaged third party manufacturers to obtain the active ingredient for CB-839 for pre-clinical testing and clinical trials. We do not have a long-term supply agreement with any third-party manufacturers, and we purchase our required drug supply on a purchase order basis.

We may be unable to establish agreements with third-party manufacturers or to do so on acceptable terms. Even if we are able to establish agreements with third-party manufacturers, reliance on third-party manufacturers entails additional risks, including:

reliance on the third party for regulatory compliance and quality assurance;

the possible breach of the manufacturing agreement by the third party; and

the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us.

Third-party manufacturers may not be able to comply with current U.S. Good Manufacturing Practice requirements, or cGMPs, or similar regulatory requirements outside the United States. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including fines, injunctions, civil penalties, delays,

suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates, operating restrictions and criminal prosecutions, any of which could adversely affect supplies of our product candidates and harm our business and results of operations.

Any product that we may develop may compete with other product candidates and products for access to these manufacturing facilities. There are a limited number of manufacturers that operate under cGMPs and that might be capable of manufacturing for us.

Any performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval. We do not currently have arrangements in place for redundant supply for bulk drug substances. If any one of our current contract manufacturers cannot perform as agreed, we may be required to replace that manufacturer. Although we believe that there are several potential alternative manufacturers who could manufacture our product candidates, we may incur added costs and delays in identifying and qualifying any such replacement.

Our current and anticipated future dependence upon others for the manufacture of our product candidates or products may adversely affect our future profit margins and our ability to commercialize any product candidates that receive marketing approval on a timely and competitive basis.

We also currently rely, and expect to continue to rely, on third parties to store and distribute drug supplies for our clinical trials. Any performance failure on the part of these third parties could delay clinical development or marketing approval of our product candidates or commercialization of our drugs, producing additional losses and depriving us of potential revenue. Although we believe that there are several potential alternative third parties who could store and distribute drug supplies for our clinical trials, we may incur added costs and delays in identifying and qualifying any such replacement.

We may seek to selectively establish collaborations, and, if we are unable to establish them on commercially reasonable terms, we may have to alter our development and commercialization plans.

Our drug development programs and the potential commercialization of our product candidates will require substantial additional cash to fund expenses. For some of our product candidates, we may decide to collaborate with additional pharmaceutical and biotechnology companies for the development and potential commercialization of those product candidates.

We may also be restricted under existing license agreements from engaging in research and development activities or entering into future agreements on certain terms with potential collaborators. For example, pursuant to our license agreement with Symbioscience. we have agreed not to develop any other arginase inhibitors for use in human healthcare outside of the scope of that agreement.

We face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator’s resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator’s evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by the FDA or similar regulatory authorities outside the United States, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing products, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge and industry and market conditions generally. The collaborator may also consider alternative product candidates for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us for our product candidate.

Collaborations are complex and time-consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators.

If we decide to collaborate with a third party in connection with any of our development programs or product candidates, we may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development program or the product candidate for which we are seeking to collaborate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop our product candidates or bring them to market and generate product revenue.

To the extent we enter into any collaborations, we may depend on such collaborations for the development and commercialization of our product candidates. If those collaborations are not successful, we may not be able to capitalize on the market potential of our product candidates.

We may selectively seek third-party collaborators for the development and commercialization of our product candidates. Our current and any future collaborators for any collaboration arrangements include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies. Pursuant to these arrangements and any potential future arrangements, we will have limited control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of our product candidates. Our ability to generate revenue from these arrangements will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements.

Collaborations involving our product candidates pose many risks to us, including that:

- Collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations.
- Collaborators may not pursue development and commercialization of our product candidates or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborator's strategic focus or available funding or external factors such as an acquisition that diverts resources or creates competing priorities.
- Collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing.
- Collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates or products if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours.
- A collaborator with marketing and distribution rights to one or more product candidates or products may not commit sufficient resources to the marketing and distribution of such drugs.
- Collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our proprietary information or expose us to potential litigation.
- Disputes may arise between the collaborators and us that result in the delay or termination of the research, development or commercialization of our product candidates or products or that result in costly litigation or arbitration that diverts management attention and resources.
- We may lose certain valuable rights under circumstances identified in our collaborations if we undergo a change of control.
- Collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates.
- Collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all. If a future collaborator of ours were to be involved in a business combination, the continued pursuit and emphasis on our product development or commercialization program under such collaboration could be delayed, diminished or terminated.

We have in-licensed portfolios of arginase inhibitors and hexokinase II inhibitors, respectively, as part of our efforts to develop product candidates for these programs, and we are substantially dependent on these in-licenses for these programs. To the extent these in-licenses are terminated, our business may be harmed.

Risks Related to Our Intellectual Property

Recent laws and rulings by U.S. courts make it difficult to predict how patents will be issued or enforced in our industry.

Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may have a significant impact on our ability to protect our technology and enforce our intellectual property rights. There have been numerous recent changes to the patent laws and to the rules of the United States Patent and Trademark Office, or the USPTO, which may have a significant impact on our ability to protect our technology and enforce our intellectual property rights. For example, the Leahy-Smith America Invents Act, which was signed into law in 2011, includes a transition from a “first-to-invent” system to a “first-to-file” system, and changes the way issued patents are challenged. Certain changes, such as the institution of inter partes review proceedings, came into effect on September 16, 2012. Substantive changes to patent law associated with the America Invents Act may affect our

ability to obtain patents, and, if obtained, to enforce or defend them in litigation or post-grant proceedings, all of which could harm our business.

Furthermore, the patent positions of companies engaged in the development and commercialization of biologics and pharmaceuticals are particularly uncertain. Two cases involving diagnostic method claims and "gene patents" have recently been decided by the Supreme Court. On March 20, 2012, the Supreme Court issued a decision in Mayo Collaborative Services v. Prometheus Laboratories, Inc., or Prometheus, a case involving patent claims directed to measuring a metabolic product in a patient to optimize a drug dosage amount for the patient. According to the Supreme Court, the addition of well-understood, routine or conventional activity such as "administering" or "determining" steps was not enough to transform an otherwise patent ineligible natural phenomenon into patent eligible subject matter. On July 3, 2012, the USPTO issued guidance indicating that process claims directed to a law of nature, a natural phenomenon or an abstract idea that do not include additional elements or steps that integrate the natural principle into the claimed invention such that the natural principle is practically applied and the claim amounts to significantly more than the natural principle itself should be rejected as directed to non-statutory subject matter. On June 13, 2013, the Supreme Court issued its decision in Association for Molecular Pathology v. Myriad Genetics, Inc., or Myriad, a case involving patent claims held by Myriad Genetics, Inc. relating to the breast cancer susceptibility genes BRCA1 and BRCA2. Myriad held that isolated segments of naturally occurring DNA, such as the DNA constituting the BRCA1 and BRCA2 genes, is not patent eligible subject matter, but that complementary DNA, which is an artificial construct that may be created from RNA transcripts of genes, may be patent eligible.

We cannot assure you that our efforts to seek patent protection for our technology and products will not be negatively impacted by the decisions described above, rulings in other cases or changes in guidance or procedures issued by the USPTO. We cannot fully predict what impact the Supreme Court's decisions in Prometheus and Myriad may have on the ability of life science companies to obtain or enforce patents relating to their products and technologies in the future.

Moreover, although the Supreme Court has held in Myriad that isolated segments of naturally occurring DNA are not patent-eligible subject matter, certain third parties could allege that activities that we may undertake infringe other gene-related patent claims, and we may deem it necessary to defend ourselves against these claims by asserting non-infringement and/or invalidity positions, or pay to obtain a license to these claims. In any of the foregoing or in other situations involving third-party intellectual property rights, if we are unsuccessful in defending against claims of patent infringement, we could be forced to pay damages or be subjected to an injunction that would prevent us from utilizing the patented subject matter. Such outcomes could harm our business.

If we are alleged to infringe intellectual property rights of third parties, our business could be harmed.

Our research, development and commercialization activities may be alleged to infringe patents, trademarks or other intellectual property rights owned by other parties. Certain of our competitors and other companies in the industry have substantial patent portfolios and may attempt to use patent litigation as a means to obtain a competitive advantage. We may be a target for such litigation. Even if our pending patent applications issue, they may relate to our competitors' activities and may therefore not deter litigation against us. The risks of being involved in such litigation may also increase as we become more visible as a public company and move into new markets and applications for our product candidates. There may also be patents and patent applications that are relevant to our technologies or product candidates that are unknown to us. For example, certain relevant patent applications may have been filed but not published. If such patents exist, or if a patent issues on any of such patent applications, that patent could be asserted against us. Third parties could bring claims against us that would cause us to incur substantial expenses and, if the claims against us are successful, could cause us to pay substantial damages, including treble damages and attorneys' fees for willful infringement. The defense of such a suit could also divert the attention of our management and technical personnel. Further, if an intellectual property infringement suit were brought against us, we could be

forced to stop or delay research, development or sales of the product that is the subject of the suit.

As a result of infringement claims, or to avoid potential claims, we may choose or be compelled to seek intellectual property licenses from third parties. These licenses may not be available on acceptable terms, or at all. Even if we are able to obtain a license, the license would likely obligate us to pay license fees or royalties or both, and the rights granted to us likely would be nonexclusive, which would mean that our competitors also could obtain licenses to the same intellectual property. Ultimately, we could be prevented from commercializing a product candidate and/or technology or be forced to cease some aspect of our business operations if, as a result of actual or threatened infringement claims, we are unable to enter into licenses of the relevant intellectual property on acceptable terms. Further, if we attempt to modify a product candidate and/or technology or to develop alternative methods or products in response to infringement claims or to avoid potential claims, we could incur substantial costs, encounter delays in product introductions or interruptions in sales.

We may become involved in other lawsuits to protect or enforce our patents or other intellectual property, which could be expensive and time-consuming, and an unfavorable outcome could harm our business.

In addition to the possibility of litigation relating to infringement claims asserted against us, we may become a party to other patent litigation and other proceedings, including inter partes review proceedings, postgrant review proceedings, derivation proceedings declared by the USPTO and similar proceedings in foreign countries, regarding intellectual property rights with respect to our current or future technologies or product candidates or products. The cost to us of any patent litigation or other proceeding, even if resolved in our favor, could be substantial. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their substantially greater financial resources. Patent litigation and other proceedings may also absorb significant management time. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could impair our ability to compete in the marketplace.

Competitors may infringe or otherwise violate our intellectual property, including patents that may issue to or be licensed by us. As a result, we may be required to file claims in an effort to stop third-party infringement or unauthorized use. Any such claims could provoke these parties to assert counterclaims against us, including claims alleging that we infringe their patents or other intellectual property rights. This can be expensive, particularly for a company of our size, and time-consuming, and even if we are successful, any award of monetary damages or other remedy we may receive may not be commercially valuable. In addition, in an infringement proceeding, a court may decide that our asserted intellectual property is not valid or is unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our intellectual property does not cover its technology. An adverse determination in any litigation or defense proceedings could put our intellectual property at risk of being invalidated or interpreted narrowly and could put our patent applications at risk of not issuing.

If the breadth or strength of our patent or other intellectual property rights is compromised or threatened, it could allow third parties to commercialize our technology or products or result in our inability to commercialize our technology and products without infringing third-party intellectual property rights. Further, third parties may be dissuaded from collaborating with us.

Interference or derivation proceedings brought by the USPTO or its foreign counterparts may be necessary to determine the priority of inventions with respect to our patent applications, and we may also become involved in other proceedings, such as re-examination proceedings, before the USPTO or its foreign counterparts. Due to the substantial competition in the pharmaceutical space, the number of such proceedings may increase. This could delay the prosecution of our pending patent applications or impact the validity and enforceability of any future patents that we may obtain. In addition, any such litigation, submission or proceeding may be resolved adversely to us and, even if successful, may result in substantial costs and distraction to our management.

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. Moreover, intellectual property law relating to the fields in which we operate is still evolving and, consequently, patent and other intellectual property positions in our industry are subject to change and are often uncertain. We may not prevail in any of these suits or other efforts to protect our technology, and the damages or other remedies awarded, if any, may not be commercially valuable. During the course of this type of litigation, there could 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, the market price for our common stock could be significantly harmed.

We may not be able to protect our intellectual property rights throughout the world, which could impair our competitive position.

Filing, prosecuting, defending and enforcing patents on all of our technologies, product candidates and products throughout the world would be prohibitively expensive. As a result, we seek to protect our proprietary position by filing patent applications in the United States and in select foreign jurisdictions and cannot guarantee that we will obtain the patent protection necessary to protect our competitive position in all major markets. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export infringing products to territories where we may obtain patent protection but where enforcement is not as strong as that in the United States. These products may compete with our current and future products in jurisdictions where we do not have any issued patents, and our patent claims or other intellectual property rights may not be effective or sufficient to prevent them from so competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing 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 the marketing of competing products in violation of our proprietary rights generally. The legal systems of certain countries make it difficult or impossible to obtain patent protection for pharmaceutical products and services. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and could divert our efforts and attention from other aspects of our business.

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

In addition to seeking patents for some of our technologies and product candidates, we also rely on trade secrets, including unpatented know-how, technology and other proprietary information, to maintain our competitive position. We seek to protect these trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, contract manufacturers, consultants, advisors and other third parties. We also enter into confidentiality and invention assignment agreements with our employees and consultants that obligate them to assign to us any inventions developed in the course of their work for us. However, we cannot guarantee that we have executed these agreements with each party that may have or have had access to our trade secrets or that the agreements we have executed will provide adequate protection. Despite these efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. As a result, we may be forced to bring claims against third parties, or defend claims that they bring against us, to determine ownership of what we regard as our intellectual property. Monitoring unauthorized disclosure is difficult and we do not know whether the procedures we have followed to prevent such disclosure are, or will be adequate. 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 may be less willing or unwilling to protect trade secrets. If any of the technology or information that we protect as trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to, or independently developed by, a competitor, our competitive position would be harmed.

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

Our trademarks or trade names may be challenged, infringed, circumvented, declared generic or determined to be infringing on other marks. As a means to enforce our trademark rights and prevent infringement, we may be required to file trademark claims against third parties or initiate trademark opposition proceedings. This can be expensive and time-consuming, particularly for a company of our size. In addition, in an infringement proceeding, a court may decide that a trademark of ours is not valid or is unenforceable, or may refuse to stop the other party from using the trademark at issue. We may not be able to protect our rights to these and other trademarks and trade names which we need to build name recognition by potential partners or customers in our markets of interest. We do not currently have any registered trademarks in the United States. Any trademark applications in the United States and in other foreign jurisdictions where we may file may not be allowed or may subsequently be opposed. In addition, other companies in the biopharmaceutical space may be using trademarks that are similar to ours and may in the future allege that our use of the trademark infringes or otherwise violates their trademarks. 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 harmed.

