

Calithera Biosciences, Inc.
Form S-1/A
September 19, 2014
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As filed with the U.S. Securities and Exchange Commission on September 19, 2014.

Registration No. 333-198355

**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION**

Washington, D.C. 20549

AMENDMENT NO. 2

TO

FORM S-1

REGISTRATION STATEMENT

UNDER

THE SECURITIES ACT OF 1933

CALITHERA BIOSCIENCES, INC.

(Exact name of registrant as specified in its charter)

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Delaware
(State or other jurisdiction of
incorporation or organization)

2834
(Primary Standard Industrial
Classification Code Number)

27-2366329
(I.R.S. Employer
Identification Number)

343 Oyster Point Blvd. Suite 200
South San Francisco, California 94080
(650) 870-1000

(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

Susan M. Molineaux, Ph.D.
President and Chief Executive Officer
Calithera Biosciences, Inc.
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South San Francisco, California 94080
(650) 870-1000

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Approximate date of commencement of proposed sale to the public: As soon as practicable after the effective date of this Registration Statement.

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, check the following box. "

If this form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. "

If this form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. "

If this form is a post-effective amendment filed pursuant to Rule 462(d) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. "

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 definitions 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 Smaller reporting company "

(Do not check if a smaller reporting company)

CALCULATION OF REGISTRATION FEE

Title of each class of securities to be registered	Proposed maximum	
	aggregate offering price(1)(2)	Amount of registration fee(3)
Common stock, \$0.0001 par value per share	\$103,500,000	\$13,331

(1) Estimated solely for the purpose of computing the amount of registration fee pursuant to Rule 457(o) under the Securities Act of 1933, as amended.

(2) Includes the offering price of shares that the underwriters have the option to purchase to cover over-allotments, if any.

(3) The Registrant previously paid a registration fee of \$10,304 with the initial filing of this registration statement.

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The Registrant hereby amends this Registration Statement on such date or dates as may be necessary to delay its effective date until the Registrant shall file a further amendment which specifically states that this Registration Statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933, as amended, or until the Registration Statement shall become effective on such date as the Commission, acting pursuant to said Section 8(a), may determine.

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The information in this prospectus is not complete and may be changed. We may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This preliminary prospectus is not an offer to sell these securities and it is not soliciting offers to buy these securities in any state where the offer or sale is not permitted.

SUBJECT TO COMPLETION, DATED SEPTEMBER 19, 2014

PRELIMINARY PROSPECTUS

6,000,000 Shares

Common Stock

This is the initial public offering of shares of common stock of Calithera Biosciences, Inc.

We are offering 6,000,000 shares of our common stock. Prior to this offering, there has been no public market for our common stock. We currently expect the initial public offering price to be between \$13.00 and \$15.00 per share of common stock. We have applied to list our common stock on the NASDAQ Global Market under the symbol CALA.

We are an emerging growth company under the federal securities laws and will be subject to reduced public company reporting requirements for this prospectus and future filings.

Investing in our common stock involves a high degree of risk. See Risk Factors beginning on page 10.

	Per Share	Total
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Initial public offering price	\$	\$
Underwriting discounts and commissions(1)	\$	\$
Proceeds, before expenses, to us	\$	\$

(1) See Underwriting for additional disclosure regarding underwriting discounts, commissions and estimated offering expenses.

Entities associated with Advanced Technology Ventures VIII, L.P., Delphi Ventures VIII, L.P., Morgenthaler Venture Partners IX, L.P. and certain other existing stockholders have indicated an interest in purchasing up to an aggregate of \$15.0 million in shares of our common stock in this offering at the initial public offering price. Because these indications of interest are not binding agreements or commitments to purchase, these existing stockholders may elect not to purchase shares in this offering or the underwriters may elect not to sell any shares in this offering to such stockholders. The underwriters will receive the same discount from any shares of our common stock purchased by these stockholders as they will from any other shares of our common stock sold to the public in this offering.

We have granted the underwriters the right to purchase up to 900,000 additional shares of common stock to cover over-allotments, if any. The underwriters can exercise this right at any time within 30 days after the date of this prospectus.

The underwriters expect to deliver the shares against payment in New York, New York on or about _____, 2014.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

Citigroup

Leerink Partners

Wells Fargo Securities

JMP Securities

, 2014

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We are responsible for the information contained in this prospectus and in any free writing prospectus we prepare or authorize. We have not, and the underwriters have not, authorized anyone to provide you with different information, and we take no responsibility for any other information others may give you. We are not, and the underwriters are not, making an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should not assume that the information contained in this prospectus is accurate as of any date other than the date on the cover of this prospectus.

Persons who come into possession of this prospectus and any applicable free writing prospectus in jurisdictions outside the United States are required to inform themselves about and to observe any restrictions as to this offering and the distribution of this prospectus and any such free writing prospectus applicable to that jurisdiction.

Until _____, 2014 (25 days after the date of this prospectus), all dealers that buy, sell or trade shares of our common stock, whether or not participating in this offering, may be required to deliver a prospectus. This delivery is in addition to a dealer's obligation to deliver a prospectus when acting as an underwriter and with respect to their unsold allotments or subscriptions.

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SUMMARY

This summary highlights information contained elsewhere in this prospectus. This summary is not complete and may not contain all the information you should consider before investing in our common stock. You should read this entire prospectus carefully, especially the risks of investing in our common stock discussed under the heading Risk Factors, and our financial statements and related notes included elsewhere in this prospectus before making an investment decision. Except as otherwise indicated herein or as the context otherwise requires, references in this prospectus to Calithera, the company, we, us and our refer to Calithera Biosciences, Inc.

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. 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 U.S. Food and Drug Administration, or 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 of CB-839 in late 2015 or early 2016. We currently hold all commercial rights to CB-839.

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 Investigational New Drug, or IND, application to the FDA near the end of 2015.

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Our management team has considerable experience and success in the discovery and development of small molecule oncology drugs. Susan Molineaux, Ph.D., our Chief Executive Officer, was the founder and Chief Executive Officer of Proteolix, Inc., where she and several members of our current management team led the group that discovered and advanced through Phase 2 registration trials carfilzomib (marketed as Kyprolis), which was approved on an accelerated basis in 2012 for the treatment of refractory multiple myeloma. Additional members of our management team bring extensive experience in medicinal chemistry and in the financial management of private and public companies.

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. Key elements of our strategy include:

Pursuing a broad clinical development program of CB-839 both as a single agent and in combination with approved therapies.

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

Maximizing the commercial value of CB-839.

Advancing our first-in-class arginase inhibitor into clinical development.

Further developing our pipeline by leveraging our expertise in tumor biology, drug discovery and clinical development.

Our Research and Development Programs

The following table summarizes our ongoing and planned clinical trials from 2014 to 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.

Note: Phase 1 trials include a dose escalation stage followed by dose expansion in select tumor types.

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Our Lead Program in Tumor Metabolism: CB-839

CB-839 is an inhibitor of glutaminase, a tumor metabolism target that, based on our preclinical studies, is critical for the growth and survival of multiple tumor types. Due to CB-839's novel mechanism of action, preclinical synergistic activity with existing cancer agents and favorable preclinical safety profile, 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 and multiple myeloma.

CB-839 in combination with standard of care drugs, initially with a cytotoxic agent for triple-negative breast cancer and an immunomodulatory agent for multiple myeloma.

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 believe this broad product development program provides the best opportunity to maximize the commercial value of CB-839.

In February 2014, we initiated three Phase 1 clinical trials in patients with solid tumors, leukemias, lymphomas and multiple myeloma 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. 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. During dose escalation, increased blood levels of CB-839 have been correlated with the inhibition of glutaminase and CB-839 has been generally well tolerated. As of July 25, 2014, 24 patients with cancers that had been heavily treated by other drugs had been enrolled in these trials, and 21 Grade 1 adverse events, or AEs, (most commonly nausea, vomiting and fatigue), two Grade 2 AEs and two Grade 3 AEs had been reported. Stable disease has been observed in several patients, including a TNBC patient who had a 13% decrease in tumor size after her third cycle of dosing with CB-839; she remains in the trial with no ongoing AEs. In addition to evaluating CB-839 as a single agent, we plan to enroll two Phase 1b combination cohorts, one in which CB-839 will be combined with paclitaxel in patients with triple-negative breast cancer and a second in which CB-839 will be combined with pomalidomide (marketed as Pomalyst) and dexamethasone in patients with multiple myeloma. Pending input from the FDA on the results of our Phase 1 trials and our Phase 2 trial protocols, we plan to initiate in late 2015 or early 2016 one or more Phase 2 clinical trials to study CB-839 as a single agent or in combination with approved therapies.

Our Lead Program in Tumor Immunology: Arginase Inhibitors

Our preclinical program in tumor immunology is focused on developing 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 immune cells, known as cytotoxic T cells. Secreted arginase is present 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. We are currently optimizing arginase inhibitors with the aim of submitting an IND application to the FDA near the end of 2015.

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Risks Associated with our Business

Our business is subject to numerous risks and uncertainties, including those highlighted in the section titled "Risk Factors" immediately following this prospectus summary. These risks include, among others, the following:

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 had an accumulated deficit of \$39.8 million as of June 30, 2014.

We will need substantial additional funding and may be unable to raise capital when needed, which would force us to delay, reduce or eliminate our product development programs or commercialization efforts.

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

Clinical trials of our product candidates will be costly and time consuming, and if they fail to demonstrate safety and efficacy to the satisfaction of the FDA, or similar regulatory authorities, we will be unable to commercialize our product candidates.

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.

If we are unable to obtain sufficient intellectual property protection or protect our intellectual property rights, our business may be harmed.

Healthcare policy and regulatory oversight in the United States and internationally are subject to rapid change, and if we are unable to respond, our business may be harmed.

We face substantial competition from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide.

If we are unable to adequately address these and other risks we face, our business, financial condition, operating results and prospects may be adversely affected.

In addition, we are an emerging growth company as defined in the Jumpstart Our Business Startups Act, or the JOBS Act, enacted in April 2012, and therefore we intend to take advantage of certain exemptions from various public company reporting requirements, including not being required to have our internal control over financial reporting audited by our independent registered public accounting firm pursuant to Section 404(b) of the Sarbanes-Oxley Act of 2002, reduced disclosure obligations regarding executive compensation in this prospectus, our periodic reports and proxy statement and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and any golden parachute payments not previously approved. We may take advantage of these exemptions for up to five years or until we are no longer an emerging growth company.

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Corporate Information

We were incorporated in Delaware in March 2010 as Protein Activation Therapeutics, Inc. and subsequently changed our name to Calithera Biosciences, Inc. Our headquarters are located at 343 Oyster Point Blvd., Suite 200, South San Francisco, California 94080, and our telephone number is (650) 870-1000. Our website address is www.calithera.com. The information contained on, or that can be accessed through, our website is not part of, and is not incorporated by reference into this prospectus and should not be considered to be part of this prospectus. Investors should not rely on any such information in deciding whether to purchase our common stock.

Calithera, the Calithera logo and other trademarks or service marks of Calithera Biosciences, Inc. appearing in this prospectus are the property of Calithera Biosciences, Inc. Other trademarks, service marks or trade names appearing in this prospectus are the property of their respective owners. We do not intend our use or display of other companies' trade names, trademarks or service marks to imply a relationship with, or endorsement or sponsorship of us by, these other companies.

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The Offering

Common stock offered by us 6,000,000 shares

Common stock to be outstanding immediately after this offering 15,881,573 shares

Over-allotment option 900,000 shares

Use of proceeds We estimate that the net proceeds from this offering will be approximately \$75.4 million, or approximately \$87.1 million if the underwriters exercise in full their over-allotment option to purchase additional shares, at an assumed initial public offering price of \$14.00 per share, the midpoint of the price range set forth on the cover page of this prospectus, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

We intend to use the net proceeds from this offering to further the clinical development of CB-839, further the development of our arginase inhibitor program, fund research and drug discovery activities related to additional product candidates, and for working capital and general corporate purposes. We may also use a portion of the net proceeds to acquire complementary businesses, products or technologies, although, we have no present commitments or agreements for any specific acquisitions.

