Calithera Biosciences, Inc.
Form 424B4
October 02, 2014
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Filed Pursuant to Rule 424(b)(4)
Registration No. 333-198355

PROSPECTUS

8,000,000 Shares

Common Stock

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

We are offering 8,000,000 shares of our common stock. Prior to this offering, there has been no public market for our common stock. The initial public offering price is $10.00 per share of common stock. Our common stock has been approved for listing on the NASDAQ Global Select 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
Initial public offering price	$ 10.00	$ 80,000,000
Underwriting discounts and commissions(1)	$ 0.70	$ 5,600,000
Proceeds, before expenses, to us	$ 9.30	$ 74,400,000

(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 that had submitted indications of interest have agreed to purchase 1,650,000 shares of our common stock in this offering at the initial public offering price. The underwriters will receive the same discount from the 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 1,200,000 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 October 7, 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**

October 1, 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 October 27, 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 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	8,000,000 shares
Common stock to be outstanding immediately after this offering	17,881,573 shares
Over-allotment option	1,200,000 shares
Use of proceeds	We estimate that the net proceeds from this offering will be approximately $71.7 million, or approximately $82.9 million if the underwriters exercise in full their over-allotment option to purchase additional shares, based on the initial public offering price of $10.00 per share, 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.
NASDAQ Global Select 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 that had submitted indications of interest have agreed to purchase 1,650,000 shares of our common stock in this offering at the initial public offering price. The underwriters will receive the same discount from the 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 ceased to be available for future issuance at the time our 2014 Equity Incentive Plan became 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 became 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 became 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 effected on September 19, 2014;

- 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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Summary Financial Data

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
			(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)	$ (366.13)	$ (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)
Balance Sheet Data:			
Cash and cash equivalents	$ 27,750	$ 40,750	$ 112,450
Working capital	23,128	39,128	110,828
Total assets	30,655	43,655	115,355
Convertible preferred stock	54,282		
Accumulated deficit	(39,782)	(39,782)	(39,782)
Total stockholders (deficit) equity	(30,043)	40,239	111,939

(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 $71.7 million in net proceeds from our sale of 8,000,000 shares of common stock in this offering at the initial public offering price of $10.00 per share, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

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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;

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,

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

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

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.

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.

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.

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 has been 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 their affiliates will, in the aggregate, beneficially own approximately 38.7% of our outstanding

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common stock, which includes the purchase of 1,150,000 shares by entities associated with Advanced Technology Ventures VIII, L.P., Delphi Ventures VIII, L.P., Morgenthaler Venture Partners IX, L.P. in this offering at the initial public offering price. 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.

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

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disclosure, including regulations implemented by the Securities and Exchange Commission, or SEC, and the NASDAQ Global Select 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.

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, 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.

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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 17,881,573 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 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 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

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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 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 $3.74 in net tangible book value per share from the price you paid, based on the initial public offering price of $10.00 per share. In addition, new investors who purchase shares in this offering will contribute approximately 50.0% of the total amount of equity capital raised by us through the date of this offering, but will only own approximately 44.7% 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.

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

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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 8,000,000 shares of common stock in this offering will be approximately $71.7 million at the initial public offering price of $10.00 per share, after deducting underwriting discounts and commissions and estimated offering expenses payable by us. If the underwriters exercise their over-allotment option in full, we estimate that the net proceeds will be approximately $82.9 million after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.

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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CAPITALIZATION

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 the initial public offering price of $10.00 per share, 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
	(in thousands, except share and per share data)		
Cash and cash equivalents	$ 27,750	$ 40,750	$ 112,450
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; 17,881,573 shares issued and outstanding, pro forma as adjusted	1	1	2
Additional paid-in capital	9,738	80,020	151,719
Accumulated deficit	(39,782)	(39,782)	(39,782)
Total stockholders (deficit) equity	(30,043)	40,239	111,939
Total capitalization	$ 24,239	$ 40,239	$ 111,939

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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 ceased to be available for future issuance at the time our 2014 Equity Incentive Plan became 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 became 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 became effective upon the execution of the underwriting agreement related to this offering.

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DILUTION

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 8,000,000 shares of common stock in this offering at the initial public offering price of $10.00 per share, 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 $111.9 million, or $6.26 per share. This represents an immediate increase in pro forma as adjusted net tangible book value of $2.19 per share to our existing stockholders and an immediate dilution of $3.74 per share to investors purchasing common stock in this offering.

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

Initial public offering price per share		$ 10.00
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	2.19	
Pro forma as adjusted net tangible book value per share after this offering		6.26
Dilution in net tangible book value per share to new investors in this offering		$ 3.74

If the underwriters exercise in full their over-allotment option to purchase 1,200,000 additional shares from us, the pro forma as adjusted net tangible book value per share after giving effect to this offering would be $6.45 per share, representing an immediate increase to existing stockholders of $2.38 per share, and immediate dilution to investors in this offering of $3.55 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, based on the initial public offering price of $10.00 per share, before deducting underwriting discounts and commissions and estimated offering expenses payable by us in connection with this offering; and

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	55.3%	$ 79,900,000	50.0%	$ 8.09
New investors	8,000,000	44.7	80,000,000	50.0	10.00
Total	17,881,573	100%	$ 159,900,000	100%	

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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 ceased to be available for future issuance at the time our 2014 Equity Incentive Plan became 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 became 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 became effective upon the execution of the underwriting agreement related to this offering.

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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SELECTED FINANCIAL DATA

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)	$ (366.13)	$ (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 December 31,		As of June 30,
	2012	2013	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

$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.

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	481
	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.

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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

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;

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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Contractual Obligations and Other Commitments

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

	Payments Due by Period				
Contractual Obligations:	**Less Than 1 Year**	**1 to 3 Years**	**3 to 5 Years**	**More Than 5 Years**	**Total**
			(in thousands)		
Operating lease obligations(1)	$ 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 Polices and Estimates

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

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 provide by the American Institute of Certified Public Accountants Practice Guide, *Valuation of Privately-Held-Company Equity Securities Issued as Compensation*. Given the absence of a public trading market for our common stock, our board of directors exercised reasonable judgment and considered a number of objective and subjective factors to determine the best estimate of the fair value of our common stock, including our stage of development; progress of our research and development efforts; the rights, preferences and privileges of our preferred stock relative to those of our common stock; equity market conditions affecting comparable public companies and the lack of marketability of our common stock.

After the closing of 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 Select Market on the date of grant.

Based on the initial public offering price of $10.00 per share, the intrinsic value of stock options outstanding at June 30, 2014 was $7.8 million, of which $0.7 million and $7.1 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.

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

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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Phase 1 Clinical Trials with CB-839

Trial Design

In February 2014, we initiated three Phase 1 clinical trials of CB-839 in patients with solid and hematological tumors. The favorable preclinical safety profile of CB-839 enabled a starting dose in these trials of 100 mg given orally three times daily, or TID. As shown in the table below, CX-839-001 is enrolling patients with solid tumors, CX-839-002 is enrolling patients with multiple myeloma or non-Hodgkin s lymphoma, and CX-839-003 is enrolling patients with acute myeloid or acute lymphocytic leukemia. 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
CX-839-001	Solid Tumors (including Triple-negative Breast Cancer (TNBC))	Dose escalation in all solid tumors Dose expansion cohorts in selected tumor types Phase 1b in TNBC in combination with paclitaxel
CX-839-002	Multiple Myeloma (MM) Non-Hodgkin s Lymphoma (NHL)	Dose escalation in MM and NHL Dose expansion cohorts in MM and selected subtypes of NHL Phase 1b in MM in combination with pomalidomide and dexamethasone
CX-839-003	Acute Lymphocytic Leukemia (ALL) Acute Myeloid Leukemia (AML)	Dose escalation in ALL and AML Dose expansion cohorts in ALL and AML

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

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 patient s 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 a 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,

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

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.

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

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

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;
- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending applications or supplements to approved applications, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- consent decrees, injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Drugs may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off label uses, and a company that is found to have improperly promoted off label uses may be subject to significant liability.

Additional Provisions

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

Federal false claims laws prohibit any person from knowingly presenting, or causing to be presented, a false claim for payment to the federal government, or knowingly making, or causing to be made, a false statement to have a false claim paid. Recently, several pharmaceutical and other healthcare companies have been prosecuted under these laws for allegedly inflating drug prices they report to pricing services, which in turn were used by the government to set Medicare and Medicaid reimbursement rates, and for allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. In addition, certain marketing practices, including off-label

promotion, may also violate false claims laws. The majority of states also have statutes or regulations similar to the federal anti-kickback law and false claims laws, which apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor.

Foreign Regulation

In order to market any product outside of the United States, we would need to comply with numerous and varying regulatory requirements of other countries regarding safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of our products. Whether or not

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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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MANAGEMENT

Executive Officers and Directors

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

Name	Age	Position
Executive Officers		
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
Non-Employee Directors		
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 Aethestics, 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 Select 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 Select 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

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 Select 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

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.

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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 Select 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 Select 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.

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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. *President and Chief Executive Officer*	2013	$ 350,000	$ 134,750	$ 17,600	$ 502,350
Mark K. Bennett, Ph.D. *Senior Vice President, Research*	2013	275,000	89,100	8,422	372,522
Eric B. Sjogren, Ph.D. *Senior Vice President, Drug Discovery*	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.

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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.