Third parties may assert ownership or commercial rights to inventions we develop.

Third parties may in the future make claims challenging the inventorship or ownership of our intellectual property. We have written agreements with collaborators that provide for the ownership of intellectual property arising from our collaborations. In some instances, there may not be adequate written provisions to address clearly the resolution of intellectual property rights that may arise from a collaboration. If we cannot successfully negotiate sufficient ownership and commercial rights to the inventions that result from our collaborations, or if disputes otherwise arise with respect to the intellectual property developed in the course of a collaboration, we may be limited in our ability to capitalize on the market potential of these inventions.

In addition, we may face claims by third parties that our agreements with employees, contractors or consultants obligating them to assign intellectual property to us are ineffective or are in conflict with prior or competing contractual obligations of assignment, which could result in ownership disputes regarding intellectual property we have developed or will develop and interfere with our ability to capture the commercial value of such inventions. Litigation may be necessary to resolve an ownership dispute, and if we are not successful, we may be precluded from using certain intellectual property, or may lose our exclusive rights in that intellectual property. Either outcome could have an adverse impact on our business.

Risks Related to Regulatory Approval of Our Product Candidates and Other Legal Compliance Matters

If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals, we will not be able to commercialize, or will be delayed in commercializing, our product candidates, and our ability to generate revenue will be impaired.

Our product candidates and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale and distribution, are subject to comprehensive regulation by the FDA and other regulatory agencies in the United States and by comparable authorities in other countries. Failure to obtain marketing approval for a product candidate will prevent us from commercializing the product

candidate. We have not received approval to market any of our product candidates from regulatory authorities in any jurisdiction. We have only limited experience in filing and supporting the applications necessary to gain marketing approvals and expect to rely on third-party contract research organizations to assist us in this process. Securing regulatory approval requires the submission of extensive preclinical and clinical data and supporting information to the various regulatory authorities for each therapeutic indication to establish the product candidate's safety and efficacy. Securing regulatory approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the relevant regulatory authority. Our product candidates may not be effective, may be only moderately effective or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining marketing approval or prevent or limit commercial use.

The process of obtaining marketing approvals, both in the United States and elsewhere, is expensive, may take many years and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. We cannot assure you that we will ever obtain any marketing approvals in any jurisdiction. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations or changes in regulatory review for each submitted product application may cause delays in the approval or rejection of an application. The FDA and comparable authorities in other countries have substantial discretion in the approval process and may refuse to accept any application or may decide that our data is insufficient for approval and require additional preclinical or other studies, and clinical trials. In addition, varying interpretations of the data obtained from preclinical testing and clinical trials could delay, limit or prevent marketing approval of a product candidate. Additionally, any marketing approval we ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable.

Any product candidate for which we obtain marketing approval could be subject to marketing 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 products.

Any product candidate for which we obtain marketing approval, along with the manufacturing processes, post-approval clinical data, labeling, advertising and promotional activities for such product, will be subject to continual requirements of and review by the FDA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, cGMP requirements, quality assurance and corresponding maintenance of records and documents and requirements regarding the distribution of samples to physicians and recordkeeping. Even if marketing approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the medicine. The FDA closely regulates the postapproval marketing and promotion of drugs to ensure that they are marketed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA imposes stringent restrictions on manufacturers' communications regarding off-label use and if we do not market our products for their approved indications, we may be subject to enforcement action for off-label marketing.

In addition, later discovery of previously unknown problems with our products, manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things:

- restrictions on such products, manufacturers or manufacturing processes;
- restrictions on the labeling, marketing, distribution or use of a product;
- requirements to conduct post-approval clinical trials;
- warning or untitled letters;
- withdrawal of the products from the market;

- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of products;
- fines, restitution or disgorgement of profits or revenue;
- suspension or withdrawal of marketing approvals;
- refusal to permit the import or export of our products;
- product seizure; and
- injunctions or the imposition of civil or criminal penalties.

Our relationships with customers and third-party payors will be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.

Healthcare providers, physicians and third-party payors play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval. Our future arrangements with third-party payors and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute our medicines for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations include the following:

the federal healthcare anti-kickback statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward 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 federal and state healthcare programs such as Medicare and Medicaid;

the federal False Claims Act imposes criminal and civil penalties, including 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, as amended by the Health Information Technology for Economic and Clinical Health Act, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program and also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;

the federal false statements statute prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services;

the federal transparency requirements under the Affordable Care Act requires manufacturers of drugs, devices, biologics and medical supplies to report to the Department of Health and Human Services information related to physician payments and other transfers of value and physician ownership and investment interests; 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, and some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring drug manufacturers to report information related to payments to physicians and other health care providers or marketing expenditures.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, exclusion from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. If any of the physicians or other providers or entities with whom we expect to do business are found to be not in compliance with applicable laws, they may be

subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

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

In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any product candidates for which we obtain marketing approval.

The Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or Medicare Modernization Act, changed the way Medicare covers and pays for pharmaceutical products. The legislation expanded Medicare coverage for drug purchases by the elderly and introduced a new reimbursement methodology based on average sales prices for physician-administered drugs. In addition, this legislation provided authority for limiting the number of drugs that will be covered in any therapeutic class. Cost reduction initiatives and other provisions of this legislation could decrease the coverage and price that we receive for any approved products.

While the Medicare Modernization Act applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates. Therefore, any reduction in reimbursement that results from the Medicare Modernization Act may result in a similar reduction in payments from private payors.

More recently, in March 2010, President Obama signed into law the Affordable Care Act, a sweeping law intended to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add new transparency requirements for health care and health insurance industries, impose new taxes and fees on the health industry and impose additional health policy reforms. Effective October 1, 2010, the Affordable Care Act revises the definition of "average manufacturer price" for reporting purposes, which could increase the amount of Medicaid drug rebates to states. Further, the new law imposes a significant annual fee on companies that manufacture or import branded prescription drug products. Substantial new provisions affecting compliance have also been enacted, which may affect our business practices with health care practitioners. We will not know the full effects of the Affordable Care Act until applicable federal and state agencies issue regulations or guidance under the new law. Although it is too early to determine the effect of the Affordable Care Act, the new law appears likely to continue the pressure on pharmaceutical pricing, especially under the Medicare program, and may also increase our regulatory burdens and operating costs.

Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We cannot be sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, may be. In addition, increased scrutiny by the U.S. Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing testing and other requirements.

Risks Related to Employee Matters and Managing Growth

Our future success depends on our ability to retain our senior management team and to attract, retain and motivate qualified personnel.

We are highly dependent upon our senior management team, as well as the other principal members of our research and development teams. All of our executive officers are employed "at will," meaning we or they may terminate the employment relationship at any time. We do not maintain "key person" insurance for any of our executives or other employees. The loss of the services of any of these persons could impede the achievement of our research, development and commercialization objectives.

Recruiting and retaining qualified scientific, clinical, manufacturing and sales and marketing personnel will also be critical to our success. We may not be able to attract and retain these personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors, may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us.

We expect to expand our operations, and may encounter difficulties in managing our growth, which could disrupt our business.

We expect to expand the scope of our operations, particularly in the areas of drug development, regulatory affairs and sales and marketing. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. We may not be able to effectively manage the expected expansion of our operations or recruit and train additional qualified personnel. Moreover, the expected expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

We may engage in acquisitions that could disrupt our business, cause dilution to our stockholders or reduce our financial resources.

In the future, we may enter into transactions to acquire other businesses, products or technologies. Because we have not made any acquisitions to date, our ability to do so successfully is unproven. If we do identify suitable candidates, we may not be able to make such acquisitions on favorable terms, or at all. Any acquisitions we make may fail to strengthen our competitive position, and these transactions may be viewed negatively by customers or investors. We may decide to incur debt in connection with an acquisition or issue our common stock or other equity securities to the stockholders of the acquired company, which would reduce the percentage ownership of our existing stockholders. We could incur losses resulting from undiscovered liabilities of the acquired business that are

not covered by the indemnification we may obtain from the seller. In addition, we may not be able to successfully integrate the acquired personnel, technologies and operations into our existing business in an effective, timely and non-disruptive manner. Acquisitions may also divert management attention from day-to-day responsibilities, increase our expenses and reduce our cash available for operations and other uses. We cannot predict the number, timing or size of future acquisitions or the effect that any such transactions might have on our operating results.

Risks Related to Our Common Stock

The trading price of our common stock is likely to be volatile, and purchasers of our common stock could incur substantial losses.

Our stock price has fluctuated in the past and is likely to be volatile in the future. From the date of our IPO through March 20, 2015, the reported sale price of our common stock has fluctuated between $6.51 and $33.48 per share. The stock market in general and the market for biotechnology companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, investors may experience losses on their investment in our common stock. The market price for our common stock may be influenced by many factors, including:

the success of competitive products or technologies;

regulatory actions with respect to our product candidates or our competitors' product and product candidates;

announcements by us or our competitors of significant acquisitions, strategic partnerships, joint ventures, collaborations or capital commitments;

results of clinical trials of our product candidates or those of our competitors;

regulatory or legal developments in the United States and other countries;

developments or disputes concerning patent applications, issued patents or other proprietary rights;

the recruitment or departure of key personnel;

the level of expenses related to any of our product candidates or clinical development programs;

the results of our efforts to in-license or acquire additional products or product candidates;

actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;

variations in our financial results or those of companies that are perceived to be similar to us;

fluctuations in the valuation of companies perceived by investors to be comparable to us;

inconsistent trading volume levels of our shares;

announcement or expectation of additional financing efforts;

sales of our common stock by us, our insiders or our other stockholders;

changes in the structure of healthcare payment systems;

market conditions in the pharmaceutical and biotechnology sectors;

general economic, industry and market conditions; and

the other factors described in this “Risk Factors” section.

In addition, in the past, stockholders have initiated class action lawsuits against companies following periods of volatility in the market prices of these companies’ stock. Such litigation, if instituted against us, could cause us to incur substantial costs and divert management’s attention and resources.

Concentration of ownership of our common stock among our existing executive officers, directors and principal stockholders may prevent new investors from influencing significant corporate decisions.

Our executive officers, directors and current beneficial owners of 5% or more of our common stock, in the aggregate, beneficially own a significant percentage of our outstanding common stock. These persons, acting together, will be able to significantly influence all matters requiring stockholder approval, including the election and removal of directors and any merger or other significant corporate transactions. The interests of this group of stockholders may not coincide with the interests of other stockholders.

Our quarterly operating results may fluctuate significantly or may fall below the expectations of investors or securities analysts, each of which may cause our stock price to fluctuate or decline.

We expect our operating results to be subject to quarterly fluctuations and will be affected by numerous factors, including:

our ability to successfully develop, obtain regulatory approvals, and market and sell CB-839 and our other product candidates;

the success of competitive products or technologies;

results of clinical trials of our product candidates or those of our competitors;

developments or disputes concerning patent applications, issued patents or other proprietary rights;

the recruitment or departure of key personnel;

the level of expenses related to any of our product candidates or clinical development programs;

the results of our efforts to discover, develop, acquire or in-license additional product candidates or medicines;

actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;

variations in our financial results or those of companies that are perceived to be similar to us;

market conditions in the pharmaceutical and biotechnology sectors;

general economic, industry and market conditions; and

the other factors described in this “Risk Factors” section.

If our quarterly operating results fall below the expectations of investors or securities analysts, the price of our common stock could decline substantially. Furthermore, any quarterly fluctuations in our operating results may, in turn, cause the price of our stock to fluctuate substantially. We believe that quarterly comparisons of our financial results are not necessarily meaningful and should not be relied upon as an indication of our future performance.

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

The trading market for our common stock will depend in part on the research and reports that securities or industry analysts publish about us or our business, our market and our competitors. We do not have any control over these analysts. If one or more of the analysts who cover us downgrade our shares or change their opinion of our shares, our share price would likely decline. If one or more of these analysts cease coverage of our company or fail to regularly publish reports on us, we could lose visibility in the financial markets, which could cause our share price or trading volume to decline.

We will incur costs and demands upon management as a result of complying with the laws and regulations affecting public companies in the United States, which may harm our operating results.

As a public company listed in the United States, we will incur significant additional legal, accounting and other expenses. In addition, changing laws, regulations and standards relating to corporate governance and public disclosure, including regulations implemented by the Securities and Exchange Commission, or the SEC, and the NASDAQ Global Market, may increase legal and financial compliance costs and make some activities more time-consuming. These laws, regulations and standards are subject to varying interpretations, and as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. We intend to invest resources to comply with evolving laws, regulations and standards, and this investment may result in increased general and administrative expenses and a diversion of management's time and attention from revenue-generating activities to compliance activities. If, notwithstanding our efforts to comply with new laws, regulations and standards, we fail to comply, regulatory authorities may initiate legal proceedings against us, and our business may be harmed.

Further, failure to comply with these laws, regulations and standards might also make it more difficult for us to obtain certain types of insurance, including director and officer liability insurance, and we might be forced to accept reduced policy limits and coverage or incur substantially higher costs to obtain the same or similar coverage. The impact of these events could also make it more difficult for us to attract and retain qualified persons to serve on our Board of Directors, on committees of our Board of Directors or as members of senior management.

We do not anticipate paying any cash dividends on our common stock so any returns will be limited to changes in the value of our common stock.

We have never declared or paid cash dividends on our common stock. We currently intend to retain our future earnings, if any, to fund the development and growth of our business. In addition, the terms of any existing or future credit facility may restrict our ability to pay dividends. Any return to stockholders will therefore be limited to the increase, if any, of our stock price.

We are an "emerging growth company," and we expect to comply with the reduced disclosure requirements applicable to emerging growth companies, which could make our common stock less attractive to investors.

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act, or JOBS Act, enacted in April 2012, and for as long as we continue to be an "emerging growth company," we expect to take advantage of exemptions from various reporting requirements applicable to other public companies but not to "emerging growth companies," including, but not limited to, not being required to comply with the auditor attestation requirements of Section 404, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved. We will continue to be an "emerging growth company" until the earlier of (1) the last day of the fiscal year (a) following the fifth anniversary of the closing of this offering, (b) in which we have total annual gross revenue of at least $1.0 billion, or (c) in which we are deemed to be a large accelerated filer, which means the market value of our common stock that is held by non-affiliates exceeds $700 million as of the prior December 31st, and (2) the date on which we have issued more than $1.0 billion in non-convertible debt during the prior three-year period. We cannot predict if investors will find our common stock less attractive if we choose to rely on these exemptions. If some investors find our common stock less attractive as a result of any choices to reduce future disclosure, there may be a less active trading market for our common stock, and our stock price may be more volatile.

If we are unable to maintain proper and effective internal controls over financial reporting, the accuracy and timeliness of our financial reporting may be adversely affected.