Risk factors You should read the section titled Risk Factors together with all the other information included in this prospectus before deciding to invest in shares of our common stock.

Proposed NASDAQ Global Market symbol CALA

Entities associated with Advanced Technology Ventures VIII, L.P., Delphi Ventures VIII, L.P., Morgenthaler Venture Partners IX, L.P. and certain other existing stockholders have indicated an interest in purchasing up to an aggregate of \$15.0 million in shares of our common stock in this offering at the initial public offering price. Because these indications of interest are not binding agreements or commitments to purchase, these existing stockholders may elect not to purchase shares in this offering or the underwriters may elect not to sell any shares in this offering to such stockholders. The underwriters will receive the same discount from any shares of our common stock purchased by these stockholders as they will from any other shares of our common stock sold to the public in this offering.

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The number of shares of our common stock to be outstanding after this offering is based on 9,881,573 shares of common stock outstanding as of June 30, 2014, and excludes:

979,388 shares of common stock issuable upon the exercise of options outstanding as of June 30, 2014 with a weighted-average exercise price of \$2.07 per share, plus options to purchase an aggregate of 306,559 shares of common stock granted subsequent to June 30, 2014, with a weighted average exercise price of \$6.94 per share;

42,120 shares of common stock reserved for future issuance under our 2010 Equity Incentive Plan as of June 30, 2014, plus an additional 439,130 shares of common stock reserved for future issuance subsequent to June 30, 2014, all of which shares will cease to be available for future issuance at the time our 2014 Equity Incentive Plan becomes effective in connection with this offering;

971,340 shares of common stock reserved for future issuance under our 2014 Equity Incentive Plan, as well as any automatic increases in the number of shares of common stock reserved for future issuance under this plan, which will become effective upon the execution of the underwriting agreement related to this offering; and

189,883 shares of common stock reserved for future issuance under our 2014 Employee Stock Purchase Plan, as well as any automatic increases in the number of shares of common stock reserved for future issuance under this plan, which will become effective upon the execution of the underwriting agreement related to this offering.

Unless otherwise noted, all information in this prospectus assumes:

a 1-for-48 reverse stock split of our common stock and preferred stock prior to the effectiveness of the registration statement of which this prospectus forms a part;

the conversion of all outstanding shares of preferred stock into 9,592,042 shares of common stock immediately upon the closing of this offering, which includes the conversion of the 1,902,583 shares of Series D preferred stock we issued and sold in July 2014;

that our amended and restated certificate of incorporation, which we will file in connection with the closing of this offering, and our amended and restated bylaws are effective;

no exercise of any outstanding options; and

no exercise of the underwriters' over-allotment option to purchase additional shares.

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The following tables summarize our financial data. We have derived the statements of operations data for the years ended December 31, 2012 and 2013 from our audited financial statements included elsewhere in this prospectus. The statements of operations data for the six months ended June 30, 2013 and 2014 and the balance sheet data as of June 30, 2014 are derived from our unaudited financial statements included elsewhere in this prospectus. We have prepared the unaudited financial statements on the same basis as the audited financial statements and have included, in our opinion, all adjustments, consisting only of normal recurring adjustments that we consider necessary for a fair presentation of the financial information set forth in those statements. Our historical results are not necessarily indicative of the results that may be expected in the future and results of interim periods are not necessarily indicative of the results for the entire year. You should read this data together with our financial statements and related notes, Selected Financial Data and Management's Discussion and Analysis of Financial Condition and Results of Operations included elsewhere in this prospectus.

	Years Ended December 31,		Six Months Ended June 30,	
	2012	2013	2013	2014
	(in thousands, except per share data)			
Statements of Operations Data:				
Operating expenses:				
Research and development	\$ 6,558	\$ 9,900	\$ 4,069	\$ 7,501
General and administrative	1,417	2,478	903	2,141
Total operating expenses	7,975	12,378	4,972	9,642
Loss from operations	(7,975)	(12,378)	(4,972)	(9,642)
Other income		1		2
Net loss	(7,975)	(12,377)	(4,972)	(9,640)
Gain on extinguishment of convertible preferred stock	2,889			
Net loss attributable to common stockholders	\$ (5,086)	\$ (12,377)	\$ (4,972)	\$ (9,640)
Net loss per share attributable to common stockholders, basic and diluted(1)	\$ (366.13)	\$ (131.53)	\$ (84.62)	\$ (47.14)
Shares used in computing net loss per share attributable to common stockholders, basic and diluted(1)	14	94	59	205
Pro forma net loss per share attributable to common stockholders, basic and diluted (unaudited)(1)		\$ (3.03)		\$ (1.22)
Shares used in computing pro forma net loss per share attributable to common stockholders, basic and diluted (unaudited)(1)		4,083		7,894

- (1) See Note 9 to our audited financial statements and Note 6 to our unaudited interim financial statements included elsewhere in this prospectus for an explanation of the calculations of our basic and diluted net loss per common share, pro forma net loss per common share, and the weighted-average number of shares used in the computation of the per share amounts.

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	As of June 30, 2014		
	Actual	Pro Forma(1) (unaudited) (in thousands)	Pro Forma As Adjusted(2)(3)
Balance Sheet Data:			
Cash and cash equivalents	\$ 27,750	\$ 40,750	\$ 116,170
Working capital	23,128	39,128	114,548
Total assets	30,655	43,655	119,075
Convertible preferred stock	54,282		
Accumulated deficit	(39,782)	(39,782)	(39,782)
Total stockholders (deficit) equity	(30,043)	40,239	115,659

- (1) The pro forma column reflects (i) the issuance and sale of 1,902,583 shares of Series D preferred stock and the receipt of net proceeds of \$16.0 million in July 2014 (of which \$3.0 million was included in cash and cash equivalents and total assets as of June 30, 2014) and (ii) the conversion of all outstanding shares of our convertible preferred stock into 9,592,042 shares of our common stock immediately upon the closing of this offering.
- (2) The pro forma as adjusted column further reflects the receipt of \$75.4 million in net proceeds from our sale of 6,000,000 shares of common stock in this offering at an assumed initial public offering price of \$14.00 per share, the midpoint of the price range set forth on the cover page of this prospectus, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.
- (3) Each \$1.00 increase or decrease in the assumed initial public offering price of \$14.00 per share would increase or decrease, respectively, the amount of cash and cash equivalents, working capital, total assets and total stockholders (deficit) equity by approximately \$5.6 million, assuming the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting underwriting discounts and commissions and estimated offering expenses payable by us. We may also increase or decrease the number of shares we are offering. An increase or decrease of 1,000,000 in the number of shares we are offering would increase or decrease, respectively, the amount of cash and cash equivalents, working capital, total assets and stockholders (deficit) equity by approximately \$13.0 million, assuming the assumed initial public offering price per share, as set forth on the cover page of this prospectus, remains the same and after deducting underwriting discounts and commissions. The pro forma as adjusted information is illustrative only, and will be adjusted based on the actual initial public offering price and other terms of this offering determined at pricing.

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RISK FACTORS

Investing in our common stock involves a high degree of risk. You should carefully consider the risks and uncertainties described below together with all of the other information contained in this prospectus, including our financial statements and the related notes appearing at the end of this prospectus, before deciding to invest in our common stock. If any of the following risks actually occur, it could harm our business, prospects, operating results and financial condition. In such event, the trading price of our common stock could decline and you might lose all or part of your investment.

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 \$8.0 million, \$12.4 million and \$9.6 million for 2012 and 2013 and the six months ended June 30, 2014, respectively. As of June 30, 2014, we had an accumulated deficit of \$39.8 million. To date, we have financed our operations primarily through private placements of our preferred stock. 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 inhibitor program and advance a candidate 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;

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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 is 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 inhibitor program. 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.

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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. 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. Furthermore, upon the closing of this offering, we expect to incur additional costs associated with operating as a public company.

We expect that the net proceeds from this offering, together with our existing cash, cash equivalents and marketable securities and anticipated interest income will enable us to fund our operating expenses and capital expenditure requirements through at least 2015. 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 inhibitor program 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 processes that take 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. Since inception, our operations have been financed primarily by net proceeds of approximately \$79.4 million from the sale of shares of our preferred stock,

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including net proceeds of \$16.0 million from the issuance and sale of 1,902,583 shares of Series D preferred stock in July 2014. As of June 30, 2014, we had cash and cash equivalents of \$27.8 million. We expect that our existing cash and cash equivalents, excluding the proceeds from this offering, will be sufficient to enable us to conduct planned preclinical studies and clinical trials for our product candidates through at least the end of 2015. 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, including purchasers of common stock in this offering, 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

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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 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 can suppress the growth of certain cancer cells, to

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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 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.

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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 program is 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 inhibitor program 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.

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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

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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;

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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.

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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 July 25, 2014, we had enrolled 24 patients in these trials and 21 Grade 1 adverse events, or AEs, (most commonly nausea, vomiting and fatigue), two Grade 2 AEs and two Grade 3 AEs had been reported. We have treated an insufficient number of patients to assess the safety of CB-839 and, as our trials

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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 inhibitor program 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

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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.

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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 Pharmaceutical, Inc., AstraZeneca plc, Cornerstone Pharmaceuticals, Inc., Eli Lilly and Company, Forma Therapeutics Holdings, LLC, GlaxoSmithKline plc, Novartis International AG, Pfizer, Inc., 3-V Biosciences, Inc., and Roche Holdings and its subsidiary Genentech Inc. Our principal competitors in the field of tumor immunology include AstraZeneca plc, Ono Pharmaceuticals, Co., Ltd., NewLink Genetics Corporation, Incyte Corporation, Merck & Co., Bristol-Myers Squibb Company, CureTech Ltd, and EMD Serono, Inc.

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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

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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.

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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

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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 expect 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 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

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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 likely collaborators for any collaboration arrangements include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies. If we enter into any such arrangements with any third parties, we will likely 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.

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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.

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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

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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, post-grant 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.

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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

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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 a 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,

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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 post-approval 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;

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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.

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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.

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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 This Offering and Our Common Stock

An active trading market for our common stock may not develop or be sustainable, and investors may not be able to resell their shares at or above the initial public offering price.

Prior to this offering, there has been no public market for our common stock. The initial public offering price for our common stock will be determined through negotiations with the underwriters and may bear no

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relationship to the price at which the common stock will trade upon the closing of this offering. An active trading market for our shares may never develop or be sustained following this offering. If an active market for our common stock does not develop, it may be difficult for investors to resell the shares purchased in this offering. We cannot predict the prices at which our common stock will trade and investors may not be able to resell their shares at a price that is at or above the initial public offering price.

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 is likely to be volatile. The stock market in general and the market in which we operate have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, investors may not be able to sell their common stock at or above the initial public offering price. 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.

Based upon shares outstanding as of June 30, 2014, upon the closing of this offering, our executive officers, directors and current beneficial owners of 5% or more of our common stock will, in the aggregate, beneficially

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own approximately 59.4% of our outstanding common stock. Entities associated with Advanced Technology Ventures VIII, L.P., Delphi Ventures VIII, L.P., Morgenthaler Venture Partners IX, L.P. and certain other existing stockholders have indicated an interest in purchasing up to an aggregate of \$15.0 million in shares of our common stock in this offering at the initial public offering price. The previously discussed ownership percentage upon the completion of this offering does not reflect the potential purchase of any shares in this offering by such stockholders. If these entities purchase all of the \$15.0 million in shares of our common stock they have indicated an interest in purchasing in this offering, the number of shares of our common stock beneficially owned by our executive officers, directors and current beneficial owners of 5% or more of our common stock and their respective affiliates will, in the aggregate, increase to 65.1% of our common stock. These stockholders, 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.