	Option Awards						Stock Awards	
Name	Grant Date	Vesting Commencement Date	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)	11/7/2011	1,216	6,993	0.48	12/13/2021		
	6/13/2012(3)	3/27/2012	1,344	7,257	0.48	6/12/2022		
	5/23/2013(4)	5/23/2013	2,362	19,376	0.96	5/22/2023		
	12/17/2013(5)	12/17/2013		37,991	2.64	12/16/2023		

(1) Reflects the unvested portion of a restricted stock grant for 11,000 shares of common stock granted on March 24, 2010. Our right to repurchase the unvested shares lapsed in equal increments on a monthly basis through June 17, 2014.
(2) The unvested shares vest in equal monthly installments through November 7, 2015, subject to continued service with us through each relevant vesting date and are subject to accelerated vesting upon a qualifying termination as set forth in the executive officer s employment agreement with us.
(3) The unvested shares vest in equal monthly installments through March 27, 2016, subject to continued service with us through each relevant vesting date and are subject to accelerated vesting upon a qualifying termination as set forth in the executive officer s employment agreement with us.
(4) The unvested shares vest in equal monthly installments through May 23, 2017, subject to continued service with us through each relevant vesting date and are subject to accelerated vesting upon a qualifying termination as set forth in the executive officer s employment agreement with us.
(5) The unvested shares vest in equal monthly installments through December 17, 2017, subject to continued service with us through each relevant vesting date and are subject to accelerated vesting upon a qualifying termination as set forth in the executive officer s employment agreement with us.
(6) Amounts calculated in accordance with ASC Topic 718 using a per share fair market value as of December 31, 2013 of $2.64.
(7) The unvested shares subject to this option fully vested on June 1, 2014.

In September 2014, we granted Drs. Susan Molineaux, Bennett and Sjogren options to purchase 63,716, 18,740 and 18,740 shares of our common stock, respectively, with exercise prices of $7.20 per share. The options vest in equal monthly installments through September 8, 2018, subject to continued service with us, and are subject to accelerated vesting upon a qualifying termination as set forth in the executive officer s employment agreement with us.

Emerging Growth Company Status

We are an emerging growth company, as defined in the JOBS Act. As an emerging growth company we will be exempt from certain requirements related to executive compensation, including, but not limited to, the

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requirements to hold a nonbinding advisory vote on executive compensation and to provide information relating to the ratio of total compensation of our Chief Executive Officer to the median of the annual total compensation of all of our employees, each as required by the Investor Protection and Securities Reform Act of 2010, which is part of the Dodd-Frank Wall Street Reform and Consumer Protection Act.

Pension Benefits

Our named executive officers did not participate in, or otherwise receive any benefits under, any pension or retirement plan sponsored by Calithera during 2013.

Nonqualified Deferred Compensation

Our named executive officers did not participate in, or earn any benefits under, a nonqualified deferred compensation plan sponsored by Calithera during 2013.

Employment, Severance and Change in Control Agreements

Employment Agreements

We have employment agreements with each of our executive officers. The agreements generally provide for at-will employment and set forth the executive officer s initial base salary, annual performance bonus opportunity, initial equity grant amount and eligibility for employee benefits. In addition, each of our named executive officers has executed a form of our standard confidential information and invention assignment agreement. The key terms of the employment agreements are described below. A qualifying termination for the purposes of the employment agreements is defined as a termination of the executive officer by us without cause, other than as a result of the executive officer s death or disability, or the resignation of the executive officer s employment with us with good reason.

Susan M. Molineaux, Ph.D.

In June 2010, we entered into an employment agreement with Dr. Molineaux, pursuant to which she commenced employment on an at-will basis as our President and Chief Executive Officer. Under the employment agreement, we agreed to pay Dr. Molineaux an annual base salary of $350,000, with an annual target bonus of 35% of that base salary, payable based on achievement of certain corporate goals to be established by us. Dr. Molineaux purchased 11,000 shares of common stock, 9,166 shares of which were subject to a right of repurchase under a restricted stock purchase agreement. Our repurchase rights had lapsed as to all shares as of June 2014.

Under the employment agreement, as amended in November 2011, if a qualifying termination occurs on or within 12 months following a change in control, she will receive a cash severance payment equal to the sum of 12 months of her annual base salary as in effect immediately prior to her termination, plus 100% of her annual target bonus. Upon a qualifying termination, other than following a change in control, Dr. Molineaux will receive a cash severance payment equal to the sum of 12 months of her annual base salary plus a pro-rated portion of her annual target bonus, based on our proportional accomplishments of that year s goal through the date of termination.

In addition, upon a qualifying termination, all of Dr. Molineaux s unvested equity awards will immediately vest and become exercisable, and outstanding options will remain exercisable for a period of up to 120 days, or until the expiration date of the award, if earlier. Also, Dr. Molineaux and her eligible dependents will be eligible to receive continued medical coverage for up to 12 months following her termination, so long as Dr. Molineaux timely elects such continued coverage. Receipt of these benefits is contingent upon Dr. Molineaux s execution and non-revocation of a release of claims in our favor, as well as her resignation from our board of directors.

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Mark K. Bennett, Ph.D.

In September 2010, we entered into an employment agreement with Dr. Bennett, pursuant to which he commenced employment on an at-will basis as our Senior Vice President, Research. Under the employment agreement, we agreed to pay Dr. Bennett an annual base salary of $275,000, with an annual target bonus of 30% of that base salary, payable based on achievement of certain corporate and individual goals to be established by us. Pursuant to the employment agreement, we granted Dr. Bennett an initial stock option to purchase 1,833 shares of common stock, which fully vested in June 2014.

If a qualifying termination of Dr. Bennett occurs on or within 12 months following a change in control, he will receive a cash severance payment equal to the sum of 50% of his annual base salary, as in effect immediately prior to his termination, plus the greater of (i) 50% of his annual target bonus and (ii) 50% of a pro-rated portion of his annual target bonus calculated based on our proportional accomplishment of that year s goals through the date of termination. Upon a qualifying termination, other than on or within twelve months following a change in control, Dr. Bennett will receive a cash severance payment equal to the sum of 50% of his annual base salary (as in effect immediately prior to his termination) plus a pro-rated portion of his annual target bonus for the year in which he terminates employment, calculated based on our proportional accomplishment of that year s goals through the date of termination.

In addition, in the case of any qualifying termination, Dr. Bennett and his eligible dependents will be eligible to receive continued medical coverage for up to six months following his termination, so long as Dr. Bennett timely elects such continued coverage. Receipt of these benefits is contingent upon Dr. Bennett s execution and non-revocation of a release of claims in our favor.

Curtis C. Hecht

In March 2014, we entered into an employment agreement with Mr. Hecht, pursuant to which he commenced employment on an at-will basis as our Vice President, Business and Corporate Development. Under the employment agreement, we agreed to pay Mr. Hecht an annual base salary of $250,000, with an annual target bonus of 28% of that base salary, payable based on achievement of certain corporate and individual goals to be established by us. Pursuant to the employment agreement, we granted Mr. Hecht an initial stock option to purchase 49,503 shares of common stock. The option vests monthly over a four-year period.

If a qualifying termination of Mr. Hecht occurs, he will receive cash severance in the form of continuing payments, in accordance with our regular payment schedules of six months of his annual base salary, as in effect immediately prior to his termination, plus a pro-rated portion of his annual target bonus. Also, Mr. Hecht and his eligible dependents will be eligible to receive continued medical coverage for up to six months following his termination, so long as Mr. Hecht timely elects such continued coverage. Receipt of these benefits is contingent upon Mr. Hecht s execution and non-revocation of a release of claims in our favor.

In addition, upon a qualifying termination in connection with or within twelve months following a change in control, all of Mr. Hecht s unvested stock options will immediately vest and become exercisable.

Christopher J. Molineaux, Ph.D.

In June 2013, we entered into an employment agreement with Dr. Molineaux, pursuant to which he commenced employment on an at-will basis as our Senior Vice President, Development. Under the employment agreement, we agreed to pay Dr. Molineaux an annual base salary of $275,000, with an annual target bonus of 30% of that base salary, payable based on achievement of certain corporate and individual goals to be established by us. Pursuant to the employment agreement, we granted Dr. Molineaux an initial stock option to purchase 52,015 shares of common stock. The option vests monthly over a four-year period.

If a qualifying termination of Dr. Molineaux occurs on or within 12 months following a change in control, he will receive a cash severance payment equal to the sum of 50% of his annual base salary, as in effect

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immediately prior to his termination, plus the greater of (i) 50% of his annual target bonus and (ii) 50% of a pro-rated portion of his annual target bonus. In addition, upon such qualifying termination, all of Dr. Molineaux s unvested equity awards will immediately vest and become exercisable, and outstanding options will remain exercisable for a period of up to 120 days, or the expiration date of the award, if earlier. Upon a qualifying termination, other than on or within twelve months following a change in control, Dr. Molineaux will receive a cash severance payment equal to the sum of 50% of his annual base salary plus a pro-rated portion of his annual target bonus.

Also, in the case of any qualifying termination, Dr. Molineaux and his eligible dependents will be eligible to receive continued medical coverage for up to six months following his termination, so long as Dr. Molineaux timely elects such continued coverage under COBRA. Receipt of these benefits is contingent upon Dr. Molineaux s execution and non-revocation of a release of claims in our favor.

Eric B. Sjogren, Ph.D.

In September 2010, we entered into an employment agreement with Dr. Sjogren, pursuant to which he commenced employment on an at-will basis as our Senior Vice President, Drug Discovery. Under the employment agreement, we agreed to pay Dr. Sjogren an annual base salary of $275,000, with an annual target bonus of 30% of that base salary, payable based on achievement of certain corporate and individual goals to be established by us. Pursuant to the employment agreement, we granted Dr. Sjogren an initial stock option to purchase 1,833 shares of common stock, which option fully vested in June 2014.