Effective internal controls are necessary for us to provide reliable financial reports and to protect from fraudulent, illegal or unauthorized transactions. If we cannot provide effective controls and reliable financial reports, our business and operating results could be harmed. We have in the past discovered, and may in the future discover, areas of our internal controls that need improvement. For example, in connection with the audit of our financial statements from inception through the year ended December 31, 2013, we and our independent public accounting firm identified a material weakness in our internal control over financial reporting. A "material weakness" is a deficiency, or a combination of deficiencies, in internal control over financial reporting such that there is a reasonable possibility that a material misstatement of our annual or interim financial statements will not be prevented or detected on a timely basis. The material weakness related to a deficiency in the operation of our internal controls over the accounting for a non-routine, complex equity transaction, which resulted in material post-closing adjustments to the convertible preferred stock and additional paid-in capital balances in the financial statements for the years ended December 31, 2011 and 2012. Specifically, we did not properly account for a reduction in the liquidation preference amount the holders of our Series A preferred stock would be entitled to receive in the event we consummate a change in control.

We have implemented changes to our disclosure controls and procedures and internal control over financial reporting to remediate the material weakness identified above. We have strengthened the operation of our internal controls over the accounting for non-routine, complex equity transactions, including increasing the depth and experience within our accounting and finance organization, as well as designing and implementing improved processes and internal controls to identify such matters. We have hired additional personnel to build our financial management and reporting

infrastructure, including the hiring of our Chief Financial Officer and Vice President, Finance, in the second quarter of 2014. While we believe, we have remediated this material weakness, neither we nor our independent registered public accounting firm has performed an evaluation of our internal control over financial reporting during any period in accordance with the provisions of the Sarbanes-Oxley Act. In light of the material weakness that was identified as a result of the limited procedures performed, we believe that it is possible that, had we and our independent registered public accounting firm performed an evaluation of our internal control over financial reporting in accordance with the provisions of the Sarbanes-Oxley Act, additional material weaknesses or significant control deficiencies may have been identified.

If material weaknesses or control deficiencies occur in the future, we may be unable to report our financial results accurately on a timely basis, which could cause our reported financial results to be materially misstated and result in the loss of investor confidence and cause the market price of our common stock to decline.

We will be required, pursuant to Section 404 of the Sarbanes-Oxley Act, to furnish a report by management on, among other things, the effectiveness of our internal control over financial reporting for the fiscal year ending December 31, 2015. This assessment will need to include disclosure of any material weaknesses identified by our management in our internal control over financial reporting. Our independent registered public accounting firm will not be required to attest to the effectiveness of our internal control

over financial reporting until our first annual report required to be filed with the SEC following the later of the date we are deemed to be an "accelerated filer" or a "large accelerated filer," each as defined in the Securities Exchange Act of 1934, as amended, or the Exchange Act, or the date we are no longer an "emerging growth company," as defined in the JOBS Act. We will be required to disclose changes made in our internal control and procedures on a quarterly basis. To comply with the requirements of being a public company, we may need to undertake various actions, such as implementing new internal controls and procedures and hiring accounting or internal audit staff. We have begun the costly and challenging process of compiling the system and processing documentation necessary to perform the evaluation needed to comply with Section 404, when applicable, and we may not be able to complete our evaluation, testing and any required remediation in a timely fashion.

Future sales of shares by existing stockholders could cause our stock price to decline.

Sales of a substantial number of shares of our common stock in the public market, or the perception that the sales might occur, could depress the market price of our common stock and could impair our ability to raise capital through the sale of additional equity securities. We are unable to predict the effect that sales may have on the prevailing market price of our common stock.

Provisions in our corporate charter documents and under Delaware law may prevent or frustrate attempts by our stockholders to change our management or hinder efforts to acquire a controlling interest in us, and the market price of our common stock may be lower as a result.

There are provisions in our certificate of incorporation and bylaws that may make it difficult for a third party to acquire, or attempt to acquire, control of our company, even if a change in control was considered favorable by our stockholders.

Our charter documents also contain other provisions that could have an anti-takeover effect, such as:

- establishing a classified Board of Directors so that not all members of our Board of Directors are elected at one time;
- permitting the Board of Directors to establish the number of directors and fill any vacancies and newly created directorships;
- providing that directors may only be removed for cause;
- prohibits cumulative voting for directors;
- requiring super-majority voting to amend some provisions in our certificate of incorporation and bylaws;
- authorizing the issuance of "blank check" preferred stock that our Board of Directors could use to implement a stockholder rights plan;
- eliminating the ability of stockholders to call special meetings of stockholders; and
- prohibiting stockholder action by written consent, which requires all stockholder actions to be taken at a meeting of our stockholders.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which prohibit a person who owns 15% or more of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner. Any provision in our certificate of incorporation or our bylaws or Delaware law that has the effect of delaying or deterring a change in control could limit the opportunity for our stockholders to receive a premium for their shares of our common stock, and could also affect the price that some investors are willing to pay for our common stock.

Our amended and restated certificate of incorporation provides 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 provides 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 bylaws; or any action asserting a claim against us that is governed by the internal affairs doctrine. The choice of forum 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. If a court were to find the choice of forum provision contained in our amended and restated certificate of incorporation to be

inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could harm our business and financial condition.

Item 1B. Unresolved Staff Comments.
None.

Item 2. Properties.
Our headquarters are located at 343 Oyster Point Blvd., Suite 200, South San Francisco, California 94080 under a lease that expires in November 2017 with an option to extend another two years to November 2019. We have subleased a portion of this laboratory space to another biotechnology company under a two-year sublease agreement. We believe that our existing facilities are adequate for our current needs, as the facilities have sufficient laboratory space to house additional scientists to be hired as we expand.

Item 3. Legal Proceedings.
From time to time, we may become involved in legal proceedings relating to claims arising from the ordinary course of business. Our management believes that there are currently no claims or actions pending against us, the ultimate disposition of which could have a material adverse effect on our results of operations, financial condition or cash flows.

Item 4. Mine Safety Disclosures.
Not applicable.

PART II

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

Price Range of Common Stock

Our common stock commenced trading on the NASDAQ Global Select Market under the symbol "CALA" on October 2, 2014. Prior to that date, there was no public trading market for our common stock. The following table sets forth, for the periods indicated, the high and low reported sales prices of our common stock as reported on the NASDAQ Global Select Market:

2014	High	Low
Fourth Quarter (from October 2, 2014)	$33.48	$6.51

As of March 20, 2015, there were 72 holders of record of our common stock.

Stock Price Performance Graph

The following stock performance graph compares our total stock return with the total return for (i) the NASDAQ Composite Index and the (ii) the NASDAQ Biotechnology Index for the period from October 2, 2014 (the date our common stock commenced trading on the NASDAQ Global Market) through December 31, 2014. The figures represented below assume an investment of $100 in our common stock at the closing price of $9.41 on October 2, 2014 and in the NASDAQ Composite Index and the NASDAQ Biotechnology Index on October 2, 2014 and the reinvestment of dividends into shares of common stock. The comparisons in the table are required by the SEC and are not intended to forecast or be indicative of possible future performance of our common stock.

$100 investment in stock or index	Ticker	October 2, 2014	December 31, 2014
Calithera Biosciences, Inc.	CALA	$100.00	$214.67
NASDAQ Composite Index	IXIC	$100.00	$106.90
NASDAQ Biotechnology Index	NBI	$100.00	$113.00

This graph shall not be deemed "soliciting material" or be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, or the Exchange Act, or otherwise subject to the liabilities under that Section, and shall not be deemed to be incorporated by reference into any of our filings under the Securities Act of 1933, as amended, or the Securities Act, whether made before or after the date hereof and irrespective of any general incorporation language in any such filing.

Dividend Policy

We have never declared or paid cash dividends on our capital stock. We intend to retain all available funds and any future earnings, if any, to fund the development and expansion of our business and we do not anticipate paying any cash dividends in the foreseeable future. Any future determination related to dividend policy will be made at the discretion of our Board of Directors.

Recent Sale of Unregistered Securities

From January 1, 2014 through December 31, 2014, we sold and issued the following unregistered securities, which share numbers have been adjusted, as appropriate, for the 48-to-1 reverse stock split that occurred on September 19, 2014:

(1) Prior to filing our registration statement on Form S-8 in October 2014, we sold an aggregate of 155,532 shares of common stock to employees, directors and consultants for cash consideration in the aggregate amount of $249,000 upon the exercise of stock options and stock awards.
(2) Prior to filing our registration statement on Form S-8 in October 2014, we granted stock options and stock awards to employees, directors and consultants under our 2010 Equity Incentive Plan covering an aggregate of 547,160 shares of common stock, at an average exercise price of $5.05 per share. Of these, options covering an aggregate of 1,885 shares were cancelled without being exercised.
(3) In July 2014, we issued 1,902,583 shares of our Series D preferred stock, par value $0.0001, to accredited investors at a price per share of $8.41 for an aggregate purchase price of $16.0 million. Upon the closing of our initial public offering, these shares converted into 1,902,583 shares of common stock.

The offers, sales and issuances of the securities described in paragraphs (1) and (2) above were deemed to be exempt from registration under the Securities Act under Rule 701 promulgated under the Securities Act as offers and sale of securities pursuant to certain compensatory benefit plans and contracts relating to compensation in compliance with Rule 701.

The offers, sales, and issuances of the securities described in paragraph (3) above were deemed to be exempt from registration under the Securities Act in reliance on Section 4(2) of the Securities Act or Regulation D promulgated thereunder as transactions by an issuer not involving a public offering. The recipients of securities in each of these transactions acquired the securities for investment only and not with a view to or for sale in connection with any distribution thereof and appropriate legends were affixed to the securities issued in these transactions. Each of the recipients of securities in these transactions was an accredited or sophisticated person and had adequate access, through employment, business or other relationships, to information about us.

Use of Proceeds from Registered Securities

On October 7, 2014, we closed our IPO, in which we issued and sold 8,000,000 shares of our common stock at a public offering price of $10.00 per share, for net proceeds of $71.6 million, after deducting underwriting discounts and commissions of $5.6 million and estimated offering expenses of $2.8 million payable by the Company. No payments for such expenses were made directly or indirectly to (i) any of our officers or directors or their associates, (ii) any persons owning 10% or more of any class of our equity securities, or (iii) any of our affiliates. The offer and sale of all of the shares in the IPO were registered under the Securities Act pursuant to a registration statement on Form S-1 (File No. 333-198355), which was declared effective by the SEC on October 1, 2014. Citigroup Global Markets and Leerink Partners acted as joint book-running managers for the offering. Wells Fargo Securities and JMP Securities acted as co-managers for the offering. Following the sale of the shares in connection with the closings of the IPO, the offering terminated.

We have been using and will continue to use the net offering proceeds to advance our product candidates through clinical trial programs and for working capital and general corporate purposes. No such payments were made directly or indirectly by us to directors, officers or persons owning ten percent or more of our common stock.

There has been no material change in the planned use of proceeds from our IPO as described in our prospectus dated October 1, 2014, filed with the SEC pursuant to Rule 424(b) under the Securities Act of 1933, as amended.

Issuer Purchases of Equity Securities

None.

Item 6. Selected Financial Data.

The statement of operations data for the years ended December 31, 2014, 2013 and 2012 and the balance sheet data as of December 31, 2014 and 2013 are derived from our audited financial statements included elsewhere in this report. The selected balance sheet data as of December 31, 2012 is derived from our audited financial statements which are not included in this report.

Our historical results are not necessarily indicative of the results to be expected in the future. You should read the selected financial data below in conjunction with the section of this report entitled "Item 7. Management's discussion and analysis of financial condition and results of operations" and our financial statements and the related notes included in this Annual Report on Form 10-K.

	Year Ended December 31,		
	2014	2013	2012
Statements of Operation Data:	(in thousands)		
Operating expenses:			
Research and development	$16,367	$9,900	$6,558
General and administrative	5,354	2,478	1,417
Total operating expenses	21,721	12,378	7,975
Loss from operations	(21,721)	(12,378)	(7,975)
Other income	9	1	—
Net loss	(21,712)	(12,377)	(7,975)
Gain on extinguishment of convertible preferred stock	—	—	2,889
Net loss attributable to common stockholders	$(21,712)	$(12,377)	$(5,086)
Net loss per share attributable to common stockholders, basic and diluted	$(4.67)	$(131.53)	$(366.13)
Shares used in computing net loss per share attributable to common stockholders, basic and diluted	4,652	94	14

	Year Ended December 31,		
	2014	2013	2012
Balance Sheet Data:	(in thousands)		
Cash and cash equivalents	$101,969	$33,820	$2,205
Working capital	99,742	32,825	1,363
Total assets	104,770	34,844	3,060
Convertible preferred stock	—	54,282	10,722
Accumulated deficit	(51,854)	(30,142)	(17,765)
Total stockholders' equity (deficit)	100,366	(20,813)	(8,571)

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

Some of the statements under in this "Management's Discussion and Analysis of Financial Condition and Results of Operations" are forward-looking statements. These forward-looking statements are based on management's beliefs and assumptions and on information currently available to our management and involve significant elements of subjective judgment and analysis. Words such as "may," "will," "should," "could," "would," "expect," "plan," "anticipate," "believe," "es "project," "predict," "potential," "seek""target," "goals,""intend," variations of such words, and similar expressions are intende identify forward-looking statements. Our actual results and the timing of events may differ significantly from the results discussed in the forward-looking statements. Factors that might cause such a difference include those discussed under the caption "Special Note Regarding Forward Looking Statements" and in "Risk Factors" and elsewhere in this Annual Report on Form 10-K. These and many other factors could affect our future financial and operating results. We undertake no obligation to update any forward-looking statement to reflect events after the date of this Annual Report.

Overview

We are a clinical-stage pharmaceutical company focused on discovering and developing novel small molecule drugs directed against tumor metabolism and tumor immunology targets for the treatment of cancer. Tumor metabolism and tumor immunology have emerged as promising new fields for cancer drug discovery, and recent clinical successes with therapeutic agents in each field have demonstrated the potential to create fundamentally new therapies for cancer patients. Our lead product candidate, CB-839, is an internally discovered, first-in-class inhibitor of glutaminase, a critical enzyme in tumor metabolism. We are currently evaluating CB-839 in three Phase 1 clinical trials in solid and hematological tumors. Our lead preclinical program in tumor immunology is directed at developing inhibitors of the enzyme arginase and may provide a first-in-class therapeutic agent for this novel target. Our ongoing research efforts are focused on discovering additional product candidates against novel tumor metabolism and immunology targets.