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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 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 will have broad discretion in the use of proceeds from this offering and may invest or spend the proceeds in ways with which you do not agree and in ways that may not yield a return.

Although we currently intend to use the net proceeds from this offering in the manner described in the section titled "Use of Proceeds" in this prospectus, we will have broad discretion over the use of proceeds from this offering. Investors may not agree with our decisions, and our use of the proceeds may not yield any return on your investment in us. Our failure to apply the net proceeds of this offering effectively could impair our ability to pursue our growth strategy or could require us to raise additional capital.

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.

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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 June 30th,

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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.

We have identified a material weakness in our internal control over financial reporting, and 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.

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 intend to take steps to remediate this material weakness, including increasing the depth and experience within our accounting and finance organization, as well as designing and implementing improved processes and internal controls. However, our efforts to remediate this material weakness may not be effective or prevent any future material weakness or significant deficiency in our internal control over financial reporting. If our efforts are not successful or other 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 first fiscal year beginning after the effective date of this offering. 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.

If our existing stockholders sell, or indicate an intention to sell, substantial amounts of our common stock in the public market after the lock-up and legal restrictions on resale discussed in this prospectus lapse, the trading price of our common stock could decline. Based on shares outstanding as of June 30, 2014, upon the closing of this offering, we will have outstanding a total of 15,881,573 shares of common stock. Of these shares, only the shares of common stock sold in this offering will be freely tradable, without restriction, in the public market immediately

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after the offering. Each of our directors and executive officers, and substantially all holders of our common stock and securities exercisable for or convertible into our common stock have entered into lock-up agreements with the

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underwriters that restrict their ability to sell or transfer their shares. The lock-up agreements pertaining to this offering will expire 180 days from the date of this prospectus, Citigroup Global Markets Inc. and Leerink Partners LLC, however, may, in their sole discretion, waive the contractual lock-up prior to the expiration of the lock-up agreements. During such 180-day period, our directors and executive officers may establish a trading plan pursuant to Rule 10b5-1 under the Exchange Act for the sale of shares of common stock to occur on or after the date of the lock-up agreements. After the lock-up agreements expire, based on shares outstanding as of June 30, 2014, an additional 9,881,573 shares of common stock will be eligible for sale in the public market. These shares will become eligible for sale in the public market to the extent permitted by the provisions of various vesting agreements, the lock-up agreements and Rules 144 and 701 under the Securities Act of 1933, as amended, or the Securities Act. We intend to file a registration statement on Form S-8 under the Securities Act covering all of the shares of common stock subject to options outstanding and reserved for issuance under our stock plans. This registration statement will become effective immediately upon filing, and shares covered by this registration statement will be eligible for sale in the public markets, subject to Rule 144 limitations applicable to affiliates and any lock-up agreements described above. If these additional shares are sold, or if it is perceived that they will be sold, in the public market, the trading price of our common stock could decline.

Purchasers in this offering will experience immediate and substantial dilution in the tangible net book value of their investment.

The assumed initial public offering price of our common stock is substantially higher than the net tangible book value per share of our common stock immediately after this offering. Therefore, if you purchase our common stock in this offering, you will incur an immediate dilution of \$6.72 in net tangible book value per share from the price you paid, based on an assumed initial public offering price of \$14.00 per share. In addition, new investors who purchase shares in this offering will contribute approximately 51.3% of the total amount of equity capital raised by us through the date of this offering, but will only own approximately 37.8% of the outstanding share capital. The exercise of outstanding options and warrants will result in further dilution, as will the exercise by the underwriters of their option to purchase additional shares. For a further description of the dilution that you will experience immediately after this offering, see the section titled Dilution.

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, as they will be in effect following this offering, 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 will 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.

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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 will provide that the Court of Chancery of the State of Delaware will be 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.

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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus contains forward-looking statements about us and our industry that involve substantial risks and uncertainties. All statements other than statements of historical facts contained in this prospectus, including statements regarding our future financial condition, business strategy and plans, and objectives of management for future operations, are forward-looking statements. In some cases, you can identify forward-looking statements by words such as anticipate, believe, continue, could, design, estimate, expect, intend, may, plan, predict, should, will or the negative of these terms or other similar expressions.

We have based these forward-looking statements largely on our current expectations and projections about future events and financial trends that we believe may affect our financial condition, results of operations, business strategy and financial needs. These forward-looking statements are subject to a number of known and unknown risks, uncertainties and assumptions, including risks described in the section titled **Risk Factors** and elsewhere in this prospectus, regarding, among other things:

our ability to fund our working capital requirements;

our ability to obtain and maintain regulatory approval of our product candidates;

our ability to successfully commercialize our product candidates;

the rate and degree of market acceptance of our products that are approved;

our estimates of our expenses, ongoing losses, future revenue, capital requirements and our needs for or ability to obtain additional financing;

our expectation that our existing capital resources and the net proceeds from this offering will be sufficient to enable us to complete our planned clinical trials;

our ability to obtain and maintain intellectual property protection for our product candidates;

our ability to identify and develop new product candidates;

our ability to retain and recruit key personnel;

our use of proceeds from this offering;

our financial performance; and

developments and projections relating to our competitors or our industry.

These risks are not exhaustive. Other sections of this prospectus may include additional factors that could harm our business and financial performance. Moreover, we operate in a very competitive and rapidly changing environment. New risk factors emerge from time to time, and it is not possible for our management to predict all risk factors nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in, or implied by, any forward-looking statements.

You should not rely upon forward-looking statements as predictions of future events. We cannot assure you that the events and circumstances reflected in the forward-looking statements will be achieved or occur. Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee future results, levels of activity, performance or achievements. Except as required by law, we undertake no obligation to update publicly any forward-looking statements for any reason after the date of this prospectus or to conform these statements to actual results or to changes in our expectations.

You should read this prospectus and the documents that we reference in this prospectus and have filed as exhibits to the registration statement of which this prospectus is a part with the understanding that our actual future results, levels of activity, performance and achievements may be materially different from what we expect. We qualify all of our forward-looking statements by these cautionary statements.

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INDUSTRY AND MARKET DATA

Unless otherwise indicated, information contained in this prospectus concerning our industry and the market in which we operate, including our general expectations and market position, market opportunity and market size, is based on information from various sources and is subject to a number of assumptions and limitations. Although we are responsible for all of the disclosure contained in this prospectus and we believe the information from the third-party sources included in this prospectus is reliable, such information is inherently imprecise. The industry in which we operate is subject to a high degree of uncertainty and risk due to a variety of factors, including those described in the section titled Risk Factors. These and other factors could cause results to differ materially from those expressed in the estimates made by the independent parties and by us.

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USE OF PROCEEDS

We estimate that the net proceeds from the sale of 6,000,000 shares of common stock in this offering will be approximately \$75.4 million at an assumed initial public offering price of \$14.00 per share, the midpoint of the price range set forth on the cover page of this prospectus, after deducting underwriting discounts and commissions and estimated offering expenses payable by us. If the underwriters exercise their overallotment option in full, we estimate that the net proceeds will be approximately \$87.1 million after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.

Each \$1.00 increase or decrease in the assumed initial public offering price of \$14.00 per share would increase or decrease, respectively, our net proceeds by \$5.6 million, assuming the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting underwriting discounts and commissions and estimated offering expenses payable by us. We may also increase or decrease the number of shares we are offering. An increase or decrease of 1,000,000 in the number of shares we are offering would increase or decrease, respectively, the net proceeds to us from this offering by approximately \$13.0 million, assuming the assumed initial public offering price of \$14.00 per share remains the same and after deducting underwriting discounts and commissions.

We currently expect to use our net proceeds from this offering as follows:

approximately \$25.0 to \$35.0 million to further the clinical development of CB-839 through completion of Phase 2 clinical trials;

approximately \$10.0 to \$15.0 million to further the development of our arginase inhibitor program through a Phase 1 clinical trial;

approximately \$5.0 to \$10.0 million to fund our research and drug discovery activities related to additional product candidates, including the advancement of a third program to submission of an Investigational New Drug application; and

the remaining proceeds for working capital and general corporate purposes.

However, due to the uncertainties inherent in the product development process, it is difficult to estimate with certainty the exact amounts of the net proceeds from this offering that may be used for the above purposes. Our management will have broad discretion over the use of the net proceeds from this offering. The amounts and timing of our expenditures will depend upon numerous factors including the results of our research and development efforts, the timing and success of preclinical studies and any ongoing clinical trials or clinical trials we may commence in the future, the timing of regulatory submissions and the amount of cash obtained through future collaborations, if any.

We believe opportunities may exist from time to time to expand our current business through acquisitions or in-licenses of complementary companies, medicines or technologies. While we have no current agreements, commitments or understandings for any specific acquisitions or in-licenses at this time, we may use a portion of the net proceeds for these purposes.

Pending the use of the proceeds from this offering as described above, we intend to invest the net proceeds in interest-bearing investment-grade securities or government securities.

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.

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The following table sets forth our cash and cash equivalents and capitalization as of June 30, 2014 on:

an actual basis;

a pro forma basis, to reflect (i) the issuance and sale of 1,902,583 shares of Series D preferred stock and the receipt of net proceeds of \$16.0 million in July 2014 (of which \$3.0 million was included in cash and cash equivalents as of June 30, 2014), (ii) the conversion of all outstanding shares of preferred stock into 9,592,042 shares of common stock immediately upon the closing of this offering and (iii) the filing of our amended and restated certificate of incorporation; and

a pro forma as adjusted basis, to give further effect to the sale of shares of common stock in this offering at an assumed initial public offering price of \$14.00 per share, the midpoint of the price range set forth on the cover page of this prospectus, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

You should read this information together with our audited financial statements and related notes appearing elsewhere in this prospectus and the information set forth under the heading Selected Financial Data and Management's Discussion and Analysis of Financial Condition and Results of Operations.

	As of June 30, 2014		
	Actual	Pro Forma (unaudited)	Pro Forma As Adjusted(1)
	(in thousands, except share and per share data)		
Cash and cash equivalents	\$ 27,750	\$ 40,750	\$ 116,170
Convertible preferred stock, \$0.0001 par value per share 11,340,166 shares authorized, 7,689,459 shares issued and outstanding, actual; no shares issued and outstanding, pro forma and pro forma as adjusted	\$ 54,282	\$	\$
Stockholders' (deficit) equity:			
Preferred stock, par value of \$0.0001 per share no shares authorized, issued or outstanding, actual; 10,000,000 shares authorized, no shares issued or outstanding, pro forma and pro forma as adjusted			
Common stock, par value of \$0.0001 per share 13,437,500 shares authorized, 289,531 shares issued and outstanding, actual; 200,000,000 shares authorized, pro forma and pro forma as adjusted; 9,881,573 shares issued and outstanding, pro forma; 15,881,573 shares issued and outstanding, pro forma as adjusted	1	1	2
Additional paid-in capital	9,738	80,020	155,439
Accumulated deficit	(39,782)	(39,782)	(39,782)
Total stockholders' (deficit) equity	(30,043)	40,239	115,659
Total capitalization	\$ 24,239	\$ 40,239	\$ 115,659

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- (1) Each \$1.00 increase or decrease in the assumed initial public offering price of \$14.00 per share, the midpoint of the price range set forth on the cover page of this prospectus, would increase or decrease, respectively, the amount of cash and cash equivalents, additional paid-in capital, total stockholder's (deficit) equity and total capitalization by \$5.6 million, assuming the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting underwriting discounts and commissions and estimated offering expenses payable by us. We may also increase or decrease the number of shares we are offering. An increase or decrease of 1,000,000 in the number of shares we are offering would increase or decrease, respectively, the amount of cash and cash equivalents and stockholders' (deficit) equity by approximately \$13.0 million, assuming the assumed initial public offering price per

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share, as set forth on the cover page of this prospectus, remains the same and after deducting underwriting discounts and commissions. The pro forma as adjusted information discussed above is illustrative only, and will be adjusted based on the actual initial public offering price and other terms of this offering determined at pricing.