If a qualifying termination of Dr. Sjogren occurs on or within 12 months following a change in control, he will receive a cash severance payment equal to the sum of 50% of his annual base salary, as in effect immediately prior to his termination, plus the greater of (i) 50% of his annual target bonus and (ii) 50% of a pro-rated portion of his annual target bonus. In addition, upon such qualifying termination, all of Dr. Sjogren s unvested equity awards will immediately vest and become exercisable. Upon a qualifying termination, other than on or within twelve months following a change in control, Dr. Sjogren will receive a cash severance payment equal to the sum of 50% of his annual base salary plus a pro-rated portion of his annual target bonus.

Also, Dr. Sjogren and his eligible dependents will be eligible to receive continued medical coverage for up to six months following his termination, so long as Dr. Sjogren timely elects such continued coverage. Receipt of these benefits is contingent upon Dr. Sjogren s execution and non-revocation of a release of claims in our favor.

William D. Waddill

In March 2014, we entered into an employment agreement with Mr. Waddill, pursuant to which he commenced employment on an at-will basis as our Senior Vice President, Chief Financial Officer, Treasurer and Secretary. Pursuant to the employment agreement, we agreed to pay Mr. Waddill an annual base salary of $310,000, with an annual target bonus of 35% of that base salary, payable based on achievement of certain corporate and individual goals to be established by us. Pursuant to the employment agreement, we granted Mr. Waddill an initial stock option to purchase 90,006 shares of common stock. The option will vest monthly over a four-year period. In addition, Mr. Waddill was paid a bonus of $15,000 in connection with his commencement of employment, which bonus must be repaid in its entirety should Mr. Waddill be terminated for cause or resign without good reason during the first six months of his employment.

If a qualifying termination of Mr. Waddill occurs on or within 12 months following a change in control, he will receive cash severance in the form of continuing payments, in accordance with our regular payment schedule, of nine months of his annual base salary plus the greater of (i) 75% of his annual target bonus or (ii) 75% of a pro-rated portion of his annual target bonus calculated based on the proportional accomplishments of that year s goals through the date of termination. In addition, all of Mr. Waddill s unvested stock option will immediately vest and become exercisable.

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Upon a qualifying termination, other than following a change in control, Mr. Waddill will receive cash severance in the form of continuing payments, in accordance with our regular payment schedule, of nine months of his annual base salary plus a pro-rated portion of his annual target bonus calculated based on our proportional accomplishments of that year s goals through the date of termination. Also, in the case of any qualifying termination, Mr. Waddill and his eligible dependents will be eligible to receive continued health care coverage for up to nine months following any qualifying termination, so long as Mr. Waddill timely elects such continued coverage. Receipt of these benefits is contingent upon Mr. Waddill s execution and non-revocation of a release of claims in our favor.

Employee Benefit Plans

We believe that our ability to grant equity-based awards is a valuable and necessary compensation tool that aligns the long-term financial interests of our employees, consultants and directors with the financial interests of our stockholders. In addition, we believe that our ability to grant options and other equity-based awards helps us to attract, retain and motivate employees, consultants and directors and encourages them to devote their best efforts to our business and financial success. The principal features of our equity incentive plans and our 401(k) plan are summarized below. These summaries are qualified in their entirety by reference to the actual text of the plans, which, other than the 401(k) plan, are filed as exhibits to the registration statement of which this prospectus is a part.

2010 Equity Incentive Plan

Our board of directors adopted our 2010 Equity Incentive Plan, or the 2010 Plan, in March 2010, and our stockholders approved our 2010 Plan in June 2010. Our 2010 Plan was amended most recently in August 2014. Our 2010 Plan provides for the grant of incentive stock options, or ISOs, within the meaning of Section 422 of the Code, to our employees, and for the grant of nonstatutory stock options, or NSOs, restricted stock awards, restricted stock unit awards and stock appreciation rights to our employees, directors and consultants.

Our 2014 Plan became effective upon the execution of the underwriting agreement related to this offering. As a result, we will not grant any additional awards under the 2010 Plan, although any awards previously granted under the 2010 Plan will remain subject to the terms of our 2010 Plan and applicable award agreements, until such outstanding awards that are stock options are exercised, or until they terminate or expire by their terms, and until any restricted stock awards become vested, terminate or are forfeited.

Authorized Shares

The maximum number of shares of our common stock that may be issued under our 2010 Plan is 1,669,398. The maximum number of shares that may be issued upon the exercise of ISOs under our 2010 Plan is 3,338,796. Shares subject to stock awards granted under our 2010 Plan that expire or terminate without being exercised in full or are settled in cash do not reduce the number of shares available for issuance under our 2010 Plan. Additionally, shares issued pursuant to stock awards under our 2010 Plan that we repurchase or that are forfeited, as well as shares used to pay the exercise price of a stock award or to satisfy the tax withholding obligations related to a stock award, become available for future grant under our 2010 Plan, although such shares may not be subsequently issued pursuant to the exercise of an ISO.

Plan Administration

Our board of directors or a duly authorized committee of our board of directors administers our 2010 Plan and the stock awards granted under it. Under our 2010 Plan, the board of directors has the authority to determine and amend the terms of awards, including recipients, the exercise, purchase or strike price of stock awards, if any, the number of shares subject to each stock award, the vesting schedule applicable to the awards, together with any vesting acceleration, and the form of consideration, if any, payable upon exercise or settlement of the award and the terms of the award agreements for use under our 2010 Plan. The board may amend the 2010 Plan in these and other respects with the consent of any adversely affected participant, although certain material amendments to the 2010 Plan require stockholder approval.

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Under the 2010 Plan, the board of directors also has the authority to modify outstanding awards, reprice any outstanding option, cancel any outstanding stock award in exchange for new stock awards, cash or other consideration, or take any other action that is treated as a repricing under GAAP, although if any such action adversely affects a participant, the written consent of that participant is required.

Corporate Transactions

Our 2010 Plan provides that in the event of certain specified significant corporate transactions, as defined under our 2010 Plan, each outstanding award will be treated as the administrator determines, unless otherwise provided in an individual award agreement or other written agreement with the holder of an award. The administrator may (1) arrange for the assumption, continuation or substitution of a stock award by a successor corporation; (2) arrange for the assignment of any reacquisition or repurchase rights held by us to a successor corporation; (3) accelerate the vesting, in whole or in part, of the stock award and provide for its termination prior to the transaction; (4) arrange for the lapse, in whole or in part, of any reacquisition or repurchase rights held by us; (5) cancel or arrange for the cancellation of the stock award prior to the transaction in exchange for a cash payment, if any, determined by the board; or (6) make a payment, in the form determined by the board, equal to the excess, if any, of the value of the property the participant would have received upon exercise of the awards prior to the transaction over any exercise price payable by the participant in connection with the exercise. The plan administrator is not obligated to treat all stock awards or portions of stock awards, even those that are of the same type, in the same manner.

Under the 2010 Plan, a corporate transaction is generally the consummation of: (1) a sale or other disposition of all or substantially all of our assets; (2) a sale or other disposition of at least 90% of our outstanding securities; (3) a merger, consolidation or similar transaction following which we are not the surviving corporation; or (4) a merger, consolidation or similar transaction following which we are the surviving corporation but the shares of our common stock outstanding immediately prior to such transaction are converted or exchanged into other property by virtue of the transaction.

In the event of a change in control, awards granted under the 2010 Plan will not receive automatic acceleration of vesting and exercisability, although this treatment may be provided for in an award agreement. Under the 2010 Plan, a change in control is defined to include: (1) the acquisition by any person of more than 50% of the combined voting power of our then outstanding stock; (2) a merger, consolidation or similar transaction in which the stockholders of the company immediately prior to the transaction do not own, directly or indirectly, more than 50% of the combined voting power of the surviving entity (or the parent of the surviving entity); (3) a sale, lease, exclusive license or other disposition of all or substantially all of the assets to an entity that did not previously hold more than 50% of the voting power of our stock; (4) our stockholders approve or our board of directors approves a plan of complete dissolution or liquidation or a complete dissolution or liquidation of the company otherwise occurs except for a liquidation into a parent corporation; and (5) incumbent board members no longer constitute a majority of the members of the board (where incumbent members include members appointed, elected, or nominated for election by a majority of the incumbent board members).

Transferability

Under our 2010 Plan, the board of directors may provide for limitations on the transferability of awards, in its sole discretion. Option awards are generally not transferable other than by will or the laws of descent and distribution, except as otherwise provided under our 2010 Plan.

Plan Amendment or Termination

Our board of directors has the authority to amend, suspend, or terminate our 2010 Plan, although certain material amendments require the approval of our stockholders, and amendments that would impair the rights of any participant require the consent of that participant.

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2014 Equity Incentive Plan

Our board of directors adopted our 2014 Plan in September 2014, and our stockholders approved the 2014 Plan in September 2014. Our 2014 Plan provides for the grant of ISOs to our employees and for the grant of NSOs, stock appreciation rights, restricted stock awards, restricted stock unit awards, performance stock awards, performance cash awards, and other forms of equity compensation to our employees, directors and consultants.