The field of tumor metabolism seeks to exploit the unique ways in which cancer cells take up and utilize nutrients in order to grow and survive. Our lead product candidate in tumor metabolism, CB-839, takes advantage of the pronounced dependency many cancers have on the nutrient glutamine for growth and survival. CB-839 inhibits glutaminase, an enzyme required by cancer cells to utilize glutamine effectively. We are currently conducting three Phase 1 clinical trials of CB-839 in the United States in patients with solid tumors, leukemias, lymphomas and multiple myeloma. The purpose of these trials is to evaluate the safety of CB-839 both as a single agent and in combination with approved therapies and to seek preliminary evidence of efficacy. Pending input from the FDA on the results of our Phase 1 trials and Phase 2 trial protocols, we plan to initiate one or more Phase 2 clinical trials of CB-839 in 2016. We currently hold all commercial rights to CB-839.

Our second program in tumor metabolism is focused on the hexokinase II enzyme. A defining characteristic of most cancer cells is their increased uptake of glucose. Cancer cells use glucose in a different manner than normal cells, but an obligate first step in all glucose utilizing pathways is phosphorylation of glucose by the enzyme hexokinase. Due to their higher glucose needs, cancer cells frequently increase the level of this critical enzyme, specifically the isoform hexokinase II. We believe inhibitors of hexokinase II will significantly impede the ability of cancer cells to survive and proliferate and may lead to new approaches in treating cancer. Our new program in hexokinase II inhibitors was in-licensed from TransTech Pharma and we seek to identify and advance a drug candidate into clinical development as quickly as possible. We will provide additional details on our development plans and timelines in the near future as we undertake pre-clinical studies to profile our portfolio of hexokinase II inhibitors.

The field of tumor immunology seeks to activate the body's own immune system to attack and kill cancer cells. Our preclinical program in tumor immunology is focused on developing selective inhibitors of the enzyme arginase. Arginase depletes arginine, a nutrient that is critical for the activation, growth and survival of the body's cancer-fighting immune cells. We believe that inhibitors of arginase can promote an anti-tumor immune response by

restoring arginine levels, thereby allowing activation of the body's cancer-fighting immune cells. We are currently optimizing arginase inhibitors with the aim of submitting an IND application to the FDA in early 2016.

Since our inception in 2010, we have devoted substantially all of our resources to identifying and developing CB-839, advancing our preclinical programs, conducting clinical trials and providing general and administrative support for these operations. We have not recorded revenue from product sales, collaboration activities or any other source. We have funded our operations to date primarily from the issuance and sale of convertible preferred stock and the initial public offering, or IPO, of our common stock that occurred in October 2014. In connection with the IPO, we sold 8,000,000 shares of common stock for proceeds of $71.6 million net of underwriting discounts and commissions and offering expenses.

We have never been profitable and have incurred net losses in each year since inception. Our net losses were $21.7 million, $12.4 million and $8.0 million for 2014, 2013 and 2012. As of December 31, 2014 we had an accumulated deficit of $51.9 million. Substantially all of our net losses have resulted from costs incurred in connection with our research and development programs and from general and administrative costs associated with our operations.

We expect to continue to incur significant expenses and increasing operating losses over at least the next several years. We expect our expenses will increase substantially in connection with our ongoing activities, as we:

- advance product candidates through clinical trials;
- pursue regulatory approval of product candidates;
- operate as a public company;
- continue our preclinical programs and clinical development efforts;
- continue research activities for the discovery of new product candidates; and
- manufacture supplies for our preclinical studies and clinical trials.

Critical Accounting Polices and Estimates

Our management's discussion and analysis of our financial condition and results of operations is based on our financial statements, which have been prepared in accordance with United States generally accepted accounting principles, or U.S. GAAP. The preparation of these financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements, as well as the reported 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 estimates under different assumptions or conditions. 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.

Accrued Research and Development Costs

We record accrued expenses for estimated costs of our research and development activities conducted by third-party service providers, which include the conduct of preclinical studies and clinical trials and contract manufacturing activities. We record the estimated costs of research and development activities based upon the estimated amount of services provided but not yet invoiced, and include these costs in accrued liabilities in the balance sheet and within research and development expense in the statement of operations and comprehensive loss. These costs are a significant component of our research and development expenses. We record accrued expenses for these costs based on the estimated amount of work completed and in accordance with agreements established with these third parties.

We estimate the amount of work completed through discussions with internal personnel and external service providers as to the progress or stage of completion of the services and the agreed-upon fee to be paid for such services. We make significant judgments and estimates in determining the accrued balance in each reporting period. As actual costs become known, we adjust our accrued estimates. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed, the number of patients enrolled, and the rate of patient enrollment may vary from our estimates and could result in us reporting amounts that are too high or too low in any particular period. Our accrued expenses are dependent, in part, upon the receipt of timely and accurate reporting from clinical research organizations and other third-party service providers. To date, there have been no material differences from our accrued expenses to actual expenses.

Stock-Based Compensation

We recognize compensation costs related to stock options granted to employees based on the estimated fair value of the awards on the date of grant, net of estimated forfeitures. We estimate the grant date fair value, and the resulting stock-based compensation expense, using the Black-Scholes option-pricing model. The grant date fair value of the stock-based awards is generally recognized on a straight-line basis over the requisite service period, which is generally

the vesting period of the respective awards.

The Black-Scholes option-pricing model requires the use of highly subjective assumptions, which determine the fair value of stock-based awards. These assumptions include:

Expected Term. Our expected term represents the period that our stock-based awards are expected to be outstanding and is determined using the simplified method (based on the mid-point between the vesting date and the end of the contractual term).

Expected Volatility. Since we have only been publicly traded for a short period and do not have adequate trading history for our common stock, the expected volatility was estimated based on the average volatility for comparable publicly traded

biopharmaceutical companies over a period equal to the expected term of the stock option grants. The comparable companies were chosen based on their similar size, stage in the life cycle, or area of specialty.

Risk-Free Interest Rate. The risk-free interest rate is based on the U.S. Treasury zero coupon issues in effect at the time of grant for periods corresponding with the expected term of option.

Expected Dividend. We have never paid dividends on our common stock and have no plans to pay dividends on our common stock. Therefore, we used an expected dividend yield of zero.

In addition to the Black-Scholes assumptions, we estimate our forfeiture rate based on an analysis of our actual forfeitures and will continue to evaluate the adequacy of the forfeiture rate based on actual forfeiture experience, analysis of employee turnover behavior, and other factors. The impact from any forfeiture rate adjustment would be recognized in full in the period of adjustment and if the actual number of future forfeitures differs from our estimates, we might be required to record adjustments to stock-based compensation in future periods.

Prior to our IPO in October 2014, the fair value of the shares of common stock underlying our share-based awards were estimated on each grant date by our Board of Directors. In order to determine the fair value of our common stock underlying option grants, our Board of Directors considered, among other things, timely valuations of our common stock prepared by an unrelated third-party valuation firm in accordance with the guidance provide by the American Institute of Certified Public Accountants Practice Guide, Valuation of Privately-Held-Company Equity Securities Issued as Compensation. Given the absence of a public trading market for our common stock, our Board of Directors exercised reasonable judgment and considered a number of objective and subjective factors to determine the best estimate of the fair value of our common stock, including our stage of development; progress of our research and development efforts; the rights, preferences and privileges of our preferred stock relative to those of our common stock; equity market conditions affecting comparable public companies and the lack of marketability of our common stock. After the closing of our IPO, our Board of Directors determines the fair value of each share of underlying common stock based on the closing price of our common stock as reported by the NASDAQ Global Market on the date of grant.

Income Taxes

As of December 31, 2014, we had approximately $48.6 million and $48.0 million, respectively, of federal and state operating loss carryforwards available to reduce future taxable income that will begin to expire in 2030 for federal and state tax purposes.

As of December 31, 2014, we also had research and development tax credit carryforwards of approximately $1.6 million and $1.4 million, respectively, for federal and state purposes available to offset future taxable income tax. If not utilized, the federal carryforwards will expire in various amounts beginning in 2030, and the state credits can be carried forward indefinitely.

Utilization of the net operating loss carryforwards may be subject to a substantial annual limitation due to the ownership change limitations provided by the Internal Revenue Code of 1986, as amended, and similar state provisions. We have performed an analysis to determine whether an "ownership change" has occurred from inception to December 31, 2014. Based on this analysis, management has determined that there was an ownership change. The annual limitation may result in the expiration of net operating losses and credits before utilization, however, we do not believe any of our net operating losses and research and development credits are limited by this potential ownership change.

Financial Operations Overview

Research and Development Expenses

Research and development expenses represent costs incurred to conduct research, such as the discovery and development of our product candidates. We recognize all research and development costs as they are incurred. Research and development expenses consist primarily of the following:

- employee-related expenses, which include salaries, benefits and stock-based compensation;
- expenses incurred under agreements with clinical trial sites that conduct research and development activities on our behalf;
- laboratory and vendor expenses related to the execution of preclinical studies and clinical trials;
- contract manufacturing expenses, primarily for the production of clinical supplies;
- facilities and other allocated expenses, which include direct and allocated expenses for rent and maintenance of facilities, depreciation and amortization expense and other supplies.

The largest component of our total operating expenses has historically been our investment in research and development activities including the clinical development of our product candidates. We allocate to research and development expenses the salaries, benefits, stock-based compensation expense, and indirect costs of our clinical and preclinical programs on a program-specific basis, and we include these costs in the program-specific expenses. The following table shows our research and development expenses for 2014, 2013 and 2012:

	Years Ended December 31,		
	2014	2013	2012
	(in thousands)		
Development candidate:			
CB-839	$12,381	$5,283	$—
Preclinical and research:			
CB-839	-	3,849	5,791
Arginase inhibitors	3,461	-	-
Other preclinical and research	525	768	767
Total preclinical and research	3,986	4,617	6,558
Total	$16,367	$9,900	$6,558

We expect our research and development expenses will increase during the next few years as we advance our product candidates into and through clinical trials, pursue regulatory approval of our product candidates, which will require a significant investment in contract manufacturing and inventory build-up related costs. In December 2014, we entered into an exclusive license agreement with Symbioscience to develop and commercialize their portfolio of arginase inhibitors and in March 2015, we entered into an exclusive license agreement with TransTech to develop and commercialize their hexokinase II inhibitors. These license agreements will result in higher research and development expenses in the future.

The process of conducting clinical trials necessary to obtain regulatory approval is costly and time consuming. We may never succeed in achieving marketing approval for our product candidates. The probability of success of our product candidates may be affected by numerous factors, including clinical data, competition, manufacturing capability and commercial viability. As a result, we are unable to determine the duration and completion costs of our research and development projects or when and to what extent we will generate revenue from the commercialization and sale of any of our product candidates.

General and Administrative Expenses

General and administrative expenses consist of personnel costs, allocated expenses and other expenses for outside professional services, including legal, audit and accounting services. Personnel costs consist of salaries, benefits and stock-based compensation. Allocated expenses consist of facilities and other allocated expenses, which include direct and allocated expenses for rent and maintenance of facilities, depreciation and amortization expense and other supplies. We expect to incur additional expenses as a result of operating as a public company, including costs to comply with the rules and regulations applicable to companies listed on a national securities exchange and costs related to compliance and reporting obligations pursuant to the rules and regulations of the SEC. In addition, we have incurred and expect to continue to incur increased expenses related to additional insurance, investor relations and other increases related to needs for additional human resources and professional services associated with being a public company.

Results of Operations

Comparison of the Years Ended December 31, 2014 and 2013

	Years Ended December 31,		Change	
	2014	2013	$	%
	(in thousands, except percentages)			
Operating expenses:				
Research and development	$16,367	$9,900	$6,467	65 %
General and administrative	5,354	2,478	2,876	116%
Total operating expenses	21,721	12,378	9,343	75 %
Loss from operations	(21,721)	(12,378)	(9,343)	75 %
Other income	9	1	8	*
Net loss	$(21,712)	$(12,377)	$(9,335)	75 %

* Percentage not meaningful.

Research and Development

Research and development expenses increased $6.5 million, or 65%, from $9.9 million for 2013 to $16.4 million for 2014. The increase was due to an increase of $3.5 million in clinical trial related expenses in connection with our CB-839 Phase 1 clinical trials which began enrolling patients in February 2014, an increase of $1.9 million in personnel-related costs primarily as a result of higher headcount, an increase of $0.8 million in costs related to CB-839 development and manufacturing to support our Phase 1 clinical trials, and $0.3 million related to our licensing arrangement for arginase inhibitors program.

General and Administrative

General and administrative expenses increased $2.9 million, or 116%, from $2.5 million for 2013, to $5.4 million for 2014. The increase was due to an increase of $1.7 million in personnel-related costs as a result of higher headcount, salary increases and stock-based compensation expense, an increase of $0.6 million in professional services costs primarily related to audit fees and an increase of $0.5 million in facility costs due to our office expansion in the second half of 2013.

Comparison of the Years Ended December 31, 2013 and 2012

	Years Ended December 31,		Change	
	2013	2012	$	%
	(in thousands, except percentages)			
Operating expenses:				
Research and development	$9,900	$6,558	$3,342	51%
General and administrative	2,478	1,417	1,061	75%
Total operating expenses	12,378	7,975	4,403	55%
Loss from operations	(12,378)	(7,975)	(4,403)	55%
Other income	1	-	1	*
Net loss	$(12,377)	$(7,975)	$(4,402)	55%

* Percentage not meaningful.

Research and Development

Research and development expenses increased $3.3 million, or 51%, from $6.6 million for 2012 to $9.9 million for 2013. The increase was due to an increase of $2.1 million in external costs related to CB-839 development activities and manufacturing to support our Phase 1 clinical trials, an increase of $0.7 million in connection with start-up activities to support our CB-839 Phase 1 clinical trials, an increase of $0.5 million in personnel-related costs as a result of increased headcount and an increase of $0.2 million in professional services costs. These increases were

partially offset by a decrease of $0.4 million in laboratory supplies costs.

General and Administrative

General and administrative expenses increased $1.1 million, or 75%, from $1.4 million for 2012, to $2.5 million for 2013. The increase was due to an increase of $0.9 million in professional consulting expenses in connection with our market evaluation of CB-839, our evaluation of potential partnership opportunities and accounting services. In addition, facility-related costs increased by $0.1 million due to our office expansion in the second half of 2013.

Liquidity and Capital Resources

As of December 31, 2014, we had cash and cash equivalents totaling $102.0 million. In connection with our IPO that closed in October 2014, we received cash proceeds of $71.6 million, net of underwriters' discounts and commissions and expenses paid by us. Prior to the IPO, our operations have been financed primarily by net proceeds from the sale of shares of our preferred stock.

Our primary uses of cash are to fund operating expenses, primarily research and development expenditures. Cash used to fund operating expenses is impacted by the timing of when we pay these expenses, as reflected in the change in our outstanding accounts payable and accrued expenses.

We believe that our existing cash and cash equivalents as of December 31, 2014 will be sufficient for us to meet our current operating plan for at least the next twelve months. However, our forecast of the period of time through which our financial resources will be adequate to support our operations is a forward-looking statement that involves risks and uncertainties, and actual results could vary materially. In order to complete the process of obtaining regulatory approval for our product candidates and to build the sales, marketing and distribution infrastructure that we believe will be necessary to commercialize our product candidates, if approved, we will require substantial additional funding.