The number of shares of common stock in the table above is based on 9,881,573 shares of common stock outstanding as of June 30, 2014, and excludes:

979,388 shares of common stock issuable upon the exercise of options outstanding as of June 30, 2014 with a weighted-average exercise price of \$2.07 per share, plus options to purchase an aggregate of 306,559 shares of common stock granted subsequent to June 30, 2014, with a weighted average exercise price of \$6.94 per share;

42,120 shares of common stock reserved for future issuance under our 2010 Equity Incentive Plan as of June 30, 2014, plus an additional 439,130 shares of common stock reserved for future issuance subsequent to June 30, 2014, all of which shares will cease to be available for future issuance at the time our 2014 Equity Incentive Plan becomes effective in connection with this offering;

971,340 shares of common stock reserved for future issuance under our 2014 Equity Incentive Plan, as well as any automatic increases in the number of shares of common stock reserved for future issuance under this plan, which will become effective upon the execution of the underwriting agreement related to this offering; and

189,883 shares of common stock reserved for future issuance under our 2014 Employee Stock Purchase Plan, as well as any automatic increases in the number of shares of common stock reserved for future issuance under this plan, which will become effective upon the execution of the underwriting agreement related to this offering.

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If you invest in our common stock in this offering, your interest will be diluted to the extent of the difference between the initial public offering price per share of our common stock and the pro forma as adjusted net tangible book value per share of our common stock immediately after the closing of this offering.

Our pro forma net tangible book value of our common stock as of June 30, 2014 was \$40.2 million, or \$4.07 per share, based on the total number of shares of our common stock outstanding as of June 30, 2014. Pro forma net tangible book value per share represents our total tangible assets less our total liabilities, divided by the number of outstanding shares of common stock, after giving effect to (i) the issuance and sale of 1,902,583 shares of Series D preferred stock and the receipt of net proceeds of \$16.0 million in July 2014 and (ii) the conversion of all outstanding shares of preferred stock into 9,592,042 shares of common stock immediately upon the closing of this offering.

After giving effect to the sale of 6,000,000 shares of common stock in this offering at an assumed initial public offering price of \$14.00 per share, the midpoint of the price range set forth on the cover page of this prospectus, after deducting underwriting discounts and commissions and estimated offering expenses payable by us, our pro forma as adjusted net tangible book value as of June 30, 2014, would have been \$115.7 million, or \$7.28 per share. This represents an immediate increase in pro forma as adjusted net tangible book value of \$3.21 per share to our existing stockholders and an immediate dilution of \$6.72 per share to investors purchasing common stock in this offering.

The following table illustrates this dilution on a per share basis to new investors:

Assumed initial public offering price per share	\$ 14.00
Pro forma net tangible book value per share at June 30, 2014	\$ 4.07
Increase in pro forma net tangible book value per share attributable to new investors in this offering	3.21
Pro forma as adjusted net tangible book value per share after this offering	7.28
Dilution in net tangible book value per share to new investors in this offering	\$ 6.72

Each \$1.00 increase (decrease) in the assumed initial public offering price of \$14.00 per share would increase (decrease) our pro forma as adjusted net tangible book value per share after this offering by \$0.35 per share and the dilution to new investors by \$0.65 per share, assuming the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting underwriting discounts and commissions and estimated offering expenses payable by us. Similarly, each increase of 1,000,000 shares in the number of shares of common stock offered by us would increase the pro forma as adjusted net tangible book value by \$0.34 per share and decrease the dilution to new investors by \$0.34 per share, assuming the assumed initial public offering price, as set forth on the cover page of this prospectus, remains the same and after deducting underwriting discounts and commissions.

If the underwriters exercise in full their over-allotment option to purchase 900,000 additional shares from us, the pro forma as adjusted net tangible book value per share after giving effect to this offering would be \$7.59 per share, representing an immediate increase to existing stockholders of \$3.52 per share, and immediate dilution to investors in this offering of \$6.41 per share.

The following table summarizes, as of June 30, 2014 on the pro forma as adjusted basis described above:

the total number of shares of common stock purchased from us by existing stockholders and by new investors purchasing shares in this offering;

the total consideration paid to us by existing stockholders and by new investors purchasing common stock in this offering, assuming an initial public offering price of \$14.00 per share, the midpoint of the price range set forth on the cover page of this prospectus, before deducting underwriting discounts and commissions and estimated offering expenses payable by us in connection with this offering; and

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the average price per share paid by existing stockholders and by new investors purchasing shares in this offering.

	Shares Purchased		Total Consideration		Average Price Per Share
	Number	Percent	Amount	Percent	
Existing stockholders	9,881,573	62.2%	\$ 79,900,000	48.7%	\$ 8.09
New investors	6,000,000	37.8	84,000,000	51.3	14.00
Total	15,881,573	100%	\$ 163,900,000	100%	

The total number of shares of common stock reflected in the discussion and tables above is based on 9,881,573 shares of common stock outstanding as of June 30, 2014, which includes the conversion of the 1,902,583 shares of Series D preferred stock we issued and sold in July 2014, and excludes:

979,388 shares of common stock issuable upon the exercise of options outstanding as of June 30, 2014 with a weighted-average exercise price of \$2.07 per share, plus options to purchase an aggregate of 306,559 shares of common stock granted subsequent to June 30, 2014, with a weighted average exercise price of \$6.94 per share;

42,120 shares of common stock reserved for future issuance under our 2010 Equity Incentive Plan as of June 30, 2014, plus an additional 439,130 shares of common stock reserved for future issuance subsequent to June 30, 2014, all of which shares will cease to be available for future issuance at the time our 2014 Equity Incentive Plan becomes effective in connection with this offering;

971,340 shares of common stock reserved for future issuance under our 2014 Equity Incentive Plan, as well as any automatic increases in the number of shares of common stock reserved for future issuance under this plan, which will become effective upon the execution of the underwriting agreement related to this offering; and

189,883 shares of common stock reserved for future issuance under our 2014 Employee Stock Purchase Plan, as well as any automatic increases in the number of shares of common stock reserved for future issuance under this plan, which will become effective upon the execution of the underwriting agreement related to this offering.

A \$1.00 increase (decrease) in the assumed initial public offering price of \$14.00 per share would increase (decrease) total consideration paid by new investors by \$6.0 million, assuming the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and without deducting underwriting discounts and commissions and estimated expenses payable by us.

To the extent that any outstanding options are exercised, new options are issued under our stock-based compensation plans or we issue additional shares of common stock in the future, there will be further dilution to investors participating in this offering.

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You should read the selected financial data together with the section titled "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our financial statements and related notes included elsewhere in this prospectus. The selected financial data included in this section are not intended to replace the financial statements and related notes included elsewhere in this prospectus.

We derived the statements of operations data for the years ended December 31, 2012 and 2013 and the balance sheet data as of December 31, 2012 and 2013 from our audited financial statements included elsewhere in this prospectus. We derived the statements of operations data for the six months ended June 30, 2013 and 2014 and the balance sheet data as of June 30, 2014 from our unaudited interim financial statements and related notes included elsewhere in this prospectus. Our unaudited interim financial statements were prepared on the same basis as our audited financial statements and include, in our opinion, all adjustments, consisting of normal recurring adjustments that we consider necessary for a fair presentation of the financial information set forth in those financial statements. Historical results are not necessarily indicative of the results that may be expected in the future and results for the six months ended June 30, 2014 are not indicative of results to be expected for the full year.

	Years Ended December 31,		Six Months Ended June 30,	
	2012	2013	2013	2014
	(unaudited)			
	(in thousands, except per share data)			
Statements of Operations Data:				
Operating expenses:				
Research and development	\$ 6,558	\$ 9,900	\$ 4,069	\$ 7,501
General and administrative	1,417	2,478	903	2,141
Total operating expenses	7,975	12,378	4,972	9,642
Loss from operations	(7,975)	(12,378)	(4,972)	(9,642)
Other income		1		2
Net loss	(7,975)	(12,377)	(4,972)	(9,640)
Gain on extinguishment of convertible preferred stock	2,889			
Net loss attributable to common stockholders	\$ (5,086)	\$ (12,377)	\$ (4,972)	\$ (9,640)
Net loss per share attributable to common stockholders, basic and diluted(1)	\$ (366.18)	\$ (131.53)	\$ (84.62)	\$ (47.14)
Shares used in computing net loss per share attributable to common stockholders, basic and diluted(1)	14	94	59	205
Pro forma net loss per share attributable to common stockholders, basic and diluted (unaudited)(1)		\$ (3.03)		\$ (1.22)
Shares used in computing pro forma net loss per share attributable to common stockholders, basic and diluted (unaudited)(1)		4,083		7,894

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- (1) See Note 9 to our audited financial statements and Note 6 to our unaudited interim financial statements included elsewhere in this prospectus for an explanation of the calculations of our basic and diluted net loss per common share, pro forma net loss per common share and the weighted-average number of shares used in the computation of the per share amounts.

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	As of December 31, 2012	As of December 31, 2013	As of June 30, 2014 (unaudited)
	(in thousands)		
Balance Sheet Data:			
Cash and cash equivalents	\$ 2,205	\$ 33,820	\$ 27,750
Working capital	1,363	32,825	23,128
Total assets	3,060	34,844	30,655
Convertible preferred stock	10,722	54,282	54,282
Accumulated deficit	(17,765)	(30,142)	(39,782)
Total stockholders' deficit	(8,571)	(20,813)	(30,043)

Recent Developments

In July 2014, we issued and sold 1,902,583 shares of Series D preferred stock and received net proceeds of \$16.0 million of which \$3.0 million was included in cash and cash equivalents and total assets as of June 30, 2014.

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MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

The following discussion and analysis of our financial condition and results of operations should be read in conjunction with our financial statements and related notes included elsewhere in this prospectus. This discussion contains forward-looking statements that involve risks and uncertainties. Our actual results could differ materially from those discussed below. Factors that could cause or contribute to such differences include, but are not limited to, those identified below and those discussed in "Risk Factors" included elsewhere in this prospectus.

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 late 2015 or early 2016. We currently hold all commercial rights to CB-839.

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 near the end of 2015.

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.

We have never been profitable and have incurred net losses in each year since inception. Our net losses were \$8.0 million and \$12.4 million for 2012 and 2013, respectively, and \$9.6 million for the six months ended June 30, 2014. As of June 30, 2014 we had an accumulated deficit of

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\$39.8 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.

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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.

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; and

facilities and other allocated expenses, which include direct and allocated expenses for rent and maintenance of facilities, depreciation and amortization expense and other supplies.

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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 2012 and 2013 and for the six months ended June 30, 2013 and 2014:

	Years Ended December 31,		Six Months Ended June 30,	
	2012	2013	2013	2014
	(in thousands)			
Product candidate:				
CB-839	\$	\$ 5,283	\$	\$ 6,066
Preclinical and research:				
CB-839		5,791	3,849	3,849
Arginase inhibitors				954
Other preclinical and research		767	768	220
		6,558	4,617	4,069
				1,435
Total	\$ 6,558	\$ 9,900	\$ 4,069	\$ 7,501

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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. We continue to evaluate opportunities to acquire or in-license other product candidates and technologies, which may result in higher research and development expenses due to license fee payments.