Authorized Shares

The maximum number of shares of our common stock that may be issued under our 2014 Plan is 971,340. In addition, the number of shares of our common stock reserved for issuance under our 2014 Plan will automatically increase on the first day of January for a period of up to 10 years, commencing on January 1, 2015, in an amount equal to 4% of the total number of shares of our capital stock outstanding on the last day of the preceding fiscal year, or a lesser number of shares determined by our board of directors. The maximum number of shares of our common stock that may be issued upon the exercise of ISOs under our 2014 Plan is 10,000,000.

Shares subject to stock awards granted under our 2014 Plan that expire or terminate without being exercised in full, or that are paid out in cash rather than in shares, do not reduce the number of shares available for issuance under our 2014 Plan. Additionally, shares issued pursuant to stock awards under our 2014 Plan that we repurchase or that are forfeited, as well as shares used to pay the exercise price of a stock award or to satisfy the tax withholding obligations related to a stock award, become available for future grant under our 2014 Plan.

Plan Administration

Our board of directors, or a duly authorized committee of our board of directors, will administer our 2014 Plan. Our board of directors may also delegate to one or more of our officers the authority to (1) designate employees (other than officers) to receive specified stock awards, and (2) determine the number of shares subject to such stock awards. Under the 2014 Plan, our board of directors has the authority to determine the terms of awards, including recipients, the exercise, purchase or strike price of stock awards, if any, the number of shares subject to each stock award, the fair market value of a share of our common stock, the vesting schedule applicable to the awards, together with any vesting acceleration, the form of consideration, if any, payable upon exercise or settlement of the award and the terms of the award agreements.

The board of directors may also modify outstanding awards under our 2014 Plan, with the consent of any adversely affected participant. The board of directors has the authority to reprice any outstanding option or stock appreciation right, cancel any outstanding stock award in exchange for new stock awards, cash or other consideration, or take any other action that is treated as a repricing under generally accepted accounting principles, with the consent of any adversely affected participant.

Stock Options

ISOs and NSOs are granted pursuant to stock option agreements adopted by the plan administrator. The plan administrator determines the exercise price for stock options, within the terms and conditions of the 2014 Plan, provided that the exercise price of a stock option generally cannot be less than 100% of the fair market value of our common stock on the date of grant. Options granted under the 2014 Plan vest at the rate specified by the plan administrator.

The plan administrator determines the term of stock options granted under the 2014 Plan, up to a maximum of 10 years. Unless the terms of an option holder s stock option agreement provide otherwise, if an option holder s service relationship with us, or any of our affiliates, ceases for any reason other than disability, death or cause, the option holder may generally exercise any vested options for a period of three months following the option holder s cessation of service. The option term may be extended in the event that exercise of the option or

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sale of the underlying shares following such a termination of service is prohibited by applicable securities laws or by our insider trading policy. If an option holder s service relationship with us or any of our affiliates ceases due to disability or death, or an option holder dies within a certain period following cessation of service, the option holder or a beneficiary may generally exercise any vested options for a period of 12 months in the event of disability and 18 months in the event of death. Options generally terminate immediately upon the termination of the individual for cause. In no event may an option be exercised beyond the expiration of its term.

The plan administrator will determine acceptable consideration for the purchase of common stock issued upon the exercise of a stock option, which may include the following methods: (1) cash, check, bank draft or money order; (2) a broker-assisted cashless exercise procedure; (3) the tender of shares of our common stock previously owned by the option holder; (4) if the option is a nonstatutory stock option, by a net exercise arrangement; and (5) other legal consideration set forth in the applicable award agreement.

In general, options are not transferable except by will, the laws of descent and distribution, or as otherwise provided by the plan administrator under our 2014 Plan. An option holder may designate a beneficiary, however, who may exercise the option following the option holder s death.

Tax Limitations on Incentive Stock Options

The aggregate fair market value, determined at the time of grant, of our common stock with respect to incentive stock options that are exercisable for the first time by an option holder during any calendar year under all of our stock plans may not exceed $100,000. Options or portions thereof that exceed such limit will generally be treated as nonstatutory stock options. No incentive stock option may be granted to any person who, at the time of grant, owns or is deemed to own stock possessing more than 10% of our total combined voting power or that of any of our affiliates unless (1) the option exercise price is at least 110% of the fair market value of the stock subject to the option on the date of grant and (2) the term of the incentive stock option does not exceed five years from the date of grant.

Restricted Stock Unit Awards

Restricted stock unit awards are granted pursuant to restricted stock unit award agreements adopted by the plan administrator. Restricted stock unit awards may be granted in consideration for any form of legal consideration that may be acceptable to our board of directors and permissible under applicable law. A restricted stock unit award may be settled by cash, delivery of stock, a combination of cash and stock as deemed appropriate by the plan administrator, or in any other form of consideration set forth in the restricted stock unit award agreement. Additionally, dividend equivalents may be credited in respect of shares covered by a restricted stock unit award. Except as otherwise provided in the applicable award agreement, restricted stock units that have not vested will be forfeited upon the participant s cessation of continuous service for any reason.

Restricted Stock Awards

Restricted stock awards are granted pursuant to restricted stock award agreements adopted by the plan administrator. A restricted stock award may be awarded in consideration for cash, check, bank draft or money order, past services to us, or any other form of legal consideration that may be acceptable to our board of directors and permissible under applicable law. The plan administrator determines the terms and conditions of

restricted stock awards, including vesting and forfeiture terms. If a participant s service relationship with us ceases for any reason, we may receive through a forfeiture condition or a repurchase right any or all of the shares of common stock held by the participant that have not vested as of the date the participant terminates service with us.

Stock Appreciation Rights

Stock appreciation rights are granted pursuant to stock appreciation grant agreements adopted by the plan administrator. The plan administrator determines the purchase price or strike price for a stock appreciation right,

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which generally cannot be less than 100% of the fair market value of our common stock on the date of grant. Upon the exercise of a stock appreciation right, we will pay the participant an amount equal to the product of (1) the excess, if any, of the per share fair market value of our common stock on the date of exercise over the purchase price or strike price, and (2) the number of shares of common stock with respect to which the stock appreciation right is exercised. This amount may be paid in shares of our common stock, in cash, in any combination of cash and shares of our common stock or in any other form of consideration, as determined by the plan administrator and set forth in the award agreement. A stock appreciation right granted under the 2014 Plan vests at the rate specified in the stock appreciation right agreement as determined by the plan administrator.

The plan administrator determines the term of stock appreciation rights granted under the 2014 Plan, which may be up to a maximum of 10 years. Unless the terms of a participant s stock appreciation right agreement provides otherwise, if a participant s service relationship with us or any of our affiliates ceases for any reason other than cause, disability or death, the participant may generally exercise any vested stock appreciation right for a period of three months following the cessation of service. The term of the stock appreciation right may be further extended in the event that exercise of the stock appreciation right following such a termination of service is prohibited by applicable securities laws or by our insider trading policy. If a participant s service relationship with us, or any of our affiliates, ceases due to disability or death, or a participant dies within a certain period following cessation of service, the participant (or, if applicable, a beneficiary) may generally exercise any vested stock appreciation right for a period of 12 months (in the case of disability) or 18 months (in the case of death). Stock appreciation rights generally terminate immediately upon the occurrence of the event giving rise to the termination of the individual for cause. In no event may a stock appreciation right be exercised beyond the expiration of its term.

Section 162(m) Limits

At such time as necessary for compliance with Section 162(m) of the Code, certain limits will apply when we make awards under the 2014 Plan. These limitations are intended to give us the flexibility to grant compensation that will not be subject to the $1,000,000 annual limitation on the income tax deductibility imposed by Section 162(m) of the Code. In the case of stock options, stock appreciation rights and other stock awards whose value is determined by reference to an increase over an exercise price or strike price of at least 100% of the fair market value of our common stock on the date of grant, such awards will not cover more than 1,000,000 shares of our common stock in any calendar year. Additionally, no participant may be granted in a calendar year a performance stock award covering more than 1,000,000 shares of our common stock or a performance cash award having a maximum value in excess of $1,000,000 under our 2014 Plan.

Performance Awards

The 2014 Plan permits the grant of performance-based stock and cash awards that may qualify as performance-based compensation that is not subject to the $1,000,000 limitation on the income tax deductibility imposed by Section 162(m) of the Code. Our compensation committee may structure awards so that the stock or cash will be issued or paid only following the achievement of certain pre-established performance goals during a designated performance period.

Our compensation committee may establish performance goals by selecting from one or more of the following performance criteria: (1) earnings (including earnings per share and net earnings); (2) earnings before interest, taxes and depreciation; (3) earnings before interest, taxes, depreciation and amortization; (4) earnings before interest, taxes, depreciation, amortization and legal settlements; (5) earnings before interest, taxes, depreciation, amortization, legal settlements and other income (expense); (6) earnings before interest, taxes, depreciation, amortization, legal settlements, other income (expense) and stock-based compensation; (7) earnings before interest, taxes, depreciation, amortization, legal settlements, other income (expense), stock-based compensation and changes in deferred revenue; (8) total stockholder return; (9) return on

equity or average stockholder s equity; (10) return on assets, investment or capital employed; (11) stock price; (12) margin (including gross margin); (13) income (before

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or after taxes); (14) operating income; (15) operating income after taxes; (16) pre-tax profit; (17) operating cash flow; (18) sales or revenue targets; (19) increases in revenue or product revenue; (20) expenses and cost reduction goals; (21) improvement in or attainment of working capital levels; (22) economic value added (or an equivalent metric); (23) market share; (24) cash flow; (25) cash flow per share; (26) share price performance; (27) debt reduction; (28) implementation or completion of projects or processes; (29) stockholders equity; (30) capital expenditures; (31) debt levels; (32) operating profit or net operating profit; (33) workforce diversity; (34) growth of net income or operating income; (35) billings; (36) bookings; (37) employee retention; (38) initiation of phases of clinical trials and/or studies by specific dates; (39) patient enrollment rates; (40) budget management; (41) submission to, or approval by, a regulatory body (including, but not limited to the U.S. Food and Drug Administration, or FDA) of an applicable filing or a product candidate; (42) regulatory milestones; (43) progress of internal research or clinical programs; (44) progress of partnered programs; (45) partner satisfaction; (46) timely completion of clinical trials; (47) submission of INDs and NDAs and other regulatory achievements; (48) research progress, including the development of programs; (49) strategic partnerships or transactions (including in-licensing and out-licensing of intellectual property; and (50) to the extent that an award is not intended to comply with Section 162(m) of the Code, other measures of performance selected by board of directors.