We have based our projections of operating capital requirements on assumptions that may prove to be incorrect and we may use all of our available capital resources sooner than we expect. Because of the numerous risks and uncertainties associated with research, development and commercialization of pharmaceutical products, we are unable to estimate the exact amount of our operating capital requirements. Our future funding requirements will depend on many factors, including, but not limited to:

the timing and costs of our planned clinical trials for our product candidates;

the timing and costs of our planned preclinical studies of our product candidates;

our success in establishing and scaling commercial manufacturing capabilities;

the number and characteristics of product candidates that we pursue;

the outcome, timing and costs of seeking regulatory approvals;

subject to receipt of regulatory approval, revenue received from commercial sales of our product candidates;

the terms and timing of any future collaborations, licensing, consulting or other arrangements that we may establish;

the amount and timing of any payments we may be required to make in connection with the licensing, filing, prosecution, maintenance, defense and enforcement of any patents or patent applications or other intellectual property rights; and

the extent to which we in-license or acquire other products and technologies.

We plan to continue to fund our operations and capital funding needs through equity and/or debt financing. We may also consider collaborations or selectively partnering for clinical development and commercialization. The sale of additional equity would result in additional dilution to our stockholders. The incurrence of debt financing would result in debt service obligations and the instruments governing such debt could provide for operating and financing covenants that would restrict our operations. 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 harm our business, results of operations and future prospects.

The following table summarizes our cash flows for the periods indicated:

	Years Ended December 31,		
	2014	2013	2012
	(in thousands)		
Cash used in operating activities	$(19,231)	$(11,837)	$(6,990)
Cash used in investing activities	$(486)	$(173)	$(49)
Cash provided by financing activities	$87,866	$43,625	$5,966

Cash Flows from Operating Activities

Cash used in operating activities for the year ended December 31, 2014 was $19.2 million, consisting of a net loss of $21.7 million, which was offset by non-cash charges $0.4 million for depreciation and amortization expense and $0.7 million for stock-based compensation. The change in our net operating assets and liabilities was primarily due to a $1.5 million increase in prepaid expenses and other current assets primarily related to our prepayment of clinical trial activities and directors and officers liability insurance, a $2.6 million increase in accounts payable and accrued liabilities related to an increase in our research and development activities, and a $0.4 million increase in deferred rent.

Cash used in operating activities for 2013 was $11.8 million, consisting of a net loss of $12.4 million, which was offset in part by non-cash charges of $0.3 million for depreciation and amortization expense and $70,000 for stock-based compensation. The change

in our net operating assets and liabilities was due to a $0.4 million increase in our accounts payable and accrued liabilities related to an increase in our research and development activities and an increase of $0.3 million in prepaid expenses and other current assets related to our prepayment for clinical trial activities.

Cash used in operating activities for 2012 was $7.0 million, consisting of a net loss of $8.0 million, which was offset in part by non-cash charges of $0.3 million for depreciation and amortization expense and $31,000 for stock-based compensation. The change in our net operating assets and liabilities was due primarily to an increase of $0.7 million in our accounts payable and accrued liabilities related to an increase in our research and development activities.

Cash Flows from Investing Activities

Cash used in investing activities for the year ended December 31, 2014 was $0.5 million and was related the purchase of property and equipment of $0.6 million, offset by the reduction in restricted cash of $70,000. Purchases of property and equipment were primarily related to leasehold improvements in connection with our office expansion.

Cash used in investing activities for the years ended December 31, 2013 and 2012, was related to our purchase of property and equipment of $0.2 million and $49,000, respectively. Purchases of property and equipment were primarily related to the expansion of our laboratory and related equipment.

Cash Flows from Financing Activities

Cash provided by financing activities for the year ended December 31, 2014 was $87.9 million and was related to net proceeds of $71.6 million from the sale of our common stock, upon our initial public offering in October 2014, $16.0 million in net proceeds from the sale and issuance of preferred stock, and $0.3 million from the issuance of common stock upon the exercise of stock options.

Cash provided by financing activities for 2013 and 2012 was primarily related to net proceeds from the sale and issuance of preferred stock of $43.6 million and $6.0 million, respectively.

Contractual Obligations and Other Commitments

The following table summarizes our contractual obligations as of December 31, 2014:

	Payments Due By Period				
Contractual Obligations:	Less Than 1 Year	1 to 3 Years	3 to 5 Years	More Than 5 Years	Total
	(in thousands)				
Operating lease obligations [1]	$969	$1,873	$ -	$ -	$2,842
Less: sublease income [2]	(154)	(92)	-	-	(246)
Total contractual obligations [3]	$815	$1,781	$ -	$ -	$2,596

(1) Represents future minimum lease payments under the non-cancelable lease for our headquarters in South San Francisco, California. The minimum lease payments above do not include any related common area maintenance charges or real estate taxes.

(2) In September 2014, we entered into a non-cancelable sublease agreement for a portion of our facilities, through July 2016.

(3) We enter into agreements in the normal course of business with organizations for collaborations or in-licensing arrangements, contract research organizations for clinical trials and vendors for preclinical studies and other services and products for operating purposes which are cancelable at any time by us, generally upon 30 to 60 days prior written notice. These payments are not included in this table of contractual obligations.

Off-Balance Sheet Arrangements

During 2014, 2013, and 2012 we did not have any off-balance sheet arrangements.

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.

Recent Accounting Pronouncements

In June 2014, the Financial Accounting Standards Board, or FASB issued ASU 2014-10, Development Stage Entities (Topic 915): Elimination of Certain Financial Reporting Requirements, Including an Amendment to Variable Interest Entities Guidance in Topic 810, Consolidation. ASU 2014-10 simplifies the accounting guidance by removing all incremental financial reporting requirements for development stage entities. The amendments related to the elimination of the inception-to-date information and other disclosure requirement of Topic 915 should be applied retrospectively, and are effective for annual reporting periods beginning after December 15, 2014, and interim periods therein. We early adopted this guidance and, accordingly, there is no inception to date information presented in the financial statements included elsewhere in this Annual Report.

In August 2014, the FASB issued ASU No. 2014-15, Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern. ASU 2014-15 requires management to evaluate whether there is substantial doubt about an entity's ability to continue as a going concern and to provide related footnote disclosures. In doing so, companies will have reduced diversity in the timing and content of footnote disclosures than under today's guidance. ASU 2014-15 is effective for the Company in the first quarter of 2016 with early adoption permitted. We are currently assessing the impact the adoption of ASU 2014-15 will have on the financial statements.

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

We are exposed to market risks in the ordinary course of our business. These risks primarily include interest rate sensitivities. We had cash and cash equivalents of $102.0 million as of December 31, 2014, which consist of bank deposits and money market funds. Such interest-earning instruments carry a degree of interest rate risk; however, historical fluctuations in interest income have not been significant. We had no outstanding debt as of December 31, 2014.

Item 8. Financial Statements and Supplementary Data.

CALITHERA BIOSCIENCES, INC.

INDEX TO FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

The Board of Directors and Stockholders of Calithera Biosciences, Inc.

We have audited the accompanying balance sheets of Calithera Biosciences, Inc. as of December 31, 2014 and 2013, and the related statements of operations and comprehensive loss, convertible preferred stock and stockholder's equity (deficit) and cash flows for each of the three years in the period ended December 31, 2014. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. We were not engaged to perform an audit of the Company's internal control over financial reporting. Our audits included consideration of internal control over financial reporting as a basis for designing audit procedures that are appropriate in the circumstances, 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. An audit also includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of Calithera Biosciences, Inc. at December 31, 2014 and 2013, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2014, in conformity with U.S. generally accepted accounting principles.

/s/ Ernst & Young LLP

Redwood City, California

March 27, 2015

Calithera Biosciences, Inc.

Balance Sheets

(in thousands, except per share amounts)

	December 31,	
	2014	2013
Assets		
Current assets:		
Cash and cash equivalents	$101,969	$33,820
Prepaid expenses and other current assets	1,894	349
Total current assets	103,863	34,169
Restricted cash	46	116
Property and equipment, net	861	559
Total assets	$104,770	$34,844
Liabilities, Convertible Preferred Stock and Stockholders' Equity (Deficit)		
Current liabilities:		
Accounts payable	$693	$150
Accrued liabilities	3,428	1,194
Total current liabilities	4,121	1,344
Deferred rent	270	31
Other non-current liabilities	13	-
Total liabilities	4,404	1,375
Commitments and contingencies (Note 5)		
Convertible preferred stock, $0.0001 par value, no shares and 7,757 shares authorized as of December 31, 2014 and 2013, respectively; no shares and 7,689 shares issued and outstanding as of December 31, 2014 and 2013, respectively	-	54,282
Stockholders' equity (deficit):		
Preferred stock, $0.0001 par value per share, 10,000 shares and no shares authorized as of December 31, 2014 and 2013, respectively; no share issued and outstanding as of December 31, 2014 and 2013	-	-
Common stock, $0.0001 par value, 200,000 and 9,896 shares authorized as of December 31, 2014 and 2013, respectively; 17,943 and 161 shares issued and outstanding as of December 31, 2014 and 2013, respectively	2	-
Additional paid-in capital	152,218	9,329
Accumulated deficit	(51,854)	(30,142)
Total stockholders' equity (deficit)	100,366	(20,813)
Total liabilities, convertible preferred stock and stockholders' equity (deficit)	$104,770	$34,844

See accompanying notes.

Calithera Biosciences, Inc.

Statements of Operations and Comprehensive Loss

(in thousands, except per share amounts)

	Year Ended December 31,		
	2014	2013	2012
Operating expenses:			
Research and development	$16,367	$9,900	$6,558
General and administrative	5,354	2,478	1,417
Total operating expenses	21,721	12,378	7,975
Loss from operations	(21,721)	(12,378)	(7,975)
Other income	9	1	—
Net loss and comprehensive loss	(21,712)	(12,377)	(7,975)
Gain on extinguishment of convertible preferred stock	—	—	2,889
Net loss attributable to common stockholders	$(21,712)	$(12,377)	$(5,086)
Net loss per share attributable to common stockholders, basic and diluted	$(4.67)	$(131.53)	$(366.13)
Weighted average shares used in computing net loss per share attributable to common stockholders, basic and diluted	4,652	94	14

See accompanying notes.

Calithera Biosciences, Inc.

Statements of Convertible Preferred Stock and Stockholders' Equity (Deficit)

(in thousands, except per share amounts)

	Convertible Preferred Stock		Common Stock		Additional Paid-In Capital	Accumulated Deficit	Total Stockholders' Equity (Deficit)
	Shares	Amount	Shares	Amount			
Balance at January 1, 2012	875	$7,689	10	$ -	$6,230	$ (9,790)	(3,560)
Issuance of Series B convertible preferred stock for cash at $4.77 per share in May 2012, net of $15 in issuance costs	838	3,985	-	-	-	-	-
Extinguishment of convertible preferred stock and related conversion to common stock	(428)	(2,930)	43	-	41	-	41
Gain on extinguishment of convertible preferred stock	-	-	-	-	2,889	-	2,889
Issuance of Series C convertible preferred stock for cash at $4.77 per share in December 2012, net of $22 in issuance costs	419	1,978	-	-	-	-	-
Vesting of common stock issued to founders	-	-	3	-	-	-	-
Exercise of stock options	-	-	2	-	3	-	3
Stock-based compensation expense	-	-	-	-	31	-	31
Net loss	-	-	-	-	-	(7,975)	(7,975)
Balance at December 31, 2012	1,704	10,722	58	-	9,194	(17,765)	(8,571)
Issuance of Series C convertible preferred stock for cash at $4.77 per share in April 2013, net of $24 in issuance costs	1,823	8,676	-	-	-	-	-
Issuance of Series D convertible preferred stock for cash at $8.41 per share in October 2013, net of $115 in issuance costs	4,162	34,884	-	-	-	-	-
Vesting of common stock issued to founders	-	-	3	-	-	-	-
Exercise of stock options	-	-	100	-	65	-	65
Stock-based compensation expense	-	-	-	-	70	-	70
Net loss	-	-	-	-	-	(12,377)	(12,377)
Balance at December 31, 2013	7,689	54,282	161	-	9,329	(30,142)	(20,813)
Issuance of Series D convertible preferred stock for cash at $8.41	1,903	15,959	-	-	-	-	-

per share in July 2014, net of $41 in issuance costs							
Conversion of preferred stock to common stock upon initial public offering	(9,592)	(70,241)	9,592	1	70,240	-	70,241
Issuance of common stock in connection with initial public offering, net of underwriting discounts, commissions and issuance costs	-	-	8,000	1	71,623	-	71,624
Issuance of common stock to nonemployees	-	-	21	-	54	-	54
Vesting of common stock issued to founders	-	-	1	-	1	-	1
Exercise of stock options	-	-	168	-	282	-	282
Stock-based compensation expense	-	-	-	-	689	-	689
Net loss	-	-	-	-	-	(21,712)	(21,712)
Balance at December 31, 2014	-	$-	17,943	$ 2	$152,218	$ (51,854)	100,366

See accompanying notes.

Calithera Biosciences, Inc.

Statements of Cash Flows

(in thousands)

	Year Ended December 31,		
	2014	2013	2012
Cash Flows From Operating Activities			
Net loss	$(21,712)	$(12,377)	$(7,975)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	361	281	269
Stock-based compensation	689	70	31
Loss on disposal of property and equipment	2	5	7
Changes in operating assets and liabilities:			
Prepaid expenses and other current assets	(1,544)	(282)	(9)
Accounts payable	543	125	25
Accrued liabilities	2,058	310	675
Deferred rent, non-current	372	31	(13)
Net cash used in operating activities	(19,231)	(11,837)	(6,990)
Cash Flows From Investing Activities			
Purchase of property and equipment	(556)	(164)	(49)
Change in restricted cash	70	(9)	-
Net cash used in investing activities	(486)	(173)	(49)
Cash Flows From Financing Activities			
Proceeds from issuance of common stock upon initial public offering, net	71,625	—	—
Net proceeds from issuance of convertible preferred stock	15,959	43,560	5,963
Proceeds from stock option exercises	282	65	3
Net cash provided by financing activities	87,866	43,625	5,966
Net increase (decrease) in cash and cash equivalents	68,149	31,615	(1,073)
Cash and cash equivalents at beginning of period	33,820	2,205	3,278
Cash and cash equivalents at end of period	$101,969	$33,820	$2,205
Supplemental Disclosure of Non-Cash Investing and Financing Information:			
Services settled through the issuance of common stock	$55	$—	$—
Unpaid amounts related to property and equipment purchases	$110	$—	$—
Conversion of preferred stock warrants to common stock warrants	$—	$—	$41
Gain on extinguishment of convertible preferred stock	$—	$—	$2,889

See accompanying notes.