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 public company, including expenses related to compliance with the rules and regulations of the SEC, and those of any national securities exchange on which our securities are traded, additional insurance expenses, investor relations activities and other administration and professional services.

Results of Operations***Comparison of the Six Months Ended June 30, 2013 and 2014***

	Six Months Ended June 30,		Change	
	2013	2014	\$	%
	(in thousands, except percentages)			
Operating expenses:				
Research and development	\$ 4,069	\$ 7,501	\$ 3,432	84%
General and administrative	903	2,141	1,238	137
Total operating expenses	4,972	9,642	4,670	94
Loss from operations	(4,972)	(9,642)	(4,670)	94
Other income		2	2	*
Net loss	\$ (4,972)	\$ (9,640)	\$ (4,668)	94

* Percentage not meaningful.

Research and Development. Research and development expenses increased \$3.4 million, or 84%, from \$4.1 million for the six months ended June 30, 2013 to \$7.5 million for the six months ended June 30, 2014. The increase was due to an increase of \$1.6 million in clinical trial related expenses in connection with our CB-839 Phase 1 clinical trials which began enrolling patients in February 2014 and an increase of \$0.8 million in costs related to CB-839 development and manufacturing to support our Phase 1 clinical trials, as well as an increase of \$0.8 million in personnel-related costs as a result of higher headcount.

General and Administrative. General and administrative expenses increased \$1.2 million, or 137%, from \$0.9 million for the six months ended June 30, 2013 to \$2.1 million for the six months ended June 30, 2014. The

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increase was due to an increase of \$0.4 million in professional services costs, an increase of \$0.5 million in personnel-related costs as a result of higher headcount, salary increases and stock-based compensation expense and an increase of \$0.3 million in facility costs due to our office expansion in the second half of 2013.

Comparison of the Years Ended December 31, 2012 and 2013

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

Since inception, our operations have been financed primarily by net proceeds of approximately \$79.4 million from the sale of shares of our preferred stock. As of June 30, 2014, we had cash and cash equivalents of \$27.8 million. In July 2014, we issued and sold 1,902,583 shares of Series D preferred stock for net proceeds of \$16.0 million.

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 plan to continue to fund our operations and capital funding needs through equity and/or debt financing. We may also consider new 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.

Table of Contents**Index to Financial Statements*****Cash Flows***

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

	Years Ended December 31,		Six Months Ended June 30,	
	2012	2013	2013	2014
	(in thousands)			
	(unaudited)			
Cash used in operating activities	\$ (6,990)	\$ (11,837)	\$ (4,704)	\$ (9,103)
Cash used in investing activities	(49)	(173)	(90)	(112)
Cash provided by financing activities	5,966	43,625	8,676	3,145

Cash Flows from Operating Activities

Cash used in operating activities for the six months ended June 30, 2014 was \$9.1 million. Our net loss of \$9.6 million was offset in part by non-cash charges of \$0.2 million for depreciation and amortization and \$0.2 million of stock-based compensation. The change in operating assets and liabilities was primarily due to a \$1.1 million increase in prepaid expenses and other current assets related to our prepayment of clinical trial activities, a \$0.6 million increase in other assets related to deferred offering costs, a \$0.3 million increase in deferred rent and a \$1.6 million increase in accounts payable and accrued liabilities related to an increase in our research and development activities.

Cash used in operating activities for the six months ended June 30, 2013 was \$4.7 million. Our net loss of \$5.0 million was offset in part by a non-cash charge of \$0.1 million for depreciation and amortization. The change in operating assets and liabilities was primarily due to a \$0.1 million increase in accounts payable and accrued liabilities related to an increase in our research and development activities.

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

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Cash used in investing activities was \$0.1 million for the six months ended June 30, 2014 and was related to the purchase of property and equipment of \$0.2 million and the reduction in restricted cash of \$0.1 million. Purchases of property and equipment were primarily related to leasehold improvements in connection with our office expansion.

Cash used in investing activities was \$0.1 million for the six months ended June 30, 2013 and was primarily related to the purchase of property and equipment of \$82,000.

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

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Cash Flows from Financing Activities

Cash provided by financing activities for the six months ended June 30, 2014 of \$3.1 million was related to \$3.0 million in proceeds received in advance for the issuance of preferred stock and \$0.1 million from the issuance of common stock upon the exercise of stock options.

Cash provided by financing activities for the six months ended June 30, 2013 was primarily related to net proceeds from the sale and issuance of preferred stock of \$8.7 million.

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

Operating Capital Requirements and Plan of Operations

To date, we have not generated any revenue. We do not know when, or if, we will generate any revenue. We do not expect to generate significant revenue from product sales unless and until we obtain regulatory approval of and commercialize one of our current or future product candidates. We anticipate that we will continue to generate losses for the foreseeable future, and we expect the losses to increase as we continue the development of and seek regulatory approvals for our product candidates, and begin to commercialize any approved products. We are subject to all of the risks incident in the development of new products, and we may encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may harm our business. Upon the closing of this offering, we expect to incur additional costs associated with operating as a public company and we anticipate that we will need substantial additional funding in connection with our continuing operations.

We expect that our existing cash and cash equivalents, excluding the proceeds from this offering, will be sufficient to enable us to conduct planned preclinical studies and clinical trials for our product candidates through at least the end of 2015. 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;

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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.

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The following table summarizes our contractual obligations as of December 31, 2013:

Contractual Obligations:	Payments Due by Period				Total
	Less Than 1 Year	1 to 3 Years	3 to 5 Years (in thousands)	More Than 5 Years	
Operating lease obligations(1)	\$ 716	\$ 1,920	\$ 880	\$	\$ 3,516
Total contractual obligations(2)	\$ 716	\$ 1,920	\$ 880	\$	\$ 3,516

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

Off-Balance Sheet Arrangements

During 2012, 2013 and the six months ended June 30, 2014, we did not have any off-balance sheet arrangements.

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 \$33.8 million and \$27.7 million as of December 31, 2013 and June 30, 2014, respectively, 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, 2013 and June 30, 2014.

Critical Accounting Policies and Estimates

Our management's discussion and analysis of our financial condition and results of operations is based on our financial statements, which 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 revenue generated and expenses incurred during the

reporting periods. Our estimates are based on our historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these 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

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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 are a privately-held company and do not have any 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.

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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.

For 2012 and 2013, stock-based compensation expense was \$31,000 and \$70,000, respectively. For the six months ended June 30, 2013 and 2014, stock-based compensation expense was \$22,000 and \$211,000, respectively. As of June 30, 2014, we had \$1.8 million of total unrecognized stock-based compensation costs, net of estimated forfeitures, which we expect to recognize over a weighted-average period of 3.5 years.

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Historically, for all periods prior to this initial public offering, 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 provided 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 this offering, our board of directors will determine 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.

Based on an assumed initial public offering price of \$14.00 per share, the midpoint of the price range set forth on the cover page of this prospectus, the intrinsic value of stock options outstanding at June 30, 2014 was \$11.7 million, of which \$1.0 million and \$10.7 million related to stock options that were vested and unvested, respectively, at that date.

Income Taxes

As of December 31, 2013, we had approximately \$29.2 million and \$28.7 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, 2013, we also had research and development tax credit carryforwards of approximately \$0.6 million and \$0.6 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 annual limitation may result in the expiration of net operating losses and credits before utilization. An analysis to determine the limitation of the net operating loss carryforwards has not been performed.

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 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 requirements 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 prospectus.

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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. We anticipate completing the ongoing single agent dose escalation stage of these trials by the end of 2014. We then plan to enroll 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 in late 2015 or early 2016 one or more Phase 2 clinical trials 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.

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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

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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. We are currently optimizing arginase inhibitors with the aim of submitting an Investigational New Drug, or IND, application to the FDA near the end of 2015.

The members of our executive management team have held senior positions at leading biotechnology and pharmaceutical companies. They possess decades of combined experience in drug discovery and clinical development, and several have been involved in bringing oncology drugs to market.

Susan M. Molineaux, Ph.D. is our founder, President and Chief Executive Officer. Prior to joining us, Dr. Molineaux was previously the founder and Chief Executive Officer of Proteolix, Inc., a biopharmaceutical company that was responsible for the discovery and development of carfilzomib (marketed as Kyprolis), a proteasome inhibitor that was granted accelerated approval in 2012 for the treatment of refractory multiple myeloma. Proteolix was sold to Onyx Pharmaceuticals, Inc. in 2009. Prior to founding Proteolix, Dr. Molineaux held various senior scientific and management positions at Rigel Pharmaceuticals, Inc., Praecis Pharmaceuticals Incorporated and Merck & Co.

William D. Waddill is our Senior Vice President and Chief Financial Officer. Prior to joining us in April 2014, Mr. Waddill was Senior Vice President and Chief Financial Officer at OncoMed Pharmaceuticals, Inc., where he was the finance lead for the successful completion of a \$94 million initial public offering in July 2013, a \$126 million private equity financing in December 2008 and three major collaborations with pharmaceutical companies. Prior to OncoMed, Mr. Waddill was Senior Vice President and Chief Financial Officer at Ilypsa, Inc., where he was the finance lead for the company's \$420 million acquisition by Amgen Inc. in 2007.

Eric B. Sjogren, Ph.D. is our Senior Vice President of Drug Discovery. Prior to joining us, Dr. Sjogren was Vice President and Head of Medicinal Chemistry at Roche Palo Alto, LLC, where he led a large chemistry discovery team. Dr. Sjogren has over 25 years of experience in small molecule drug discovery in the pharmaceutical industry.

Mark K. Bennett, Ph.D. is our Senior Vice President of Research. Prior to joining us, Dr. Bennett was Vice President of Research at Proteolix, where he led the research efforts in the discovery of carfilzomib, oprozomib, and PR-957. Dr. Bennett previously was Director of Cell Biology at Rigel Pharmaceuticals, Inc. and an Assistant Professor of Molecular and Cell Biology at the University of California, Berkeley.

Christopher J. Molineaux, Ph.D. is our Senior Vice President of Development. Dr. Molineaux leads our drug development efforts and is currently our project leader for the CB-839 program. Prior to joining us, Dr. Molineaux was Vice President of Development at Proteolix, where he led the team that developed carfilzomib through the completion of Phase 2 clinical trials that led to the accelerated approval in the United States of the drug for the treatment of refractory multiple myeloma. Prior to joining Proteolix, Dr. Molineaux led the oral anemia project team at FibroGen, Inc. and prior to that, led the team at Praecis that discovered and developed abarelix (marketed as Plenaxis), which was approved for the treatment of prostate cancer.

Our Strategy

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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

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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 and multiple myeloma.

CB-839 in combination with standard of care drugs, initially with a cytotoxic agent for triple-negative breast cancer and an immunomodulatory agent for multiple myeloma.

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 dose escalation trials of CB-839 in solid and hematological tumors. We will expand 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 late 2015 or early 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 near the end of 2015.

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. To date, we have utilized this expertise to internally discover CB-839, our first-in-class oncology product candidate that is now in clinical testing. 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.

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Our Research and Development Programs

The following table summarizes our ongoing and planned clinical trials from 2014 to 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.

Note:
Phase 1
trials
include a
dose
escalation
stage
followed
by dose
expansion
in select
tumor
types.

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

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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.

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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 a-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.

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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.

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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.

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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 each of: the epidermal growth factor receptor, or EGFR, inhibitor erlotinib (marketed as Tarceva) in NSCLC cells; the multikinase inhibitors sunitinib (marketed as Sutent), sorafenib (marketed as Nexavar), 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; the mutant B-Raf inhibitor dabrafenib (marketed as Tafinlar) in melanoma cells; the MEK inhibitors trametinib (marketed as Mekinist) and selumetinib (in development by AstraZeneca); and the AKT inhibitor MK-2206 (in development by Merck) in multiple cancer cell types. We believe these synergistic activities reflect the fact that growth factor inhibitors and CB-839 disrupt the utilization of glucose and glutamine, respectively, which are both important substances on which metabolically re-wired tumor cells rely to produce energy and building blocks.