Our board of directors may establish performance goals on a company-wide basis, with respect to one or more business units, divisions, affiliates or business segments, and in either absolute terms or relative to the performance of one or more comparable companies or the performance of one or more relevant indices. Unless otherwise specified by our board of directors (i) in the award agreement at the time the award is granted or (ii) in such other document setting forth the performance goals at the time the performance goals are established, our board of directors will appropriately make adjustments in the method of calculating the attainment of the performance goals as follows: (1) to exclude restructuring and/or other nonrecurring charges; (2) to exclude exchange rate effects; (3) to exclude the effects of changes to generally accepted accounting principles; (4) to exclude the effects of any statutory adjustments to corporate tax rates; (5) to exclude the effects of any extraordinary items as determined under generally accepted accounting principles; (6) to exclude the dilutive effects of acquisitions or joint ventures; (7) to assume that any business divested by us achieved performance objectives at targeted levels during the balance of a performance period following such divestiture; (8) to exclude the effect of any change in the outstanding shares of our common stock by reason of any stock dividend or split, stock repurchase, reorganization, recapitalization, merger, consolidation, spin-off, combination or exchange of shares or other similar corporate change or any distributions to common stockholders other than regular cash dividends; (9) to exclude the effects of stock-based compensation and the award of bonuses under our bonus plans; (10) to exclude costs incurred in connection with potential acquisitions or divestitures that are required to be expensed under generally accepted accounting principles; (11) to exclude the goodwill and intangible asset impairment charges that are required to be recorded under generally accepted accounting principles; (12) to exclude the effect of any other unusual, non-recurring gain or loss or other extraordinary item and (13) to exclude the effects of the timing of acceptance for review and/or approval of submission to the FDA or any other regulatory body.

Other Stock Awards

The plan administrator may grant other awards based in whole or in part by reference to our common stock. The plan administrator will set the number of shares under the stock award and all other terms and conditions of such awards.

Changes to Capital Structure

In the event there is a specified type of change in our capital structure, such as a stock split, reverse stock split, or recapitalization, appropriate adjustments will be made to (1) the class and maximum number of shares reserved for issuance under the 2014 Plan, (2) the class and maximum number of shares by which the share reserve may increase automatically each year, (3) the class and maximum number of shares that may be issued upon the exercise of incentive stock options, (4) the class and maximum number of shares subject to stock

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awards that can be granted in a calendar year (as established under the 2014 Plan pursuant to Section 162(m) of the Code), and (5) the class and number of shares and exercise price, strike price, or purchase price, if applicable, of all outstanding stock awards.

Corporate Transactions

Our 2014 Plan provides that in the event of certain specified significant corporate transactions, as defined under our 2014 Plan, each outstanding award will be treated as the administrator determines, unless otherwise provided in an individual award agreement or other written agreement with the holder of an award. The administrator may (1) arrange for the assumption, continuation or substitution of a stock award by a successor corporation; (2) arrange for the assignment of any reacquisition or repurchase rights held by us to a successor corporation; (3) accelerate the vesting, in whole or in part, of the stock award and provide for its termination prior to the transaction; (4) arrange for the lapse, in whole or in part, of any reacquisition or repurchase rights held by us; (5) cancel or arrange for the cancellation of the stock award prior to the transaction in exchange for a cash payment, if any, determined by the board; or (6) make a payment, in the form determined by the board, equal to the excess, if any, of the value of the property the participant would have received upon exercise of the awards prior to the transaction over any exercise price payable by the participant in connection with the exercise. The plan administrator is not obligated to treat all stock awards or portions of stock awards, even those that are of the same type, in the same manner.

In the event of a change in control, awards granted under the 2014 Plan will not receive automatic acceleration of vesting and exercisability, although this treatment may be provided for in an award agreement. Under the 2014 Plan, a change in control is defined to include (1) the acquisition of any person of more than 50% of the combined voting power of the company s then outstanding stock; (2) a merger, consolidation or similar transaction in which the stockholders of the company immediately prior to the transaction do not own, directly or indirectly, more than 50% of the combined voting power of the surviving entity (or the parent of the surviving entity); (3) a sale, lease, exclusive license or other disposition of all or substantially all of the assets to an entity that did not previously hold more than 50% of the voting power over company stock and (4) the stockholders of the company approve and the board approves a plan of complete dissolution or liquidation or a complete dissolution or liquidation of the company otherwise occurs except for a liquidation into a parent corporation.

Transferability

Under our 2014 Plan, the board of directors may provide for limitations on the transferability of awards. Generally, a participant may not transfer stock awards under our 2014 Plan other than by will, the laws of descent and distribution or as otherwise provided under our 2014 Plan.

Plan Amendment or Termination

Our board of directors has the authority to amend, suspend or terminate our 2014 Plan, provided that such action does not materially impair the existing rights of any participant without such participant s written consent. No incentive stock options may be granted after the tenth anniversary of the date our board of directors adopted our 2014 Plan. No stock awards may be granted under our 2014 Plan while it is suspended or after it is terminated.

2014 Employee Stock Purchase Plan

Our board of directors adopted the ESPP in September 2014, and our stockholders approved the ESPP in September 2014. The ESPP became effective immediately upon the execution and delivery of the underwriting agreement related to this offering. The purpose of the ESPP is to secure the services of new employees, to retain the services of existing employees and to provide incentives for such individuals to exert maximum efforts toward our success and that of our affiliates. The ESPP is intended to qualify as an employee stock purchase plan within the meaning of Section 423 of the Code.

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Share Reserve

Following this offering, the ESPP authorizes the issuance of 189,883 shares of our common stock pursuant to purchase rights granted to our employees or to employees of any of our designated affiliates. The number of shares of our common stock reserved for issuance will automatically increase on January 1 of each calendar year, from January 1, 2015 (assuming the ESPP becomes effective in 2014) through January 1, 2024, by the lesser of (1) 1% of the total number of shares of our common stock outstanding on December 31 of the preceding calendar year, and (2) 250,000 shares; provided, that prior to the date of any such increase, our board of directors may determine that such increase will be less than the amount set forth in clauses (1) and (2). As of the date hereof, no shares of our common stock have been purchased under the ESPP.

Administration

Our board of directors has delegated its authority to administer the ESPP to our compensation committee. The ESPP is implemented through a series of offerings under which eligible employees are granted purchase rights to purchase shares of our common stock on specified dates during such offerings. Under the ESPP, we may specify offerings with durations of not more than 27 months, and may specify shorter purchase periods within each offering. Each offering will have one or more purchase dates on which shares of our common stock will be purchased for employees participating in the offering. We currently intend to have 24-month offerings with four purchase periods (of approximately six months in duration) per offering, except that the first purchase period under our first offering may be shorter or longer than six months, depending on the date on which the underwriting agreement relating to this offering becomes effective. An offering under the ESPP may be terminated under certain circumstances.

Payroll Deductions

Generally, all regular employees, including executive officers, employed by us or by any of our designated affiliates, may participate in the ESPP and may contribute, normally through payroll deductions, up to 15% of their earnings (as defined in the ESPP) for the purchase of our common stock under the ESPP. Unless otherwise determined by our board of directors, common stock will be purchased for the accounts of employees participating in the ESPP at a price per share equal to the lower of (a) 85% of the fair market value of a share of our common stock on the first date of an offering or (b) 85% of the fair market value of a share of our common stock on the date of purchase. For the initial offering, which we expect will commence upon the execution and delivery of the underwriting agreement relating to this offering, the fair market value on the first day of the offering period will be the price at which shares are first sold to the public.

Limitations

Employees may have to satisfy one or more of the following service requirements before participating in the ESPP, as determined by our board of directors, including: (1) being customarily employed for more than 20 hours per week; (2) being customarily employed for more than five months per calendar year; or (3) continuous employment with us or one of our affiliates for a period of time (not to exceed two years). No employee may purchase shares under the ESPP at a rate in excess of $25,000 worth of our common stock based on the fair market value per share of our common stock at the beginning of an offering for each year such a purchase right is outstanding and the maximum number of shares an employee may purchase during a single purchase period is 2,500. Finally, no employee will be eligible for the grant of any purchase rights under the ESPP if immediately after such rights are granted, such employee has voting power over 5% or more of our outstanding capital stock

measured by vote or value pursuant to Section 424(d) of the Code.