Calithera Biosciences, Inc.

Notes to Financial Statements

1. Organization and Basis of Presentation

Calithera Biosciences, Inc. (the "Company") was incorporated in the State of Delaware on March 9, 2010. The Company is a clinical-stage biopharmaceutical company focused on discovering and developing novel small molecule drugs directed against tumor metabolism and tumor immunology targets for the treatment of cancer. The Company's principal operations are based in South San Francisco, California, and it operates in one segment.

Initial Public Offering

In October 2014, the Company completed an initial public offering ("IPO") of its common stock. In connection with its IPO, the Company issued and sold 8,000,000 shares of its common stock, at a price to the public of $10.00 per share. As a result of the IPO, the Company received $71.6 million in net proceeds, after deducting underwriting discounts and commissions of $5.6 million and offering expenses of $2.8 million paid by the Company.

At the closing of the IPO, 9,592,042 shares of outstanding convertible preferred stock were automatically converted into 9,592,042 shares of common stock with the related carrying value of $70.2 million reclassified to common stock and additional paid-in capital. In connection with the IPO, the Company amended and restated its Amended and Restated Certificate of Incorporation to change the authorized capital stock to 200,000,000 shares designated as common stock and 10,000,000 shares designated as preferred stock, all with a par value of $0.0001 per share. There are no shares of preferred stock outstanding at December 31, 2014.

Liquidity

In the course of its development activities, the Company has sustained operating losses and expects such losses to continue over the next several years. The Company's ultimate success depends on the outcome of its research and development activities. The Company has incurred net losses from operations since inception and has an accumulated deficit of $51.9 million as of December 31, 2014. The Company intends to raise additional capital through the issuance of additional equity, and potentially through strategic alliances with partner companies. However, if such financing is not available at adequate levels, the Company will need to reevaluate its operating plans. Management believes that the currently available resources will provide sufficient funds to enable the Company to meet its operating plan for at least the next twelve months. However, if the Company's anticipated operating results are not achieved in future periods, management believes that planned expenditures may need to be reduced in order to extend the time period over which the then-available resources would be able to fund the Company's operations.

Reverse Stock Split

On September 18, 2014, the Company's Board of Directors, and on September 19, 2014, the Company's stockholders, approved the amendment and restatement of the Company's certificate of incorporation to effect a reverse split of the Company's common stock and convertible preferred stock at a 1-for-48 ratio (the "Reverse Stock Split"). The Reverse Stock Split became effective on September 19, 2014, upon the filing of the Company's amended and restated certificate of incorporation. The par value of the common and convertible preferred stock was not adjusted as a result of the Reverse Stock Split. All issued and outstanding common stock, convertible preferred stock, options for common stock and per share amounts contained in the financial statements have been retroactively adjusted to reflect this Reverse Stock Split for all periods presented.

2. Summary of Significant Accounting Policies

Use of Estimates

The accompanying financial statements have been prepared in accordance with U.S. generally accepted accounting principles ("GAAP"). The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities as of the date of the financial statements and the reported amounts of revenue and expenses during the reporting period. On an ongoing basis, management evaluates its estimates, including those related to clinical trial accrued liabilities, fair value of common stock, income taxes, and stock-based compensation. Management bases its estimates on historical experience and on various other market specific and relevant assumptions that management believes to be reasonable under the circumstances. Actual results could differ from those estimates.

Cash and Cash Equivalents

The Company considers all highly liquid investments with original maturities of three months or less at the time from the date of purchase to be cash equivalents. Cash equivalents, which consist primarily of amounts invested in money market accounts, are stated at fair value.

Restricted Cash

Restricted cash consists of money market funds held by the Company's financial institution as collateral for the Company's obligations under its facility lease for the Company's corporate headquarters in South San Francisco, California.

Concentration of Credit Risk

Financial instruments that potentially subject the Company to a concentration of credit risk consist of cash and cash equivalents. The Company's cash and cash equivalents are held by a financial institution in the United States. Amounts on deposit may at times exceed federally insured limits. Management believes that the financial institution is financially sound, and accordingly, minimal credit risk exists with respect to the financial institution.

Property and Equipment

Property and equipment are stated at cost, less accumulated depreciation and amortization. Depreciation and amortization is computed using the straight-line method over the estimated useful lives of the respective assets. Depreciation and amortization begins at the time the asset is placed in service. Maintenance and repairs are charged to operations as incurred. Upon sale or retirement of assets, the cost and related accumulated depreciation and amortization are removed from the balance sheet and the resulting gain or loss is reflected in operations.

The useful lives of property and equipment are as follows:

Research and development	5 years
Furniture and office equipment	5 years
Computer equipment	3 years
Software	3 years
Leasehold improvements	Shorter of remaining lease term or estimated useful life

Impairment of Long-Lived Assets

The Company evaluates its long-lived assets, including property and equipment, for impairment whenever events or changes in circumstances indicate that the carrying value of these assets may not be recoverable. Recoverability of these assets is measured by comparison of the carrying amount of each asset to the future undiscounted cash flows the asset is expected to generate over its remaining life. If the asset is considered to be impaired, the amount of any impairment is measured as the difference between the carrying value and the fair value of the impaired asset. The Company has not recorded impairment of any long-lived assets during any of the periods presented.

Accrued Research and Development Costs

The Company accrues for estimated costs of research and development activities conducted by third-party service providers, which include the conduct of preclinical studies and clinical trials, and contract manufacturing activities.

The Company records the estimated costs of research and development activities based upon the estimated amount of services provided but not yet invoiced, and include these costs in accrued liabilities in the balance sheets and within research and development expense in the statements of operations and comprehensive loss. These costs are a significant component of the Company's research and development expenses. The Company accrues for these costs based on factors such as estimates of the work completed and in accordance with agreements established with its third-party service providers. The Company makes significant judgments and estimates in determining the accrued liabilities balance in each reporting period. As actual costs become known, the Company adjusts its accrued liabilities. The Company has not experienced any material differences between accrued costs and actual costs incurred. However, the status and timing of actual services performed, number of patients enrolled, and the rate of patient enrollment may vary from the Company's estimates, resulting in adjustments to expense in future periods. Changes in these estimates that result in material changes to the Company's accruals could materially affect the Company's results of operations.

Research and Development Costs

Research and development costs are expensed as incurred and consist of salaries and benefits, stock-based compensation expense, laboratory supplies and allocated facility costs, as well as fees paid to third parties that conduct certain research and development activities on the Company's behalf. Amounts incurred in connection with license agreements are also included in research and development costs. Nonrefundable advance payments for goods or services to be rendered in the future for use in research and development activities are deferred and capitalized. The capitalized amounts are expensed as the related goods are delivered or the services are performed.

Deferred Rent

Rent expense is recognized on a straight-line basis over the noncancelable term of the Company's operating lease and, accordingly, the Company records the difference between cash rent payments and the recognition of rent expense as a deferred rent liability. Incentives granted under the Company's facility leases, including allowances to fund leasehold improvements, are deferred and are recognized as adjustments to rental expense on a straight-line basis over the term of the lease.

Stock-Based Compensation

Stock-based awards issued to employees and directors, including stock options, are recorded at fair value as of the grant date using the Black-Scholes option-pricing model and recognized as expense on a straight-line basis over the employee or director's requisite service period (generally the vesting period). Because noncash stock compensation expense is based on awards ultimately expected to vest, it is reduced by an estimate for future forfeitures. Forfeitures are estimated at the time of grant and revised, if necessary, in subsequent periods if actual forfeitures differ from estimates.

Income Taxes

The Company uses the liability method of accounting for income taxes. Under this method, deferred tax assets and liabilities are determined based on the differences between the financial reporting and the tax bases of assets and liabilities and are measured using the enacted tax rates and laws that will be in effect when the differences are expected to reverse. The Company must then assess the likelihood that the resulting deferred tax assets will be realized. A valuation allowance is provided when it is more likely than not that some portion or all of a deferred tax asset will not be realized. Due to the Company's lack of earnings history, the net deferred tax assets have been fully offset by a valuation allowance.

The Company recognizes benefits of uncertain tax positions if it is more likely than not that 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's policy is to recognize interest and penalties related to the underpayment of income taxes as a component of income tax expense or benefit. To date, there have been no interest or penalties charged in relation to the unrecognized tax benefits.

Net Loss per Share Attributable to Common Stockholders

Basic net loss per share attributable to common stockholders is calculated by dividing the net loss attributable to common stockholders by the weighted average number of shares of common stock outstanding during the period without consideration of common stock equivalents. The net loss attributable to common stockholders is calculated by adjusting the net loss of the Company for the gain on the extinguishment of convertible preferred stock. Since the Company was in a loss position for all periods presented, basic net loss per share attributable to common stockholders

is the same as diluted net loss per share attributable to common stockholders for all periods as the inclusion of all potential common shares outstanding would have been anti-dilutive.

Reclassification

Certain reclassifications have been made to prior period amounts to conform to current period presentation. These reclassifications did not have an impact on the Company's results of operations or financial condition as of December 31, 2014 and 2013.

Recent Accounting Pronouncements

In June 2014, the Financial Accounting Standards Board, ("FASB") issued Accounting Standards Update ("ASU") 2014-10, Development Stage Entities (Topic 915): Elimination of Certain Financial Reporting Requirements, Including an Amendment to Variable Interest Entities Guidance in Topic 810, Consolidation. ASU 2014-10 simplifies the accounting guidance by removing all

incremental financial reporting requirements for development stage entities. The amendments related to the elimination of the inception-to-date information and other disclosure requirement of Topic 915 should be applied retrospectively, and are effective for annual reporting periods beginning after December 15, 2014, and interim periods therein. The Company early adopted this guidance as of January 1, 2012.

In August 2014, the FASB issued ASU No. 2014-15, Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern. ASU 2014-15 requires management to evaluate whether there is substantial doubt about an entity's ability to continue as a going concern and to provide related footnote disclosures. In doing so, companies will have reduced diversity in the timing and content of footnote disclosures than under today's guidance. ASU 2014-15 is effective for the Company in the first quarter of 2016 with early adoption permitted. The Company is currently assessing the impact the adoption of ASU 2014-15 will have on the financial statements.

3. Fair Value Measurements

Fair value accounting is applied for all financial assets and liabilities that are recognized or disclosed at fair value in the financial statements on a recurring basis (at least annually). Financial instruments include cash and cash equivalents, accounts payable and accrued liabilities that approximate fair value due to their relatively short maturities.

Assets and liabilities recorded at fair value on a recurring basis in the balance sheets are categorized based upon the level of judgment associated with the inputs used to measure their fair values. Fair value is defined as the exchange price that would be received for an asset or an exit price that would be paid to transfer a liability in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. The authoritative guidance on fair value measurements establishes a three tier fair value hierarchy for disclosure of fair value measurements as follows:

Level 1—Inputs are unadjusted, quoted prices in active markets for identical assets or liabilities at the measurement date;

Level 2—Inputs are observable, unadjusted quoted prices in active markets for similar assets or liabilities, unadjusted quoted prices for identical or similar assets or liabilities in markets that are not active, or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the related assets or liabilities; and

Level 3—Unobservable inputs that are significant to the measurement of the fair value of the assets or liabilities that are supported by little or no market data.

The Company's financial instruments consist only of Level 1 assets, which are highly liquid money market funds. As of December 31, 2014 and 2013, the Company had $46,000 and $116,000 in money market funds that are included in restricted cash on the balance sheets.

4. Balance Sheet Components

Property and Equipment, Net

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

	December 31,	
	2014	2013
Research and development equipment	$1,427	$1,137
Furniture and office equipment	75	52
Computer equipment	211	156
Software	58	38
Leasehold improvements	321	47
Total property and equipment	2,092	1,430
Less: accumulated depreciation and amortization	(1,231)	(871)
Property and equipment, net	$861	$559

Property and equipment depreciation and amortization expense for the years ended December 31, 2014, 2013 and 2012 was $361,000, $281,000 and $269,000, respectively.

Accrued Liabilities

Accrued liabilities consist of the following (in thousands):

	December 31,	
	2014	2013
Accrued bonus and payroll expenses	$1,476	$934
Accrued professional and consulting services	490	127
Accrued clinical and manufacturing expenses	1,029	107
Other	433	26
Total accrued liabilities	$3,428	$1,194

5. Commitments and Contingencies

Facilities

In July 2010, the Company entered into a lease agreement for office and laboratory facilities in South San Francisco, California. The lease commenced in November 2010 and initially expired one year after the commencement date. The Company entered into addendums to the lease agreement at various points in time to add space to the arrangement and extend the lease term through June 2013.

In February 2013, the Company entered into a non-cancelable facility lease agreement for office and laboratory facilities in South San Francisco, California. The lease commenced on July 2013 and expires two years after the commencement date. In October 2013, the Company signed an addendum to the lease agreement for additional space and to extend the lease term through November 2017. The lease has a two-year renewal option prior to expiration. In addition the lease provides for a tenant improvement allowance of up to $230,000, which was fully utilized in 2014 and included in deferred rent. The lease has rent escalation clauses through the lease term, as well as reduced rent on the additional space for the first 12 months. The Company recognizes rent expense on a straight-line basis over the noncancelable term of the lease.

Under the terms of the lease agreement for its new South San Francisco facility, the Company provided the lessor with an irrevocable letter of credit in the amount of $46,000. The lessor shall be entitled to draw on the letter of credit in the event of any uncured default by the Company under the terms of the lease.

Future aggregate minimum lease payments under the noncancelable operating leases as of December 31, 2014 (in thousands) are as follows:

Year ending December 31:	
2015	$969
2016	977
2017	896
Total	$2,842

In September 2014, the Company entered into a non-cancelable sublease agreement for a portion of its facilities, through July 2016. Future annual minimum sublease proceeds as of December 31, 2014 (in thousands) are as follows:

Year ending December 31:	
2015	$154
2016	92
Total	$246

Expenses and income associated with the Company's operating leases were as follows (in thousands):

	Year Ended December 31,		
	2014	2013	2012
Rent expense	$ 1,309	$ 866	$ 782
Sublease income	(73)	—	—

Indemnifications

The Company indemnifies each of its officers and directors for certain events or occurrences, subject to certain limits, while the officer or director is or was serving at the Company's request in such capacity, as permitted under Delaware law and in accordance with its certificate of incorporation and bylaws. The term of the indemnification period lasts as long as an officer or a director may be subject to any proceeding arising out of acts or omissions of such officer or director in such capacity. The maximum amount of potential future indemnification is unlimited; however, the Company currently holds director and officer liability insurance. This insurance allows the transfer of risk associated with the Company's exposure and may enable it to recover a portion of any future amounts paid. The Company believes that the fair value of these indemnification obligations is minimal. Accordingly, it has not recognized any liabilities relating to these obligations for any period presented.