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.

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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. In all three trials, patients will be treated until there is evidence of progression of the disease or unacceptable toxicity, or the patient withdraws from the trial. 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 two Phase 1b combination cohorts, one in which CB-839 will be combined with paclitaxel in patients with TNBC and a second 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 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.

Phase 1 Clinical Trials with CB-839

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

We anticipate enrolling approximately 130 patients among the three trials listed above. 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 Trial Status

We are currently enrolling patients in the dose escalation stage in all three trials. As of July 25, 2014, we had enrolled a total of 24 patients across the three ongoing trials. All patients in these trials were relapsed and refractory to approved therapies. On average, these patients had

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received five prior lines of drug treatment, with some patients having received up to 15 prior drug treatments.

We have conducted a periodic analysis of the data available to us from these trials as of July 25, 2014. As of that date, we had enrolled patients at a dose up to 250 mg TID in the solid tumor trial (001) and in one of our blood tumor trials (002) and up to 600 mg TID in our other blood tumor trial (003). Of the patients originally enrolled as of July 25, 2014 in the 001 trial, five are colorectal cancer patients, five are TNBC patients, two are RCC patients and one each are cholangiocarcinoma, sarcoma, and mesothelioma patients. In the 002 trial, we had enrolled three multiple myeloma patients. In the 003 trial, we had enrolled five acute myeloid leukemia patients and one acute lymphocytic leukemia patient. Of these 24 patients, the best response as of July 25, 2014 was stable disease, observed in one mesothelioma patient, two multiple myeloma patients, and one TNBC patient.

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The mesothelioma patients and both multiple myeloma patients' disease progressed after more than five cycles of dosing with CB-839. The TNBC patient had actively progressing disease at the time she enrolled in the trial and is continuing treatment with CB-839 with no ongoing AEs at 250 mg TID after having a 13% decrease in tumor size at the end of three cycles of dosing with CB-839.

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 six to eight hours, which may allow for twice-daily administration. 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. Based on the data available as of July 25, 2014, we expect a dose of between 400 to 800 mg TID will achieve this goal. In the dose expansion stage of the Phase 1 solid tumor trial, we will measure the glutaminase inhibition in tumor samples from a subset of patients to confirm that we have selected an appropriate dose.

We plan to evaluate several biomarkers during our Phase 1 clinical trials that may allow us to better identify patients likely to respond to CB-839 in subsequent clinical trials. Based upon the observation that the activity of glutaminase is correlated with response to CB-839 in TNBC and certain other tumor cell lines, we plan to use an immunohistochemical method for evaluating the expression of glutaminase in archived or freshly biopsied tumor samples from all patients in our Phase 1 trials. We will also evaluate the expression of approximately 40 genes related to glutamine uptake and metabolism by measuring mRNA. In addition, we intend to explore the potential use of positron emission tomography, or PET, metabolic imaging to identify responsive patients.

CB-839 has been generally well tolerated. As of July 25, 2014, 21 Grade 1 AEs, two Grade 2 AEs and two Grade 3 AEs deemed possibly or probably related to CB-839 by the investigators have been reported. Toxicity grades are derived from the National Cancer Institute's Common Toxicity Criteria for Adverse Events. Grade 3 events are considered severe or medically significant but not immediately life-threatening, Grade 2 events are considered moderate, and Grade 1 events are considered mild. The most common Grade 1 AEs were nausea, vomiting and fatigue, which were observed across all three trials. Grade 2 anemia was observed in a patient with multiple myeloma who had Grade 1 anemia at baseline, and Grade 2 worsening fatigue occurred also in a multiple myeloma patient. Transient Grade 3 reduced white blood cell count occurred in an RCC patient with Grade 2 reduced white blood cell count at baseline. A Grade 3 increase in creatinine was seen in another colorectal cancer patient receiving 250 mg TID who had preexisting diabetic nephropathy and severe proteinuria. This was deemed a dose limiting toxicity, or DLT, and was considered a serious adverse event because the patient was hospitalized for observation and hydration. Creatinine levels returned to normal when the patient was taken off CB-839 and hydrated. There have been no further DLTs and the trial proceeded to the next higher dose level (400 mg TID). We have not observed any other drug-related AEs due to a creatinine increase in patients at any doses, including doses at or above 250 mg TID, across all three trials.

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 2014. It is

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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 24,050 new cases of myeloma diagnosed in the United States in 2014.

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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 believe we have identified a biomarker, pyruvate carboxylase, that correlates inversely 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 CB-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 plan to include additional myeloma patients treated with CB-839 as a single agent and a Phase 1b cohort of myeloma patients who will receive CB-839 in combination with pomalidomide and dexamethasone.

Non-Small Cell Lung Cancer (NSCLC)

According to the American Cancer Society, an estimated 224,000 new cases of lung cancer will be diagnosed in the United States in 2014. 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 also plan to evaluate CB-839 in combination with an EGFR inhibitor in NSCLC patients bearing EGFR mutations in future clinical trials.

Renal Cell Carcinoma (RCC)

According to the National Cancer Institute, renal cell carcinoma is diagnosed in approximately 64,000 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.

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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 plan to evaluate 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 combination with one or more currently marketed therapies for RCC in future clinical trials.

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. Drs. Mark Dunphy and James Hsieh of the Memorial Sloan-Kettering Cancer Center have also seen an uptake of fluoro-glutamine, or F-Gln, in tumors using PET imaging in a patient with metastatic RCC with a SDH mutation enrolled in their ongoing Phase 1 clinical trial evaluating F-Gln in cancer patients. This observation was made in a patient who had not received CB-839. 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, and a rare adrenal or extra-adrenal cancer, known as pheochromocytoma, and rare subset clear cell RCC. 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, acute myeloid leukemia, high-risk myelodysplasia/myeloproliferative disorders, a group of blood disorders, have IDH1 or IDH2 driver mutations.

We plan to evaluate CB-839 in patients with FH, SDH or IDH mutations in our ongoing Phase 1 clinical trials.

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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.

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 near the end of 2015.

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 June 30, 2014, we have one issued U.S. patent and approximately 23 pending U.S. and foreign patent applications in the following foreign jurisdictions: Argentina, Australia, Brazil, Canada, the Eurasian Patent Organization, Europe, India, Israel, Japan, Mexico, New Zealand, Singapore, South Africa, South Korea and Taiwan.

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As of June 30, 2014, the intellectual property portfolio for our tumor metabolism program, which includes CB-839, consists of one issued U.S. patent directed to composition of matter for CB-839, which expires in 2032. We also have six pending U.S. patent applications and 17 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.

With respect to our tumor immunology program, which includes the preclinical development of our arginase inhibitor, we consider trade secrets and know-how to be our primary intellectual property. Trade secrets and know-how can be difficult to protect. Despite our efforts to protect our trade secrets, our competitors may discover our trade secrets, either through breach of our confidentiality agreements, independent development, or publication of information including our trade secrets.

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

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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 inhibitor program 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 \$6.6 million and \$9.9 million in 2012 and 2013, respectively, and \$7.5 million in the six months ended June 30, 2014.

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 Pharmaceutical, Inc., AstraZeneca plc, Cornerstone Pharmaceuticals, Inc., Eli Lilly and Company, Forma Therapeutics Holdings, LLC, GlaxoSmithKline plc, Novartis International AG, Pfizer, Inc., 3-V Biosciences, Inc., and Roche Holdings, and its subsidiary Genentech Inc. Our principal competitors in the field of tumor immunology include AstraZeneca plc, Ono Pharmaceuticals, Co., Ltd., NewLink Genetics Corporation, Incyte Corporation,

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Merck & Co., Bristol-Myers Squibb Company, CureTech Ltd, and EMD Serono, 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.

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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

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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

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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.

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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.

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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.

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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.

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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

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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

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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

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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

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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;

fining, 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

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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 June 30, 2014, we had 36 full-time employees, including 15 employees with Ph.D. or M.D. degrees. Of these full-time employees, 27 employees are engaged in research and development activities. None of our employees are 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 rented to Cytomix, Inc. under a two-year sublease. 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.

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The following table sets forth certain information with respect to our executive officers and directors as of June 30, 2014:

Name	Age	Position
<i>Executive Officers</i>		
Susan M. Molineaux, Ph.D.	60	President, Chief Executive Officer and Director
William D. Waddill	57	Senior Vice President, Chief Financial Officer, Treasurer and Secretary
Mark K. Bennett, Ph.D.	55	Senior Vice President, Research
Christopher J. Molineaux, Ph.D.	61	Senior Vice President, Development
Eric B. Sjogren, Ph.D.	57	Senior Vice President, Drug Discovery
Curtis C. Hecht	43	Vice President, Business and Corporate Development
<i>Non-Employee Directors</i>		
Ralph E. Christoffersen, Ph.D.(1)	76	Director
Jonathan Drachman, M.D.(1)(2)	52	Director
Jean M. George(2)(3)	56	Director
Deepa R. Pakianathan, Ph.D.(1)(3)	49	Director

- (1) Member of the audit committee.
- (2) Member of the compensation committee.
- (3) Member of the nominating and corporate governance committee.

Executive Officers

Susan M. Molineaux, Ph.D. Dr. Molineaux has served as our President, Chief Executive Officer and as a member of our board of directors since she co-founded Calithera in March 2010. Dr. Molineaux co-founded Proteolix, Inc., a biopharmaceutical company, where she served as Chief Scientific Officer from 2003 to 2005, Chief Executive Officer from January 2006 to January 2009 and again as Chief Scientific Officer from February 2009 until Proteolix's acquisition by Onyx Pharmaceuticals, Inc. in November 2009. From 2000 to 2003, Dr. Molineaux served as Vice President of Biology at Rigel Pharmaceuticals, Inc., a drug development company. From 1999 to 2000, she served as Vice President of Biology at Praelux, Inc., a biopharmaceutical company, and from 1994 through 1999, she served as Vice President of Drug Development at Praecis Pharmaceuticals, Inc., a biopharmaceutical company. From 1989 until 1994, she was a scientist in the Immunology group at Merck & Co. Dr. Molineaux currently serves as a member of the board of directors of Geron Corporation, a biopharmaceutical company. She also serves as the Chairman of Bay Bio, Northern California's Life Science Association, and as a member of the board of directors of We Teach Science, a San Francisco Bay Area mentoring program for students in math and science. Dr. Molineaux holds a B.S. in Biology from Smith College and a Ph.D. in Molecular Biology from Johns Hopkins University, and she completed a postdoctoral fellowship at Columbia University.

We believe Dr. Molineaux's experience on our board of directors and as our Chief Executive Officer, as well as her experience in our industry qualifies her to serve on our board of directors.

William D. Waddill. Mr. Waddill has served as our Senior Vice President, Chief Financial Officer, Treasurer and Secretary since April 2014. From October 2007 to March 2014, Mr. Waddill served as Senior Vice President and Chief Financial Officer at OncoMed Pharmaceuticals, Inc., a biopharmaceutical company. From October 2006 to September 2007, Mr. Waddill served as the Senior Vice President, Chief Financial Officer of Ilypsa, Inc., a biotechnology company that was acquired in 2007 by Amgen, Inc. From February 2000 to September 2006, Mr. Waddill served as a Principal at Square One Finance, a financial consulting business. From December 1996 to February 2000, Mr. Waddill served as Senior Director of Finance and Administration at Exelixis, Inc., a

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biotechnology company. Mr. Waddill received a B.S. in Accounting from the University of Illinois, Chicago, and a certification as a public accountant, which is currently inactive, after working at PricewaterhouseCoopers LLP and Deloitte LLP.