Changes to Capital Structure

In the event that there occurs a change in our capital structure through such actions as a stock split, merger, consolidation, reorganization, recapitalization, reincorporation, stock dividend, dividend in property other than

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cash, large nonrecurring cash dividend, liquidating dividend, combination of shares, exchange of shares, change in corporate structure or similar transaction, the board of directors will make appropriate adjustments to (1) the number of shares reserved under the ESPP, (2) the maximum number of shares by which the share reserve may increase automatically each year, (3) the number of shares and purchase price of all outstanding purchase rights, and (4) the number of shares that are subject to purchase limits under ongoing offerings.

Corporate Transactions

In the event of certain significant corporate transactions, including: (1) a sale of all or substantially all of our assets, (2) the sale or disposition of 90% of our outstanding securities, (3) the consummation of a merger or consolidation where we do not survive the transaction and (4) the consummation of a merger or consolidation where we do survive the transaction but the shares of our common stock outstanding immediately prior to such transaction are converted or exchanged into other property by virtue of the transaction, any then-outstanding rights to purchase our stock under the ESPP may be assumed, continued or substituted for by any surviving or acquiring entity (or its parent company). If the surviving or acquiring entity (or its parent company) elects not to assume, continue or substitute for such purchase rights, then the participants accumulated payroll contributions will be used to purchase shares of our common stock within 10 business days prior to such corporate transaction, and such purchase rights will terminate immediately after such purchase.

ESPP Amendments, Termination

Our board of directors has the authority to amend or terminate our ESPP, provided that except in certain circumstances such amendment or termination may not materially impair any outstanding purchase rights without the holder s consent. We will obtain stockholder approval of any amendment to our ESPP as required by applicable law or listing requirements.

401(k) Plan

We maintain a tax-qualified retirement plan that provides eligible U.S. employees with an opportunity to save for retirement on a tax advantaged basis. Eligible employees are able to defer eligible compensation up to certain Code limits, which are updated annually. We have the ability to make matching and discretionary contributions to the 401(k) plan but have not done so to date. Employee contributions are allocated to each participant s individual account and are then invested in selected investment alternatives according to the participants directions. Employees are immediately and fully vested in their own contributions. The 401(k) plan is intended to be qualified under Section 401(a) of the Code, with the related trust intended to be tax exempt under Section 501(a) of the Code. As a tax-qualified retirement plan, contributions to the 401(k) plan are deductible by us when made, and contributions and earnings on those amounts are not taxable to the employees until withdrawn or distributed from the 401(k) plan.

Insurance Premiums

We pay premiums for medical insurance and dental insurance for all full-time employees, including our named executive officers. We also pay premiums for life insurance and long-term disability insurance benefits for all full-time employees, including our named executive officers. These benefits are available to all full-time employees, subject to applicable laws.

Limitations on Liability and Indemnification Matters

Upon the closing of this offering, our certificate of incorporation will contain provisions that limit the liability of our current and former directors for monetary damages to the fullest extent permitted by Delaware law. Delaware law provides that directors of a corporation will not be personally liable for monetary damages for any breach of fiduciary duties as directors, except liability for:

any breach of the director s duty of loyalty to the corporation or its stockholders;

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any act or omission not in good faith or that involves intentional misconduct or a knowing violation of law;

unlawful payments of dividends or unlawful stock repurchases or redemptions; or

any transaction from which the director derived an improper personal benefit. Such limitation of liability does not apply to liabilities arising under federal securities laws and does not affect the availability of equitable remedies such as injunctive relief or rescission.

Our certificate of incorporation will authorize us to indemnify our directors, officers, employees and other agents to the fullest extent permitted by Delaware law. Our bylaws will provide that we are required to indemnify our directors and officers to the fullest extent permitted by Delaware law and may indemnify our other employees and agents. Our bylaws will also provide that, upon satisfaction of certain conditions, we shall advance expenses incurred by a director or officer in advance of the final disposition of any action or proceeding, and permit us to secure insurance on behalf of any officer, director, employee or other agent for any liability arising out of his or her actions in that capacity regardless of whether we would otherwise be permitted to indemnify him or her under the provisions of Delaware law. We have entered and expect to continue to enter into agreements to indemnify our directors, executive officers and other employees as determined by the board of directors. With certain exceptions, these agreements provide for indemnification for related expenses including, among other things, attorneys fees, judgments, fines and settlement amounts incurred by any of these individuals in any action or proceeding. We believe that these certificate of incorporation and bylaw provisions and indemnification agreements are necessary to attract and retain qualified persons as directors and officers. We also maintain customary directors and officers liability insurance.

The limitation of liability and indemnification provisions in our certificate of incorporation and bylaws may discourage stockholders from bringing a lawsuit against our directors for breach of their fiduciary duty. They may also reduce the likelihood of derivative litigation against our directors and officers, even though an action, if successful, might benefit us and other stockholders. Further, a stockholder s investment may be adversely affected to the extent that we pay the costs of settlement and damage awards against directors and officers as required by these indemnification provisions.

At present, there is no pending litigation or proceeding involving any of our directors, officers or employees for which indemnification is sought and we are not aware of any threatened litigation that may result in claims for indemnification.

Insofar as indemnification for liabilities arising under the Securities Act of 1933, as amended, may be permitted for directors, executive officers or persons controlling us, we have been informed that in the opinion of the SEC such indemnification is against public policy as expressed in the Securities Act and is therefore unenforceable.

Rule 10b5-1 Sales Plans

Our directors and executive officers may adopt written plans, known as Rule 10b5-1 plans, in which they will contract with a broker to buy or sell shares of our common stock on a periodic basis. Under a Rule 10b5-1 plan, a broker executes trades pursuant to parameters established by the director or officer when entering into the plan, without further direction from them. The director or officer may amend a Rule 10b5-1 plan in some circumstances and may terminate a plan at any time. Our directors and executive officers also may buy or sell additional shares outside of a Rule 10b5-1 plan when they are not in possession of material nonpublic information subject to compliance with the terms of our insider trading policy. Prior to 180 days after the date of this offering (subject to early termination), the sale of any shares under such plan would be subject to the lock-up agreement that the director or officer has entered into with the underwriters.

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CERTAIN RELATIONSHIPS AND RELATED PERSON TRANSACTIONS

The following is a summary of transactions since January 1, 2011 to which we have been a participant, in which the amount involved exceeded or will exceed $120,000 and in which any of our directors, executive officers or holders of more than five percent of our capital stock, or any member of the immediate family of the foregoing persons, had or will have a direct or indirect material interest, other than compensation and other arrangements that are described in the section titled Executive Compensation or that were approved by our compensation committee.

We believe the terms obtained or consideration that we paid or received, as applicable, in connection with the transaction described below were comparable to terms available or the amounts that would be paid or received, as applicable, in arm s-length transactions.

Series B Preferred Stock Financing

In November 2011 and May 2012, we issued an aggregate of 1,676,724 shares of our Series B preferred stock at a purchase price of $4.7712 per share for an aggregate purchase price of $8.0 million. The following table summarizes purchases of Series B preferred stock by holders of more than five percent of our capital stock and their affiliated entities and our directors. None of our executive officers purchased shares of Series B preferred stock.

Name	Series B Preferred Stock	Aggregate Purchase Price
Advanced Technology Ventures VIII, L.P.(1)	419,181	$ 2,000,000
Entities affiliated with Delphi Ventures VIII, L.P.(2)	419,181	2,000,000
Morgenthaler Venture Partners IX, L.P.(3)	419,181	2,000,000
Entities affiliated with U.S. Ventures Partners X L.P.(4)	419,181	2,000,000

(1) Ms. George, a member of our board of directors, is a General Partner at Advanced Technology Ventures.
(2) Includes (a) 415,128 shares of Series B preferred stock purchased by Delphi Ventures VIII, L.P., and (b) 4,053 shares of Series B preferred stock purchased by Delphi BioInvestments VIII, L.P. Dr. Pakianathan, a member of our board of directors, is a Managing Member at Delphi Ventures.
(3) Dr. Christoffersen, a member of our board of directors, is a Partner at Morgenthaler Ventures.
(4) Includes (a) 406,187 shares of Series B preferred stock purchased by U.S. Venture Partners X L.P., and (b) 12,994 shares of Series B preferred stock purchased by USVP X Affiliates L.P. Laurence Lasky, a former member of our board of directors, was a Partner at U.S. Venture Partners. These shares converted into common stock in December 2012.

Immediately upon the closing of this offering, each share of Series B preferred stock will convert into one share of common stock. For a description of the material rights and privileges of the Series B preferred stock, please see Note 5 to the notes to our audited financial statements included elsewhere in this prospectus.

Series C Preferred Stock Financing

In December 2012 and April 2013, we issued an aggregate of 2,242,620 shares of our Series C preferred stock at a purchase price of $4.7712 per share for an aggregate purchase price of $10.7 million. The following table summarizes purchases of the Series C preferred stock by holders of more than five percent of our capital stock and their affiliated entities and our directors. None of our executive officers purchased shares of Series C preferred stock.

Name	Series C Preferred Stock	Aggregate Purchase Price
Advanced Technology Ventures VIII, L.P.(1)	747,540	$ 3,566,667
Entities affiliated with Delphi Ventures VIII, L.P.(2)	747,540	3,566,667
Morgenthaler Venture Partners IX, L.P.(3)	747,540	3,566,667

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(1) Ms. George, a member of our board of directors, is a General Partner at Advanced Technology Ventures.
(2) Includes (a) 740,312 shares of Series C preferred stock purchased by Delphi Ventures VIII, L.P., and (b) 7,228 shares of Series C preferred stock purchased by Delphi BioInvestments VIII, L.P. Dr. Pakianathan, a member of our board of directors, is a Managing Member at Delphi Ventures.
(3) Dr. Christoffersen, a member of our board of directors, is a Partner at Morgenthaler Venture Partners.