Other Matters

In October 2014, the Company received an invoice of approximately $1.3 million relating to a contingent amount associated with a terminated license agreement, incurred as a result of the closing of its IPO in October 2014. The Company believes that the invoice amount is substantially in excess of the amount actually owed pursuant to the agreement and has initiated discussions with the third party to resolve the matter. The Company does not believe that the ultimate resolution of this matter will be material to the Company's results of operations, financial condition or cash flows.

6. Convertible Preferred Stock and Stockholders' Equity (Deficit)

Convertible Preferred Stock

As of December 31, 2013, the Company had outstanding convertible preferred stock as follows (in thousands, except share amounts):

Convertible Preferred Stock:	Shares Authorized	Shares Issued and Outstanding	Carrying Values	Liquidation Preference
Series A	27,499	27,497	$2,786	$ 3,750
Series B	1,257,545	1,257,543	5,958	6,000
Series C	2,242,622	2,242,620	10,654	10,700
Series D	4,229,166	4,161,799	34,884	35,000
Total convertible preferred stock	7,756,832	7,689,459	$54,282	$ 55,450

In July 2014, the Company issued 1,902,583 shares of Series D convertible preferred stock at a price of $8.41 per share, with the same provisions of previously issued Series D convertible preferred stock. Aggregate net proceeds were approximately $16.0 million.

Immediately prior to the completion of the Company's IPO, all of the outstanding shares of convertible preferred stock automatically converted into 9,592,042 shares of common stock on a one-to-one basis. In connection with the IPO, the Company amended and restated its Amended and Restated Certificate of Incorporation to change the authorized

capital stock to 200,000,000 shares designated as common stock and 10,000,000 shares designated as preferred stock, all with a par value of $0.0001 per share.

Extinguishment of Preferred Stock

Pursuant to the Company's then-effective Certificate of Incorporation, if a holder of Series B did not purchase such holder's pro rata share in the Company's Series C financing by a specified time (a "nonparticipating holder"), then each share of Preferred Stock held by the non-participating holder would be converted into 1/10th of a share of common stock at that specified time. In connection with Series C financing during 2012, one of the Company's investors did not purchase its pro rata share of the Series C. Such holder was therefore a non-participating holder and, as a result, the 9,166 shares Series A and 419,181 Series B held by such non-participating holder automatically converted into an aggregate of 42,834 shares of common stock.

The Company has accounted for the conversion of the Series A and Series B as an extinguishment of the converted Preferred Stock and issuance of common stock due to the significance of the change in the fair value from the Preferred Stock to the common stock. Accordingly, for the year ended December 31, 2012, the Company recorded an aggregate gain of $2.9 million within stockholders' deficit equal to the difference between the $41,000 fair value of the shares of common stock issued and the $2.9 million carrying amount of the converted shares of Preferred Stock Extinguished. The gain on extinguishment is reflected in the calculation of net loss attributable to common stockholders.

Restricted Stock

In March 2010, the Company entered into a restricted stock purchase agreement with two founders of the Company. The individuals purchased a total of 17,416 shares of common stock for a total purchase price of $836. These agreements contain a repurchase option that gives the Company an irrevocable option for a period of ninety days after the individual's employment is terminated either voluntarily or involuntarily to repurchase the unvested restricted stock at a price that is the lower of the original price per share paid by the founder for such stock or the fair value as of the date of such repurchase. The restricted stock vested and the repurchase option lapsed over 48 months measured from the date that the first share of Series A was issued, which was June 17, 2010. As of December 31, 2014 and 2013, zero and 1,146 of these shares, respectively, remained subject to repurchase.

7. Equity Incentive Plans

2010 Plan

In 2010, the Company adopted the 2010 Equity Incentive Plan (the "2010 Plan"). Under the Plan, shares of the Company's common stock have been reserved for the issuance of stock options to employees, directors, and consultants under terms and provisions established by the Board of Directors. A total of 1,456,950 shares were reserved for issuance under the 2010 Plan at December 31, 2014, of which zero shares are available for future grant. Under the terms of the 2010 Plan, options may be granted at an exercise price not less than fair market value. For employees holding more than 10% of the voting rights of all classes of stock, the exercise prices for incentive and nonstatutory stock options may not be less than 110% of fair market value, as determined by the Board of Directors. The terms of options granted under the 2010 Plan may not exceed ten years. The vesting schedule of newly issued option grants is typically four years.

The Company granted options under the 2010 Plan until October 2014 when it was terminated as to future awards, although it continues to govern the terms of options that remain outstanding under the 2010 Plan.

As of December 31, 2014, a total of 1,186,420 shares of common stock are subject to options outstanding under the 2010 Plan.

2014 Plan

On September 18, 2014, the Company's Board of Directors, and on September 19, 2014, the Company's stockholders, approved the 2014 Equity Incentive Plan (the "2014 Plan") which became effective in October 2014, at which time the 2010 Equity Incentive Plan was terminated. The 2014 Plan provides for the grant of stock options, other forms of equity compensation, and performance cash awards. The maximum number of shares of common stock that may be issued under the 2014 Plan is 971,340. In addition, the number of shares of common stock reserved for issuance under the 2014 Plan will automatically increase on January 1 of each year, beginning on January 1, 2015 and ending on and including January 1, 2024, by 4% of the total number of shares of the Company's capital stock outstanding on December 31 of the preceding calendar year, or a lesser number of shares determined by the Company's Board of Directors.

As of December 31, 2014, a total of 971,340 shares of common stock were reserved for issuance under the 2014 Plan, of which 946,840 shares of common stock are available for future grant.

69

The following summarizes option activity (in thousands, except share and price per option data):

	Options Outstanding		
	Number of Options	Weighted-Average Exercise Price per Option	Aggregate Value Intrinsic
Outstanding — December 31, 2011	134,781	$ 1.08	
Shares reserved	-	$ -	
Options granted	127,452	$ 0.48	
Options exercised	(1,765)	$ 1.46	
Options canceled	(15,540)	$ 0.92	
Outstanding — December 31, 2012	244,928	$ 0.77	
Shares reserved	-	$ -	
Options granted	725,161	$ 1.99	
Options exercised	(100,273)	$ 0.64	
Options canceled	(4,986)	$ 1.05	
Outstanding — December 31, 2013	864,830	$ 1.80	$ 769
Shares reserved	-		
Options granted	571,660	$ 5.24	
Options exercised	(168,523)	$ 1.67	
Options canceled	(57,047)	$ 1.87	
Outstanding — December 31, 2014	1,210,920	$ 3.44	$ 20,292
Exercisable — December 31, 2014	184,881	$ 2.45	$ 3,282
Vested and expected to vest — December 31, 2014	1,173,415	$ 3.42	$ 19,684

The aggregate intrinsic values of options outstanding, exercisable, vested and expected to vest were calculated as the difference between the exercise price of the options and the fair value of the Company’s common stock of $20.20 per share as of December 31, 2014.

The weighted-average fair value per share of employee options granted during the years ended December 31, 2014, 2013 and 2012 were $4.90, $1.44 and $0.48, respectively. The total fair value of options that vested during the years ended December 31, 2014, 2013 and 2012 was $582,000, $60,000 and $32,000, respectively.

As of December 31, 2014, the weighted-average remaining contractual life was 8.33 years and 8.94 years for exercisable options and vested and expected to vest options, respectively.

Stock-Based Compensation Expense

Total stock-based compensation recognized related to the 2010 and 2014 Plans was as follows (in thousands):

	Year Ended December, 31

	2014	2013	2012
Research and development	$275	$ 47	$ 21
General and administrative	345	23	10
Total stock-based compensation	$620	$ 70	$ 31

As of December 31, 2014, the total unrecognized compensation expense related to unvested options, net of estimated forfeitures, was $3.1 million, which the Company expects to recognize over an estimated weighted average period of 3.3 years.

Prior to the Company's IPO on October 2014, the fair value of the shares of common stock underlying stock options were historically determined by the Company's Board of Directors. Because there had been no public market for the Company's common stock, the Board of Directors had determined fair value of the common stock at the time of grant of the option by considering a number of objective and subjective factors including important developments in the Company's operations, valuations performed by an independent third party, sales of convertible preferred stock, actual operating results and financial performance, the conditions in

the biotechnology industry and the economy in general, the stock price performance and volatility of comparable public companies, and the lack of liquidity of the Company's common stock, among other factors.

In each of the periods presented, the exercise price per share for each stock option was the same as the fair value of the Company's common stock on the date of grant.

In determining the fair value of the stock-based awards, the Company uses the Black-Scholes option-pricing model and assumptions discussed below. Each of these inputs is subjective and generally requires significant judgment to determine.

Expected Term—The Company's expected term represents the period that the Company's stock-based awards are expected to be outstanding and is determined using the simplified method (based on the midpoint between the vesting date and the end of the contractual term).

Expected Volatility—Since the Company has only been publicly traded for a short period and does not have adequate trading history for its common stock, the expected volatility was estimated based on the average volatility for comparable publicly traded biopharmaceutical companies over a period equal to the expected term of the stock option grants. The comparable companies were chosen based on their similar size, stage in the life cycle, or area of specialty.

Risk-Free Interest Rate—The risk-free interest rate is based on the U.S. Treasury zero coupon issues in effect at the time of grant for periods corresponding with the expected term of option.

Expected Dividend—The Company has never paid dividends on its common stock and has no plans to pay dividends on its common stock. Therefore, the Company used an expected dividend yield of zero.

The fair value of stock option awards was estimated at the date of grant using a Black-Scholes option pricing model with the following assumptions:

	Year Ended December 31,		
	2014	2013	2012
Expected term	5.9 - 6.6 years	6.3 years	5.9 years
Volatility	78.6 - 97.7%	87.1 - 96.0%	79.80%
Risk-free interest rate	0.9% - 2.3%	1.1 - 1.9%	0.90%
Expected dividend rate	—%	—%	—%

ESPP

On September 18, 2014, the Company's Board of Directors, and on September 19, 2014, the Company's stockholders, approved the 2014 Employee Stock Purchase Plan (the "ESPP") which became effective in October 2014. The initial number of shares of common stock that may be issued under the ESPP is 189,883 shares and the number of shares reserved for the ESPP will increase automatically each year, beginning on January 1, 2015 and continuing through and including January 1, 2024, by the lesser of (1) 1% of the total number of shares of common stock outstanding on

December 31 of the preceding calendar year; (2) 250,000 shares of common stock; or (3) such lesser number as determined by the Company's Board of Directors.

The ESPP allows eligible employees to purchase shares of the Company's common stock at a discount through payroll deductions of up to 15% of their eligible compensation, subject to any plan limitations. The ESPP provides for 24-month offering periods with four 6-month purchase periods, and at the end of each purchase period, employees are able to purchase shares at 85% of the lower of the fair market value of the Company's common stock on the first trading day of the offering period or on the last day of the purchase period. As of December 31, 2014, no shares of common stock have been issued to employees participating in the ESPP and 189,883 shares were available for issuance under the ESPP. The ESPP is a compensatory plan as defined by the authoritative guidance for stock compensation. As such stock-based compensation expense has been recorded for the year ended December 31, 2014.

Total stock-based compensation expense recognized related to the ESPP was as follows (in thousands):

	Year Ended December 31, 2014
Research and development	$ 41
General and administrative	28
Total stock based compensation	$ 69

The Company used the following assumptions to estimate the fair value of the ESPP offered for the year ended December 31, 2014: expected term of 0.37 years to 2.13 years, weighted-average volatility of 65.2% to 81.0%, risk-free interest rate of 0.05% to 0.58% and expected dividend yield of zero.

8. Income Taxes

No provision for income taxes was recorded for the years ended December 31, 2014, 2013 and 2012. The Company has incurred net operating losses for all the periods presented. The Company has not reflected any benefit of such net operating loss carryforwards in the accompanying financial statements.

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

	Year Ended December, 31		
	2014	2013	2012
Federal statutory income tax rate	34.0 %	34.0 %	34.0 %
State income taxes, net of federal benefit	5.8	5.8	5.8
Federal and state tax credits	1.1	3.8	1.2
Change in valuation allowance	(40.9)	(43.6)	(41.0)
	0 %	0 %	0 %

The components of the deferred tax assets and liabilities are as follows (in thousands):

	Year Ended December, 31	
	2014	2013
Deferred tax assets:		
Net operating loss carryforwards	$19,323	$11,584
Tax credits	1,512	963
Accrued liabilities	712	384
Stock based compensation	21	—
Other	241	91
Gross deferred tax assets	21,809	13,022
Valuation allowance	(21,809)	(13,022)
Net deferred tax assets	$-	$-

Due to the Company’s lack of earnings history, the deferred tax assets have been fully offset by a valuation allowance as of December 31, 2014 and 2013. The valuation allowance increased by $8.8 million and $5.4 million during the years ended December 31, 2014 and 2013, respectively. ASC Topic 740 requires that the tax benefit of deductible temporary differences of carryforwards be recorded as a deferred tax assets to the extent that management assesses that realization is "more likely than not." Future realization of the tax benefit ultimately depends on the existence of sufficient taxable income within the carryback or carryforward period available under the tax law. The Company has set up the valuation allowance against the federal and state deferred tax assets because based on all available evidence, these deferred tax assets are not more likely than not to be realizable.

As of December 31, 2014, the Company had approximately $48.6 million and $48.0 million, respectively, of federal and state operating loss carryforwards available to reduce future taxable income that will begin to expire in 2030 for federal and state tax purposes.

As of December 31, 2014, the Company also had research and development tax credit carryforwards of approximately $1.6 million and $1.4 million, respectively, for federal and state purposes available to offset future taxable income tax. If not utilized, the federal carryforwards will expire in various amounts beginning in 2030, and the state credits can be carried forward indefinitely.

Utilization of the net operating loss carryforwards may be subject to a substantial annual limitation due to the ownership change limitations provided by the Internal Revenue Code of 1986, as amended, and similar state provisions. The Company has performed an analysis to determine whether an "ownership change" has occurred from inception to December 31, 2014. Based on this analysis, management has determined that there was an ownership change. The annual limitation may result in the expiration of net operating losses and credits before utilization, however, the Company does not believe any of its net operating losses and research and development credits are limited by this potential ownership change.

Uncertain Tax Positions

As of December 31, 2014, the Company's total unrecognized tax benefit was $1.2 million, of which none of the tax benefit, if recognized, would affect the effective income tax rate due to the valuation allowance that currently offsets deferred tax assets. A reconciliation of the Company's unrecognized tax benefits for the years ended December 31, 2014, 2013 and 2012 is as follows (in thousands):

	Year Ended December, 31		
	2014	2013	2012
Balance at beginning of year	$773	$388	$271
Additions based on tax positions related to current year	421	385	117
Balance at end of year	$1,194	$773	$388

The unrecognized tax benefits, if recognized and in absence of full valuation allowance, would increase our credit carryforwards and hence deferred tax assets. The Company does not expect the unrecognized tax benefits to change significantly over the next 12 months.