Mark K. Bennett, Ph.D. Dr. Bennett has served as our Senior Vice President of Research since June 2010. Dr. Bennett served as Vice President of Research at Proteolix, Inc. from January 2006 to December 2009 and as Director of Biological Research from 2003 to 2005. From 1999 to 2003, Dr. Bennett was Director of Cell Biology at Rigel Pharmaceuticals, Inc. From 1993 to 1999, Dr. Bennett was an Assistant Professor in the Department of Molecular and Cell Biology at the University of California, Berkeley. Dr. Bennett received a B.S. in Biochemistry and Biophysics from Oregon State University, a Ph.D. in Neuroscience from the California Institute of Technology, and completed postdoctoral fellowships at the European Molecular Biology Laboratory and Stanford University.

Christopher J. Molineaux, Ph.D. Dr. Molineaux has served as our Senior Vice President of Development since April 2013. From March 2010 to March 2013, Dr. Molineaux served as the President of INDStrat LLC, a consulting firm. From July 2004 to November 2009, Dr. Molineaux served as Vice President of Development at Proteolix, Inc. From 2000 to 2004, Dr. Molineaux served as Senior Director of Drug Development at FibroGen, Inc., a biotechnology company. From 1999 to 2000, he served as Research Manager of Toxicology at Johnson & Johnson Pharmaceutical Research and Development. From 1994 to 1999, Dr. Molineaux served as Senior Director of Pharmacology at Praecis. From 1991 to 1994, he served in staff scientist positions at Enzon Pharmaceuticals, Inc. and Merck & Co. From 1985 to 1991, Dr. Molineaux served as an Assistant Professor of Pharmacology of Mount Sinai School of Medicine in New York City. He received a B.S. in Zoology from University of Maryland, College Park, a Ph.D. in Immunology and Infectious Diseases from Johns Hopkins University and completed his postdoctoral fellowship at the Uniformed Services University of the Health Sciences.

Eric B. Sjogren, Ph.D. Dr. Sjogren has served as our Senior Vice President of Drug Discovery since June 2010. From 2003 to 2009, Dr. Sjogren was Vice President and Head of Medicinal Chemistry at Roche Palo Alto, LLC, where he directed a small molecule drug discovery team in the areas of inflammation, virology and central nervous system disorders. Dr. Sjogren received a B.A. in Chemistry from the University of California, San Diego and a Ph.D. in Chemistry from Harvard University.

Curtis C. Hecht. Mr. Hecht has served as our Vice President of Business and Corporate Development since April 2014. From September 2013 to April 2014, Mr. Hecht served as Vice President of Business Development at inVentiv Health, a global healthcare commercialization and consulting services company. Since March 2011, he has also served as a Partner at DNA Ink, a life sciences business development and licensing firm. From June 2002 to February 2011, Mr. Hecht served in a number of roles at Hoffman La-Roche Inc., including as Global Alliance Director from 2008 to 2011 and Director of Global Business Development from 2006 to 2008. Mr. Hecht received a B.S. in Chemistry from California State University, Sacramento and an M.B.A. from Carnegie Mellon University.

Non-Employee Directors

Ralph E. Christoffersen, Ph.D. Dr. Christoffersen has served as a member of our board of directors since September 2010. Since July 2001, Dr. Christoffersen has been a Partner of the life sciences group at Morgenthaler Ventures, a private equity firm. From July 2001 to May 2002, he was Chairman of the board of directors of Ribozyme Pharmaceuticals, Inc., now Sirna Therapeutics, a biotechnology company. From June 1992 to July 2001, he was Chief Executive Officer and President of Ribozyme Pharmaceuticals. From August 1989 until June 1992, he was the Senior Vice President of Research at SmithKline Beecham Corporation. From September 1983 to August 1989, he was Vice President of Discovery Research at The Upjohn Company. From 1981 to 1983, he served as President and a Professor at Colorado State University. Dr. Christoffersen also serves as a director of a number of private biotechnology companies. He received a B.S. in Chemistry and Mathematics from Cornell College, a Ph.D. in Physical Chemistry from Indiana University and did his post-doctorate work at Nottingham University, United Kingdom and

Iowa State University.

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We believe Dr. Christoffersen's experience as an investor in, and management of, biopharmaceutical and life sciences companies qualifies him to serve on our board of directors.

Jonathan Drachman, M.D. Dr. Drachman has served as a member of our board of directors since December 2013. Since November 2004, Dr. Drachman has served in a number of roles at Seattle Genetics, Inc., most recently Chief Medical Officer and Executive Vice President of Research and Development since October 2013 and its Senior Vice President, Research and Translational Medicine from May 2010 to October 2013. From 1998 to 2004, Dr. Drachman served as a faculty member in the Hematology Division, Department of Medicine at the University of Washington in Seattle, and as a Senior Investigator in the Division of Research and Education at the Puget Sound Blood Center. Dr. Drachman received a B.A. in Biochemistry from Harvard University and an M.D. from Harvard Medical School. He completed his residency in Internal Medicine and fellowship in Medical Oncology at the University of Washington.

We believe Dr. Drachman's experience in the biotechnology industry qualifies him to serve on our board of directors.

Jean M. George. Ms. George has served as a member of our board of directors since September 2012. Since February 2002, she has been a General Partner at Advanced Technology Ventures, a venture capital fund. From September 1998 to January 2002, Ms. George served as director of BancBoston Ventures, a venture capital fund. Ms. George currently serves as a member of the board of directors of Acceleron Pharma, Inc. and Zeltiq Aesthetics, Inc. Ms. George holds a B.S. in Biology from the University of Maine and an M.B.A. from Simmons College Graduate School of Management.

We believe Ms. George's extensive investment and financial experience and her experience with biotechnology companies, qualifies her to serve on our board of directors.

Deepa R. Pakianathan, Ph.D. Dr. Pakianathan has served as a member of our board of directors since September 2012. Since 2001, Dr. Pakianathan has served as a Managing Member at Delphi Ventures, a venture capital firm. From 1998 to 2001, Dr. Pakianathan served as a Vice President in the healthcare group at JP Morgan Chase & Company. From 1993 to 1997, Dr. Pakianathan served as a postdoctoral scientist in the Immunology Department at Genentech Corporation. Dr. Pakianathan currently serves on the board of directors of Alder Biopharmaceuticals, Inc., Alexza Pharmaceuticals, Inc., Oncomed Pharmaceuticals, Inc. and Karyopharm Therapeutics, Inc. Dr. Pakianathan holds an M.S. and a Ph.D. from Wake Forest University, a B.Sc. from the University of Bombay, India and an M.Sc. from The Cancer Research Institute at the University of Bombay, India.

We believe Dr. Pakianathan's experience as a venture capital investor in and as a director for multiple biotechnology companies, as well as her experience as a biotechnology investment banker, qualify her to serve on our board of directors.

Family Relationships

Christopher J. Molineaux, Ph.D., our Senior Vice President of Development, is the spouse of Susan M. Molineaux Ph.D., a member of our board of directors and our President and Chief Executive Officer. There are no other family relationships among the directors and executive officers.

Board Composition

Certain members of our board of directors were elected pursuant to the provisions of a voting agreement. Under the terms of this voting agreement, the stockholders who are party to the voting agreement have agreed to vote their respective shares so as to elect as (1) one director designated by Morgenthaler Venture Partners IX, L.P., currently Dr. Christoffersen; (2) one director designated by Advanced Technology Ventures VIII, L.P., currently

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Ms. George; (3) one director designated by Delphi Ventures VIII, L.P., currently Dr. Pakianathan; and (4) the person serving as our chief executive officer, currently Dr. Susan Molineaux. The holders of a majority of our preferred stock and common stock, voting together as a single class, further designated Dr. Drachman for election to our board of directors. The voting agreement will terminate upon the closing of this offering and none of our stockholders will have any special rights regarding the election or designation of members of our board of directors.

Our board of directors will consist of five members upon the closing of this offering. In accordance with our certificate of incorporation to be filed in connection with this offering, immediately after this offering, our board of directors will be divided into three classes. At each annual general meeting of stockholders, the successors to directors whose terms then expire will be elected to serve from the time of election and qualification until the third annual meeting following election. Our directors will be divided among the three classes as follows:

The Class I directors will be Dr. Christoffersen and Ms. George, and their terms will expire at the annual meeting of stockholders to be held in 2015;

The Class II directors will be Dr. Drachman and Dr. Pakianathan, and their terms will expire at the annual meeting of stockholders to be held in 2016; and

The Class III director will be Dr. Susan Molineaux, and her term will expire at the annual meeting of stockholders to be held in 2017.

We expect that any additional directorships resulting from an increase in the number of directors will be distributed among the three classes so that, as nearly as possible, each class will consist of one-third of the directors. The division of our board of directors into three classes with staggered three-year terms may delay or prevent a change of our management or a change in control.

Director Independence

Under the listing requirements and rules of the NASDAQ Global Market, independent directors must comprise a majority of our board of directors within one year after the closing of this offering.

Our board of directors has undertaken a review of its composition, the composition of its committees and the independence of each director. Based upon information requested from and provided by each director concerning his or her background, employment and affiliations, including family relationships, our board of directors has determined that Drs. Christoffersen, Drachman and Pakianathan, and Ms. George do not have any relationships that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director and that each of these directors is independent as that term is defined under the applicable rules and regulations of the SEC and the listing requirements and rules of the NASDAQ Global Market. In making this determination, our board of directors considered the current and prior relationships that each non-employee director has with our company and all other facts and circumstances our board of directors deemed relevant in determining their independence, including the beneficial ownership of our capital stock by each non-employee director.

Board Committees

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Our board of directors has established an audit committee, a compensation committee and a nominating and corporate governance committee. Our board of directors may establish other committees to facilitate the management of our business. Members serve on these committees until their resignation or until otherwise determined by our board of directors. The composition and functions of each committee are described below.

All of our committees will comply with all applicable requirements of the Sarbanes-Oxley Act of 2002, the NASDAQ Global Market and SEC rules and regulations, except that with respect to the audit committee independence requirements, our audit committee will rely upon the phase-in rules of the NASDAQ Global Market and the SEC, as further described below.

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Audit Committee

Our audit committee consists of Dr. Christoffersen, Dr. Drachman and Dr. Pakianathan. The chair of our audit committee is Dr. Pakianathan. Our board of directors has determined that Dr. Pakianathan is an audit committee financial expert within the meaning of SEC regulations and that Dr. Drachman is independent as independence is defined in Rule 10A-3 of the Exchange Act and under NASDAQ listing standards. Drs. Christoffersen and Pakianathan are not considered independent directors in connection with their service on the audit committee. We are permitted to phase-in our compliance with the independent audit committee requirements set forth in NASDAQ rules and relevant SEC rules as follows: (1) one independent member at the time of listing, (2) a majority of independent members within 90 days of listing and (3) all independent members within one year of listing. Our board of directors has also determined that each member of our audit committee can read and understand fundamental financial statements in accordance with applicable requirements. In arriving at these determinations, the board of directors has examined each audit committee member's scope of experience and the nature of their employment in the corporate finance sector.

The primary purpose of our audit committee is to discharge the responsibilities of our board of directors with respect to our accounting, financial and other reporting and internal control practices and to oversee our independent registered accounting firm. Specific responsibilities of our audit committee include:

selecting a qualified firm to serve as the independent registered public accounting firm to audit our financial statements;

helping to ensure the independence and performance of the independent registered public accounting firm;

discussing the scope and results of the audit with the independent registered public accounting firm, and reviewing, with management and the independent accountants, our interim and year-end operating results;

developing procedures for employees to submit concerns anonymously about questionable accounting or audit matters;

reviewing our policies on risk assessment and risk management;

reviewing related party transactions;

obtaining and reviewing a report by the independent registered public accounting firm at least annually, that describes our internal quality control procedures, any material issues with such procedures, and any steps taken to deal with such issues when required by applicable law; and

approving (or, as permitted, pre-approving) all audit and all permissible non-audit services, other than de minimis non-audit services, to be performed by the independent registered public accounting firm.