Immediately upon the closing of this offering, each share of Series C preferred stock will convert into one share of common stock. For a description of the material rights and privileges of the Series C preferred stock please see Note 5 to the notes to our audited financial statements included elsewhere in this prospectus.

Series D Preferred Stock Financing

In October 2013 and July 2014, we issued an aggregate of 6,064,382 shares of our Series D preferred stock at a purchase price of $8.4096 per share for an aggregate purchase price of $51.0 million. The following table summarizes purchases of the Series D preferred stock by holders of more than five percent of our capital stock and their affiliated entities and our directors. None of our executive officers purchased shares of Series D preferred stock.

Name	Series D Preferred Stock	Aggregate Purchase Price
Adage Capital Management, LP	1,783,675	$ 15,000,000
Entities affiliated with T. Rowe Price Associates, Inc.(1)	713,466	6,000,000
Entities affiliated with Delphi Ventures VIII, L.P.(2)	753,107	6,333,333
Advanced Technology Ventures VIII, L.P.(3)	634,195	5,333,333
Morgenthaler Venture Partners IX, L.P.(4)	634,195	5,333,333
Entities affiliated with Wellington Management Company, LLP(5)	594,455	4,999,150
Longwood Fund II LP	576,721	4,850,000

(1) Includes (a) 265,839 shares purchased by T. Rowe Price Health Sciences Fund, Inc., (b) 12,920 shares purchased by TD Mutual Funds TD Health Sciences Fund, (c) 16,555 shares purchased by Valic Company I Health Sciences Fund, (d) 11,124 shares purchased by T. Rowe Price Health Sciences Portfolio, (e) 8,493 shares purchased by John Hancock Variable Insurance Trust Health Sciences Trust, (f) 19,261 shares purchased by John Hancock Funds II Health Sciences Fund, (g) 344,944 shares purchased by T. Rowe Price New Horizons Fund, Inc., (h) 33,644 shares purchased by T. Rowe Price New Horizons Trust, and (i) 686 shares purchased by T. Rowe Price U.S. Equities Trust.
(2) Includes (a) 745,825 shares of Series D preferred stock purchased by Delphi Ventures VIII, L.P., and (b) 7,282 shares of Series D preferred stock purchased by Delphi BioInvestments VIII, L.P. Dr. Pakianathan, a member of our board of directors, is a Managing Member at Delphi Ventures.
(3) Ms. George, a member of our board of directors, is a General Partner at Advanced Technology Ventures.
(4) Dr. Christoffersen, a member of our board of directors, is a Partner at Morgenthaler Venture Partners.
(5) Includes (a) 188,587 shares purchased by Salthill Partners, L.P., (b) 119,341 shares purchased by North River Partners, L.P., (c) 118,911 shares purchased by Hawkes Bay Master Investors (Cayman) L.P., (d) 108,591 shares held by Salthill Investors (Bermuda) L.P., and (e) 59,025 shares purchased by North River Investors (Bermuda) L.P.

Immediately upon the closing of this offering, each share of Series D preferred stock will convert into one share of common stock. For a description of the material rights and privileges of the Series D preferred stock please see Note 5 to the notes to our audited financial statements included elsewhere in this prospectus.

Investor Rights Agreement

In October 2013, we entered into an amended and restated investor rights agreement, as amended, with certain holders of our outstanding preferred stock, including entities affiliated with certain of our directors. After

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the closing of this offering, the holders of 9,592,042 shares of our common stock, including common stock issuable upon the conversion of our preferred stock, will be entitled to rights with respect to the registration of their shares of common stock under the Securities Act pursuant to this amended and restated investor rights agreement. For a description of these registration rights, see the section titled Description of Capital Stock Stockholder Registration Rights.

Voting Agreement

In October 2013, we entered into an amended and restated voting agreement, as amended, with certain holders of our preferred stock, including entities affiliated with certain of our directors. The parties to the voting agreement have agreed to vote in a certain way on certain matters, including with respect to the election of directors. Pursuant to the voting agreement, the holders of a majority of our preferred stock, voting as a separate class, have designated Dr. Christoffersen, Ms. George and Dr. Pakianathan for election to our board of directors; the holders of a majority of our common stock, voting as a separate class, have designated Dr. Susan Molineaux for election to our board of directors; and the holders of a majority of our preferred stock and common stock, have designated Dr. Drachman for election to our board of directors. Upon the closing of this offering, the board election voting provisions contained in the voting agreement will terminate and none of our stockholders will have any special rights regarding the election or designation of members of our board of directors.

Employment Agreements

We have employment agreements with each of our executive officers. For more information regarding these employment agreements, see the section titled Executive Compensation Employment, Severance and Change in Control Agreements.

Indemnification Agreements

Our amended and restated certificate of incorporation will contain provisions limiting the liability of directors, and our bylaws will provide that we will indemnify each of our directors and officers to the fullest extent permitted under Delaware law. Our amended and restated certificate of incorporation and bylaws will also provide our board of directors with discretion to indemnify our employees and agents when determined appropriate by the board. In addition, we have entered into an indemnification agreement with each of our directors and executive officers, which requires us to indemnify our directors and executive officers. For more information regarding these agreements, see the section titled Executive Compensation Limitations on Liability and Indemnification Matters.

Other Transactions

We have granted stock options to our executive officers. For a description of these stock options, see the section titled Executive Compensation. We have also granted stock options to certain members of the board of directors. For a description of these stock options, see the section titled Management Non-Employee Director Compensation.

Related-Party Transaction Policy

We have adopted a formal written policy that our executive officers, directors, holders of more than five percent of any class of our voting securities, and any member of the immediate family of and any entity affiliated with any of the foregoing persons, will not be permitted to enter into a related-party transaction with us without the prior consent of our audit committee, or other independent members of our board of directors in the event it is inappropriate for our audit committee to review such transaction due to a conflict of interest. Any request for us to enter into a transaction with an executive officer, director, principal stockholder, or any of their immediate

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family members or affiliates, in which the amount involved exceeds $120,000 must first be presented to our audit committee for review, consideration and approval. In approving or rejecting any such proposal, our audit committee will consider the relevant facts and circumstances available and deemed relevant to our audit committee, including, but not limited to, whether the transaction will be on terms no less favorable than terms generally available to an unaffiliated third-party under the same or similar circumstances and the extent of the related-party s interest in the transaction.

All of the transactions described in this section were entered into prior to the adoption of this policy.

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PRINCIPAL STOCKHOLDERS

The following table sets forth certain information with respect to the beneficial ownership of our common stock as of June 30, 2014 by:

- each person, or group of affiliated persons, known by us to beneficially own more than five percent of our common stock;
- each of our named executive officers;
- each of our directors; and
- all of our executive officers and directors as a group.

The percentage of shares beneficially owned before the offering shown in the table is based on 9,881,573 shares of common stock outstanding as of June 30, 2014 after giving effect to the conversion of all of our outstanding preferred stock into shares of common stock immediately upon the closing of this offering, which includes the issuance and sale of 1,902,583 shares of Series D preferred stock in July 2014. The information relating to the number and percentage of shares beneficially owned after the offering assumes the sale by us of 8,000,000 shares of common stock in this offering. The percentage ownership information assumes no exercise of the underwriters over-allotment option to purchase additional shares.

Beneficial ownership is determined in accordance with the rules of the SEC and generally includes any shares over which a person exercises sole or shared voting or investment power. Unless otherwise indicated, the persons or entities identified in this table have sole voting and investment power with respect to all shares shown beneficially owned by them, subject to applicable community property laws. Shares of common stock issuable under options or warrants that are exercisable within 60 days after June 30, 2014 are deemed beneficially owned and such shares are used in computing the percentage ownership of the person holding the options or warrants, but are not deemed outstanding for the purpose of computing the percentage ownership of any other person. The information contained in the following table is not necessarily indicative of beneficial ownership for any other purpose, and the inclusion of any shares in the table does not constitute an admission of beneficial ownership of those shares.

Except as otherwise noted below, the address for persons listed in the table is c/o Calithera Biosciences, Inc., 343 Oyster Point Blvd., Suite 200, South San Francisco, California 94080.

	Shares Beneficially Owned Prior to this Offering		Shares Beneficially Owned Following this Offering	
Name of Beneficial Owner	**Shares**	**%**	**Shares**	**%**
Five Percent Stockholders:				
Entities affiliated with Delphi Ventures VIII, L.P.(1)	1,926,702	19.5%	2,426,702	13.6%
Morgenthaler Venture Partners IX, L.P.(2)	1,811,915	18.3	2,161,915	12.1
Advanced Technology Ventures VIII, L.P.(3)	1,810,082	18.3	2,110,082	11.8

Adage Capital Management, LP(4)	1,783,675	18.1	2,583,675	14.4
Entities affiliated with T. Rowe Price Associates, Inc.(5)	713,466	7.2	1,263,466	7.1
Entities affiliated with Wellington Management Company, LLP(6)	594,455	6.0	594,455	3.3
Longwood Fund II LP(7)	576,721	5.8	676,721	3.8
Named Executive Officers and Directors:				
Susan M. Molineaux, Ph.D.(8)	142,023	1.4	142,023	*
Mark K. Bennett, Ph.D.(9)	33,081	*	33,081	*
Eric B. Sjogren, Ph.D.(10)	33,080	*	33,080	*
Non-Employee Directors:				
Deepa R. Pakianathan, Ph.D.(1)(11)	1,926,702	19.5	2,426,702	13.6
Ralph E. Christoffersen, Ph.D.(2)(12)	1,811,915	18.3	2,161,915	12.1
Jean M. George(3)(13)	1,810,082	18.3	2,110,082	11.8
Jonathan Drachman, M.D.(14)	3,750	*	3,750	*
All executive officers and directors as a group (10 persons)(15)(16)	5,772,258	58.4	6,922,258	38.7

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* Represents beneficial ownership of less than one percent of the outstanding common stock.