Interest and penalties are zero, and the Company's policy is to account for interest and penalties in tax expense on the statement of operations and comprehensive loss. The Company files income tax returns in the U.S. federal and California tax jurisdictions. All periods since inception are subject to examination by U.S. federal and California tax jurisdictions, none of which are currently under examination.

9. Net Loss per Common Share

Since the Company was in a loss position for all periods presented, basic net loss per share is the same as diluted net loss per share for all periods as the inclusion of all potential common shares outstanding would have been anti-dilutive. Potentially dilutive securities that were not included in the diluted per share calculations because they would be anti-dilutive were as follows (in thousands):

	December 31,		
	2014	2013	2012
Options to purchase common stock	1,211	865	245
Common stock subject to repurchase	—	1	4
Convertible preferred stock	—	7,689	1,704
Total	1,211	8,555	1,953

10. Licensing Agreements

Arginase License Agreement

In December 2014, the Company entered into an exclusive license agreement with Mars, Inc., by and through its Mars Symbioscience division, or Symbioscience, under which the Company has been granted the exclusive, worldwide license rights to develop and commercialize Symbioscience's portfolio of arginase inhibitors for use in human healthcare. Under the terms of the License Agreement, the Company will pay Symbioscience an upfront license fee of $0.3 million and potential development and regulatory milestone payments totaling up to $24.4 million for the first licensed product. Symbioscience is eligible for an additional $95.0 million in potential sales-based milestones, as well as royalty payments based on sales of such licensed product. If the Company develops additional licensed products, after achieving regulatory approval of the first licensed product, the Company would owe additional regulatory milestone payments and additional royalty payments based on sales of such additional licensed products.

Under the License Agreement, the Company will be responsible for the worldwide development and commercialization of the licensed products, at its cost, is required to use commercially reasonable efforts with respect to such development and

commercialization activities, and must meet certain general diligence obligations. The Company holds the first right to prosecute and to enforce all licensed rights under the Licenses Agreement throughout the world, and Symbioscience will retain certain step-in enforcement rights. Under the exclusivity provisions of the License Agreement, each party agrees not to develop any other arginase inhibitors for use in human healthcare outside of the scope of the License Agreement.

For the year ended December 31, 2014, the Company recorded a payment totaling $0.3 million related to its licensing arrangements with Symbioscience, in research and development expense in the statements of operations and comprehensive loss.

11. Related Party Transactions

The spouse of the Company's Chief Executive Officer is the founder of a management consulting firm that provided services to the Company through March 2013. For the years ended December 31, 2014, 2013 and 2012, the Company recognized zero, $62,000 and $41,000, respectively, paid to this management consulting firm, for consulting services which were primarily included in research and development expenses in the statements of operations and comprehensive loss. As of December 31, 2014 and 2013, the Company had no outstanding liability to the management consulting firm.

The spouse of one of the Company's executive officers was a consultant who provided accounting services for the Company through May 2014. For the years ended December 31, 2014, 2013 and 2012, the Company recognized consulting services of $61,000, $91,000 and $36,000, respectively, within general and administrative expenses in the statements of operations and comprehensive loss. As of December 31, 2014 and 2013, the Company had an outstanding liability to the individual of nil and $12,000, respectively.

12. Selected Quarterly Financial Data (Unaudited)

Selected quarterly results from operations for the years ended December 31, 2014 and 2013 are as follows (in thousands, except per share amounts):

	2014 Quarter Ended			
	March 31,	June 30,	September 30,	December 31,
Operating expenses	$4,150	$5,492	$ 5,241	6,838
Net loss	(4,149)	(5,491)	(5,239)	(6,833)
Basic and diluted net loss per common share	$(22.80)	$(24.22)	$ (16.85)	$ (0.39)

	2013 Quarter Ended			
	March 31,	June 30,	September 30,	December 31,
Operating expenses	$2,281	$2,691	$ 3,318	$ 4,088
Net loss	(2,281)	(2,691)	(3,318)	(4,087)

Basic and diluted net loss per common share	$(39.11)	$(45.47)	$ (34.22)	$ (25.42)

13. Subsequent Event

In March 2015, the Company entered into a License and Research agreement with High Point Pharmaceuticals, LLC and TransTech Pharma LLC, or collectively TransTech, under which the Company obtained an exclusive, worldwide license to develop and commercialize TransTech's hexokinase II inhibitors.

Under the terms of the License Agreement, the Company will pay TransTech an initial license fee of $0.6 million, and potential development and regulatory milestone payments totaling up to $30.5 million for the first licensed product. TransTech is eligible for an additional $77.0 million in potential sales-based milestones, as well as royalty payments, at mid-single digit royalty rates, based on tiered sales of the first commercialized licensed product. In addition, the Company will fund up to $1.1 million during the first 12 months of the License Agreement for the costs associated with up to four full-time employees for TransTech to develop additional hexokinase inhibitors. If the Company develops additional licensed products, after achieving regulatory approval of the first licensed product, the Company would owe additional regulatory milestone payments and additional royalty payments based on sales of such additional licensed products. The License Agreement will not impact the Company's ability to fund its operating expenses and capital expenditure requirements for at least the next twelve months.

Except for the research program funded by the Company at TransTech, the Company will be responsible for the worldwide development and commercialization of the licensed products, at its cost, is required to use commercially reasonable efforts with respect to such development and commercialization activities, and must meet certain specified diligence obligations. The Company holds the first right to prosecute and to enforce all licensed patents under the License Agreement throughout the world, and TransTech will retain certain step-in enforcement rights.

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

As of December 31, 2014, management, with the participation of our Chief Executive Officer and Chief Financial Officer, performed an evaluation of the effectiveness of the design and operation of our disclosure controls and procedures as defined in Rules 13a-15(e) and 15d-15(e) of the Exchange Act. Our disclosure controls and procedures are designed to ensure that information required to be disclosed in the reports we file or submit under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the Securities and Exchange Commission's rules and forms, and that such information is accumulated and communicated to our management, including the Chief Executive Officer and the Chief Financial Officer, to allow timely decisions regarding required disclosures.

Any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objective and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on this evaluation, our Chief Executive Officer and Chief Financial Officer concluded that, as of December 31, 2014, the design and operation of our disclosure controls and procedures were effective at a reasonable assurance level.

Management's Annual Report on Internal Control Over Financial Reporting

This Annual Report on Form 10-K does not include a report of management's assessment regarding internal control over financial reporting or an attestation report of our registered public accounting firm due to a transition period established by rules of the SEC for newly public companies.

Changes in Internal Control over Financial Reporting

There were no changes in our internal control over financial reporting identified in connection with the evaluation required by Rule 13a-15(d) and 15d-15(d) of the Exchange Act that occurred during the quarter ended December 31, 2014 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

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."

Item 9B. Other Information.

None.

75

PART III

Item 10. Directors, Executive Officers and Corporate Governance.
Information required by this item will be contained in our definitive proxy statement to be filed with the Securities and Exchange Commission on Schedule 14A in connection with our 2015 Annual Meeting of Stockholders or the Proxy Statement, which is expected to be filed not later than 120 days after the end of our fiscal year ended December 31, 2014, under the headings “Executive Officers,” “Election of Directors,” “Corporate Governance,” and “ Section 16(a) Beneficial Ownership Reporting Compliance,” and is incorporated herein by reference.

We have adopted a Code of Business Conduct and Ethics that applies to our officers, directors and employees which is available on our website at www.calithera.com. The Code of Business Conduct and Ethics is intended to qualify as a “code of ethics” within the meaning of Section 406 of the Sarbanes-Oxley Act of 2002 and Item 406 of Regulation S-K. In addition, we intend to promptly disclose (1) the nature of any amendment to our Code of Business Conduct and Ethics that applies to our principal executive officer, principal financial officer, principal accounting officer or controller or persons performing similar functions and (2) the nature of any waiver, including an implicit waiver, from a provision of our code of ethics that is granted to one of these specified officers, the name of such person who is granted the waiver and the date of the waiver on our website in the future.

Item 11. Executive Compensation.
The information required by this item regarding executive compensation is incorporated by reference to the information set forth in the sections titled “Executive Compensation” in our Proxy Statement.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters.
The information required by this item regarding security ownership of certain beneficial owners and management is incorporated by reference to the information set forth in the section titled “Security Ownership of Certain Beneficial Owners and Management” and “Equity Compensation Plan Information” in our Proxy Statement.

Item 13. Certain Relationships and Related Transactions, and Director Independence.
The information required by this item regarding certain relationships and related transactions and director independence is incorporated by reference to the information set forth in the sections titled “Transactions Related Persons” and “Election of Directors – Independence of the Board of Directors,” respectively, in our Proxy Statement.

Item 14. Principal Accounting Fees and Services.
The information required by this item regarding principal accountant fees and services is incorporated by reference to the information set forth in the section titled “Principal Accountant Fees and Services” in our Proxy Statement.

PART IV

Item 15. Exhibits, Financial Statement Schedules.
(a) The following documents are filed as part of this report:

1. Financial Statements

See Index to Financial Statements at Item 8 herein.

2. Financial Statement Schedules

All schedules are omitted because they are not applicable or the required information is shown in the financial statements or notes thereto.

3. Exhibits

See the Exhibit Index immediately following the signature page of this Annual Report on Form 10-K.

SIGNATURES

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

Calithera Biosciences, Inc.

Date: March 27, 2015 By: /s/ Susan M. Molineaux
Susan M. Molineaux, Ph.D.
President and Chief Executive Officer

POWER OF ATTORNEY

Each person whose individual signature appears below hereby authorizes and appoints Susan M. Molineaux and William D. Waddill, and each of them, with full power of substitution and resubstitution and full power to act without the other, as his or her true and lawful attorney-in-fact and agent to act in his or her name, place and stead and to execute in the name and on behalf of each person, individually and in each capacity stated below, and to file any and all 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 attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing, ratifying and confirming all that said attorneys-in-fact and agents or any of them or their 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, as amended, this Report has been signed below by the following persons on behalf of the Registrant in the capacities and on the dates indicated.

Name	Title	Date
/s/ Susan M. Molineaux Susan M. Molineaux, Ph.D.	President, Chief Executive Officer and Director (Principal Executive Officer)	March 27, 2015
/s/ William D. Waddill William D. Waddill	Senior Vice President, Chief Financial Officer, Treasurer and Secretary (Principal Financial and Accounting Officer)	March 27, 2015
/s/ Ralph E. Christoffersen Ralph E. Christoffersen, Ph.D.	Director	March 27, 2015
/s/ Jonathan Drachman Jonathan Drachman M.D.	Director	March 27, 2015
/s/ Jean M. George	Director	

		March 27, 2015
Jean M. George		
/s/ Deepa R. Pakianathan Deepa R. Pakianathan, Ph.D.	Director	March 27, 2015
/s/ H. Ward Wolff H. Ward Wolff	Director	March 27, 2015

Exhibit Index

Exhibit Number	Exhibit Description	Incorporation By Reference			
		Form	SEC File No.	Exhibit	Filing Date
3.1	Amended and Restated Certificate of Incorporation of the Registrant	8-K	001-36644	3.1	10/07/2014
3.2	Amended and Restated Bylaws of the Registrant	S-1	333-198355	3.4	9/19/2014
4.1	Reference is made to Exhibits 3.1 through 3.2.				
4.2	Form of common stock certificate of the Registrant.	S-1	333-198355	4.1	9/25/2014
10.1	Amended and Restated Investor Rights Agreement, among the Registrant and certain of its security holders, dated October 7, 2013, as amended.	S-1	333-198355	10.1	8/25/2014
10.2	2014 Equity Incentive Plan.	S-1	333-198355	10.4	9/25/2014
10.3	Form of Stock Option Grant Notice (2014 Equity Incentive Plan).	S-1	333-198355	10.5	9/25/2014
10.4	2014 Employee Stock Purchase Plan.	S-1	333-198355	10.6	9/25/2014
10.5	Employment Agreement between the Registrant and Susan Molineaux, dated June 1, 2010, as amended.	S-1	333-198355	10.7	8/25/2014
10.6	Offer Letter between the Registrant and William Waddill, dated March 10, 2014.	S-1	333-198355	10.8	8/25/2014
10.7	Employment Agreement between the Registrant and Mark Bennett, dated June 1, 2010.	S-1	333-198355	10.9	8/25/2014
10.8	Employment Agreement between the Registrant and Eric Sjogren, dated June 1, 2010.	S-1	333-198355	10.10	8/25/2014
10.9	Employment Agreement between the Registrant and Christopher Molineaux, dated April 8, 2013.	S-1	333-198355	10.11	8/25/2014
10.10	Offer Letter between the Registrant and Curtis Hecht, dated March 28, 2014.	S-1	333-198355	10.12	8/25/2014
10.11	Form of Indemnification Agreement between the Registrant and each of its directors and executive officers.	S-1	333-198355	10.13	9/19/2014
10.14	Lease between Are-Technology Center SSF, LLC and the Registrant, dated February 14, 2013.	S-1	333-198355	10.14	8/25/2014

10.15	Amendment to lease between Are-Technology Center SSF, LLC and the Registrant, dated October 30, 2013.	S-1	333-198355	10.15	8/25/2014
10.16†	Collaboration and License Agreement by and between the Registrant and Mars, Inc., dated December 9, 2014				
23.1	Consent of Independent Registered Public Accounting Firm.				
24.1	Power of Attorney (included on signature page to this Annual Report on Form 10-K).				
31.1	Certifications of Principal Executive Officer pursuant to Rule 13a-14(a).				
31.2	Certifications of Principal Financial Officer pursuant to Rule 13a-14(a).				
32.1*	Certification of Principal Executive Officer pursuant to Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended, and 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.				
32.2*	Certification of Principal Financial Officer pursuant to Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended, and 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.				
101.INS	XBRL Instance Document.				
101.SCH**	XBRL Taxonomy Extension Schema Document.				
101.CAL**	XBRL Taxonomy Extension Calculation Linkbase Document.				

101.DEF**	XBRL Taxonomy Extension Definition Linkbase Document.
101.LAB**	XBRL Taxonomy Extension Label Linkbase Document.
101.PRE**	XBRL Taxonomy Extension Presentation Linkbase Document.

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

** Attached as Exhibit 101 to this Annual Report on Form 10-K formatted in XBRL (Extensible Business Reporting Language): (i) Balance Sheets, (ii) Statements of Operations, (iii) Statements of Comprehensive Income (Loss), (iv) Statements of Cash Flows, and (v) Notes to Financial Statements, tagged as blocks of text and including detailed tags.

† Confidential treatment has been requested with respect to certain portions of this exhibit. Omitted portions have been filed separately with the Securities and Exchange Commission.