Compensation Committee

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Our compensation committee consists of Dr. Drachman and Ms. George. The chair of our compensation committee is Ms. George. Our board of directors has determined each member of the compensation committee is independent under the NASDAQ listing standards, are non-employee directors as defined in Rule 16b-3 promulgated under the Exchange Act and are outside directors as that term is defined in Section 162(m) of the Internal Revenue Code of 1986, as amended, or Section 162(m).

The primary purpose of our compensation committee is to discharge the responsibilities of our board of directors to oversee our compensation policies, plans and programs and to review and determine the compensation to be paid to our executive officers, directors and other senior management, as appropriate. Specific responsibilities of our compensation committee include:

reviewing and approving, or recommending that our board of directors approve, the compensation of our executive officers;

reviewing and recommending to our board of directors the compensation of our directors;

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reviewing and approving, or recommending that our board of directors approve, the terms of compensatory arrangements with our executive officers;

administering our stock and equity incentive plans;

selecting independent compensation consultants and assessing whether there are any conflicts of interest with any of the committees compensation advisers;

reviewing and approving, or recommending that our board of directors approve, incentive compensation and equity plans, severance agreements, change-of-control protections and any other compensatory arrangements for our executive officers and other senior management, as appropriate; and

reviewing and establishing general policies relating to compensation and benefits of our employees and reviewing our overall compensation philosophy.

Nominating and Corporate Governance Committee

Our nominating and corporate governance committee consists of Ms. George and Dr. Pakianathan. The chair of our nominating and corporate governance committee is Ms. George. Each member of the nominating and corporate governance committee is independent within the meaning of applicable listing standards, is a non-employee director and is free from any relationship that would interfere with the exercise of his or her independent judgment, as determined by the board of directors in accordance with the applicable NASDAQ listing standards.

Specific responsibilities of our nominating and corporate governance committee include:

identifying, evaluating and selecting, or recommending that our board of directors approve, nominees for election to our board of directors;

evaluating the performance of our board of directors and of individual directors;

considering and making recommendations to our board of directors regarding the composition of the committees of the board of directors;

reviewing developments in corporate governance practices;

evaluating the adequacy of our corporate governance practices and reporting;

reviewing management succession plans;

developing and making recommendations to our board of directors regarding corporate governance guidelines and matters; and

overseeing an annual evaluation of the board of directors performance.

Code of Business Conduct and Ethics

We have adopted a code of business conduct and ethics that applies to all of our employees, officers, including our principal executive officer, principal financial officer and principal accounting officer or controller, or persons performing similar functions and agents and representatives, including directors and consultants. The full text of our code of business conduct and ethics will be posted on our website at www.calithera.com. We intend to disclose future amendments to certain provisions of our code of business conduct and ethics, or waivers of such provisions applicable to any principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions, and our directors, on our website identified above.

Compensation Committee Interlocks and Insider Participation

None of the members of the compensation committee is currently, or has been at any time, one of our officers or employees. None of our executive officers currently serves, or has served during the last year, as a member of the board of directors or compensation committee of any entity that has one or more executive officers serving as a member of our board of directors or compensation committee.

Table of Contents**Index to Financial Statements****Non-Employee Director Compensation**

The following table sets forth information concerning the compensation paid to our non-employee directors during 2013.

Name	Fees Paid in Cash	Option Awards \$(1)	Total (\$)
Ralph E. Christoffersen, Ph.D.	\$	\$	\$
Jonathan Drachman, M.D.	10,000	485(2)	10,485
Jean M. George			
Deepa R. Pakianathan, Ph.D.			

- (1) The amount shown in this column does not reflect dollar amount actually received by this director. Instead, this amount reflects the aggregate grant date fair value of this stock option granted in 2013, computed in accordance with the provisions of FASB ASC Topic 718. Assumptions used in the calculation of this amount are included in Note 9 to our financial statements included in this prospectus. As required by SEC rules, the amount shown excludes the impact of estimated forfeitures related to service-based vesting conditions. Our director will only realize compensation to the extent the trading price of our common stock is greater than the exercise price of this stock option.
- (2) Represents an option to purchase 22,501 shares of our common stock. The option vests monthly over four years. In the event there is an acquisition or sale of all, or substantially all, of our assets, all of the unvested shares subject to the option will immediately vest and become exercisable. In September 2014, we granted Dr. Drachman an option to purchase 5,854 shares of our common stock with an exercise price of \$7.20 per share. This option vests monthly over four years and, in the event of an acquisition or sale of all, or substantially all, of our assets, all of the unvested shares subject to the option will immediately vest and become exercisable.

Non-Employee Director Compensation Policy

We have adopted a non-employee director compensation policy, pursuant to which our non-employee directors will be eligible to receive compensation for service on our board of directors and committees of our board of directors.

Equity Compensation***Initial Grant***

Each new non-employee director who joins our board of directors after our initial public offering will be granted a stock option to purchase 22,000 shares of common stock under our 2014 Equity Incentive Plan, or the 2014 Plan, vesting monthly over three years from the grant date, subject to continued service as a director through each applicable vesting date.

Annual Grant

On the date of each annual meeting of our stockholders, each continuing non-employee director will be granted an annual stock option to purchase 11,000 shares of common stock under our 2014 Plan, vesting monthly over one year from the grant date, subject to continued service as a director through each applicable vesting date.

Vesting Acceleration

In the event of a change of control or a corporate transaction (each as defined in our 2014 Plan), any unvested portion of an equity award granted under the policy will fully vest and become exercisable immediately prior to the effective date of such change of control or corporate transaction, subject to the non-employee director's continuous service with us on the effective date of the change of control or corporate transaction.

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The exercise price per share of each stock option granted under the non-employee director compensation policy will be the closing price of our common stock as reported by the NASDAQ Global Market on the date of grant. Each stock option will have a term of ten years from the date of grant, subject to earlier termination in connection with a termination of the non-employee director's continuous service with us.

Cash Compensation

Commencing with our first annual meeting of stockholders in 2015, each non-employee director will receive an annual cash retainer of \$40,000 for serving on our board of directors. The chairperson of our board of directors will receive an additional annual cash retainer of \$25,000.

The chairperson and members of the three standing committees of our board of directors will be entitled to the following additional annual cash retainers:

Board Committee	Chairperson Fee	Member Fee
Audit Committee	\$ 15,000	\$ 7,500
Compensation Committee	10,000	5,000
Nominating and Corporate Governance Committee	7,000	3,500

All annual cash compensation amounts will be payable in equal quarterly installments in arrears, on the last day of each fiscal quarter for which the service occurred, pro-rated based on the days served in the applicable fiscal quarter.

A non-employee director may elect to receive a stock option grant in lieu of his or her annual cash compensation. Such election would apply to all such cash compensation. A non-employee director must make this election prior to the date of the annual meeting of stockholders and such election will apply until the next annual meeting of our stockholders.

The number of shares of common stock to be issuable upon exercise of stock options granted in lieu of annual cash compensation will be determined by dividing (i) the amount of annual compensation that would otherwise be paid during the upcoming year of service, by (ii) the Black-Scholes value of one share of our common stock on the applicable grant date, or such other method that may be set forth in the non-employee director compensation policy on that date. Such stock options will be nonstatutory stock options and will be granted on the date of the annual meeting of our stockholders. The stock options will have an exercise price per share equal to the closing price of our common stock as reported by the NASDAQ Global Market on the date of grant and will vest monthly over one year from the grant date, subject to continued service as a director through each applicable vesting date. The stock options will have a term of ten years from the date of grant.

Table of Contents**Index to Financial Statements****EXECUTIVE COMPENSATION**

Our named executive officers, consisting of our principal executive officer and the next two most highly compensated executive officers as of December 31, 2013, were:

Susan M. Molineaux, Ph.D., President and Chief Executive Officer;

Mark K. Bennett, Ph.D., Senior Vice President, Research; and

Eric B. Sjogren, Ph.D., Senior Vice President, Drug Discovery.

2013 Summary Compensation Table

The following table sets forth all of the compensation awarded to, earned by or paid to our named executive officers during 2013.

Name and Principal Position	Year	Salary (\$)	Bonus (\$)(1)	Option Awards (\$)(2)	Total (\$)
Susan M. Molineaux, Ph.D. <i>President and Chief Executive Officer</i>	2013	\$ 350,000	\$ 134,750	\$ 17,600	\$ 502,350
Mark K. Bennett, Ph.D. <i>Senior Vice President, Research</i>	2013	275,000	89,100	8,422	372,522
Eric B. Sjogren, Ph.D. <i>Senior Vice President, Drug Discovery</i>	2013	275,000	89,100	8,422	372,522

- (1) Represent amounts earned in 2013, which were paid in 2014 under our bonus program based on the achievement of corporate performance goals and other factors deemed relevant by our board of directors. Our 2013 corporate goals related to the advancement of our preclinical programs, business and corporate development objectives, collaboration objectives and financial management objectives. For 2013, we determined our named executive officers' annual performance bonus based on attainment of company objectives, which bonus our board of directors determined was appropriate given each of the named executive officer's responsibility for the overall direction and success of our business. For 2013, our board of directors determined that Drs. Molineaux, Bennett and Sjogren were entitled to 110% of their target bonuses.
- (2) Amounts shown in this column do not reflect dollar amounts actually received by our named executive officers. Instead, these amounts reflect the aggregate grant date fair value of each stock option granted computed in accordance with the provisions of FASB ASC Topic 718. Assumptions used in the calculation of these amounts are included in Note 6 to our financial statements included in this prospectus. As required by SEC rules, the amounts shown exclude the impact of estimated forfeitures related to service-based vesting conditions. Our named executive officers will only realize compensation to the extent the trading price of our common stock is greater than the exercise price of such stock options.

Table of Contents**Index to Financial Statements****Outstanding Equity Awards at December 31, 2013**

The following table provides information regarding outstanding equity awards held by each of our named executive officers as of December 31, 2013. All awards were granted under our 2010 Equity Incentive Plan.

Name	Grant Date	Vesting Commencement Date	Option Awards				Stock Awards	
			Number of Securities Underlying Unexercised Options (#) Exercisable	Number of Securities Underlying Unexercised Options (#) Unexercisable	Option Exercise Price (\$)	Option Expiration Date	Number of Shares or Units of Stock That Have Not Vested (#)	Market Value of Shares or Units of Stock That Have Not Vested (\$)(6)
Susan M. Molineaux, Ph.D.	3/24/2010(1)	6/17/2010					1,145	\$ 3,025
	12/14/2011(2)	11/7/2011	5,458	25,107	\$ 0.48	12/13/2021		
	6/13/2012(3)	3/27/2012	5,511	29,763	0.48	6/12/2022		
	5/23/2013(4)	5/23/2013	6,306	51,711	0.96	5/22/2023		
	12/17/2013(5)	12/17/2013		129,169	2.64	12/16/2023		
Mark K. Bennett, Ph.D.	9/30/2010(7)	6/1/2010	1,604	229	9.60	9/29/2020		
	12/14/2011(2)	11/7/2011	912	6,993	0.48	12/13/2021		
	6/13/2012(3)	3/27/2012	1,075	7,257	0.48	6/12/2022		
	5/23/2013(4)	5/23/2013	1,890	19,376	0.96	5/22/2023		
	12/17/2013(5)	12/17/2013		37,991	2.64	12/16/2023		
Eric B. Sjogren, Ph.D.	9/30/2010(7)	6/1/2010	1,604	229	9.60	9/29/2020		
	12/14/2011(2)							