(1) Includes (a) 1,908,073 shares held by Delphi Ventures VIII, L.P. and (b) 18,629 shares held by Delphi BioInvestments VIII, L.P. (together, the Delphi VIII Funds). The general partner of the Delphi VIII Funds is Delphi Management Partners VIII, LLC (DMP VIII). DMP VIII may be deemed to have sole voting and dispositive power over the shares held by the Delphi VIII Funds. Each of Deepa R. Pakianathan, a member of our board of directors, James J. Bochnowski, David L. Douglass and Douglas A. Roeder, managing members of DMP VIII, shares voting and dispositive power over, and each of these individuals disclaims beneficial ownership of, the reported securities held by the Delphi VIII Funds except to the extent of such individual s pecuniary interest therein. The address for the entities affiliated with Delphi Ventures is 3000 Sand Hill Road, Building 1, Suite 135, Menlo Park, California 94025. The entities affiliated with Delphi Ventures VIII, L.P. have agreed to purchase 500,000 shares of our common stock in this offering at the initial public offering price.

(2) Represents 1,811,915 shares held by Morgenthaler Venture Partners IX, L.P. (Morgenthaler). The general partner of Morgenthaler is Morgenthaler Management Partners IX, LLC (Morgenthaler Management). The managing members of Morgenthaler Management are Ralph E. Christoffersen, a member of our board of directors, Robert C. Bellas, James W. Broderick, Rebecca Lynn, Gary J. Morgenthaler, Scott D. Walters, Gary R. Little, Robert D. Pavey and Henry A. Plain. Each of these individuals shares voting and dispositive power over, and disclaims beneficial ownership of, such securities except to the extent of such individual s pecuniary interest therein. The address of Morgenthaler is 2710 Sand Hill Road, Suite 100, Menlo Park, California 94025. Morgenthaler has agreed to purchase 350,000 shares of our common stock in this offering at the initial public offering price.

(3) Represents 1,810,082 shares held by Advanced Technology Ventures VIII, L.P. (ATV VIII). No natural person holds voting or dispositive power for the shares held by ATV VIII. ATV Associates VIII, LLC (ATV VIII LLC) is the general partner of ATV VIII and controls its investment and voting decisions. Decisions of ATV VIII LLC are made by a board of five managing directors (the ATV Managing Directors). The ATV Managing Directors are Steve Baloff, Michael Carusi, Jean M. George, a member of our board of directors, Bob Hower and William Wiberg. Each of the ATV Managing Directors shares voting and dispositive power over, and disclaims beneficial ownership of, the securities held by ATV VIII except to the extent of any pecuniary interest therein. ATV VIII has agreed to purchase 300,000 shares of our common stock in this offering at the initial public offering price.

(4) Represents 1,783,675 shares held by Adage Capital Management, L.P. (Adage). The general partner of Adage is Adage Capital Partners GP, LLC. The managing member of Adage is Adage Capital Advisors, LLC. Each of Robert Atchinson and Phillip Gross, the managing members of Adage Capital Advisors, LLC, shares voting and dispositive power over, and disclaims beneficial ownership of, the securities held by Adage except to the extent of such individual s pecuniary interest therein. Adage has agreed to purchase 800,000 shares of our common stock in this offering at the initial public offering price.

(5) Includes (a) 265,839 shares held by T. Rowe Price Health Sciences Fund, Inc., (b) 12,920 shares held by TD Mutual Funds TD Health Sciences Fund, (c) 16,555 shares held by Valic Company I Health Sciences Fund, (d) 11,124 shares held by T. Rowe Price Health Sciences Portfolio, (e) 8,493 shares held by John Hancock Variable Insurance Trust Health Sciences Trust, (f) 19,261 shares held by John Hancock Funds II Health Sciences Fund, (g) 344,944 shares held by T. Rowe Price New Horizons Fund, Inc., (h) 33,644 shares held by T. Rowe Price New Horizons Trust, and (i) 686 shares held by T. Rowe Price U.S. Equities Trust. The foregoing funds and accounts are advised or sub-advised by T. Rowe Price Associates, Inc. T. Rowe Price Associates, Inc. serves as investment adviser with power to direct investments and/or sole power to vote the securities owned by these funds and accounts other than Valic Company I Health Sciences Fund, with respect to which T. Rowe Price Associates, Inc. does not have voting power. T. Rowe Price Associates, Inc. may be deemed to be the beneficial owner of all the shares listed. T. Rowe Price Associates, Inc. disclaims beneficial ownership of such securities. T. Rowe Price Associates, Inc. is the wholly-owned subsidiary of T. Rowe Price Group, Inc., which is a publicly traded financial services holding company. The address for T. Rowe Price Associates, Inc. is 100 East Pratt Street, Baltimore, Maryland 21202. The entities affiliated with T. Rowe Price Associates, Inc. have agreed to purchase 550,000 shares of our common stock in this offering at the initial public offering price.

(6) Includes (a) 188,587 shares held by Salthill Partners, L.P., (b) 119,341 shares held by North River Partners, L.P., (c) 118,911 shares held by Hawkes Bay Master Investors (Cayman) L.P., (d) 108,591 shares held by Salthill Investors (Bermuda) L.P., and (e) 59,025 shares held by North River Investors (Bermuda) L.P.

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Wellington Management Company, LLP, in its capacity as investment adviser, may be deemed to beneficially own the number of shares of common stock set forth in the table above, which are held of record by clients of Wellington Management Company, LLP.

(7) Represents 576,721 shares held by Longwood Fund II LP (Longwood). The general partner of Longwood is Longwood Fund GP, LLC (Longwood GP). Longwood GP may be deemed to have sole voting and dispositive power over the shares held by Longwood. Each of Michelle Dipp, M.D., Ph.D. and Cristoph Westphal, M.D., Ph.D. shares voting and dispositive power over, and each of these members disclaim beneficial ownership of, the reported securities held by Longwood, except to the extent of such individuals pecuniary interest therein. Longwood has agreed to purchase 100,000 shares of our common stock in this offering at the initial public offering price.

(8) Includes (a) 117,962 shares held by the Molineaux Family Trust Dated November 9, 2000, of which Dr. Susan Molineaux and Dr. Christopher Molineaux are trustees and share voting and dispositive power and (b) 24,061 shares issuable pursuant to stock options exercisable within 60 days after June 30, 2014.

(9) Includes (a) 26,043 shares held by Mark K. Bennett and Grace T. Bennett 1991 Revocable Trust and (b) 7,038 shares issuable pursuant to stock options exercisable within 60 days of June 30, 2014.

(10) Includes (a) 11,631 shares held by Dr. Sjogren and (b) 21,449 shares issuable pursuant to stock options exercisable within 60 days after June 30, 2014.

(11) Ms. Pakianathan is a Managing Member of Delphi Ventures III, L.P.

(12) Dr. Christoffersen is a Managing Member of Morgenthaler Management Partners IX, LLC.

(13) Ms. George is a Managing Director of Advanced Technology Ventures VIII, L.P.

(14) Represents 3,750 shares issuable pursuant to stock options exercisable within 60 days after June 30, 2014.

(15) Includes (a) 5,704,335 shares held by the directors and executive officers and (b) 67,923 shares issuable pursuant to stock options exercisable within 60 days after June 30, 2014.

(16) Entities associated with Advanced Technology Ventures VIII, L.P., Delphi Ventures VIII, L.P. and Morgenthaler Venture Partners IX, L.P. have agreed to purchase 1,150,000 shares of our common stock in this offering at the initial public offering price.

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DESCRIPTION OF CAPITAL STOCK

Upon the closing of this offering and the filing of our amended and restated certificate of incorporation, our authorized capital stock will consist of 200,000,000 shares of common stock, par value $0.0001 per share, and 10,000,000 shares of preferred stock, par value $0.0001 per share. The following is a summary of the rights of our common and preferred stock and some of the provisions of our amended and restated certificate of incorporation and amended and restated bylaws, which will each become effective upon the closing of this offering, our outstanding warrants, the investor rights agreement and Delaware General Corporation Law. Because it is only a summary, it does not contain all the information that may be important to you. For a complete description, you should refer to our amended and restated certificate of incorporation, amended and restated bylaws, the warrants and investor rights agreement, copies of which have been filed as exhibits to the registration statement of which this prospectus is a part, as well as the relevant provisions of Delaware General Corporation Law.

Common Stock

As of June 30, 2014, there were 289,531 shares of common stock and 9,592,042 shares of preferred stock outstanding, which includes the issuance and sale of 1,902,583 shares of Series D preferred stock in July 2014. After giving effect to the conversion of all outstanding shares of our preferred stock into shares of common stock immediately upon the closing of this offering, there would have been 9,881,573 shares of common stock outstanding on that date held by 72 stockholders of record. As of June 30, 2014, there were outstanding options to purchase 979,388 shares of common stock.

Voting Rights

Each holder of common stock is entitled to one vote for each share on all matters submitted to a vote of the stockholders. The affirmative vote of holders of at least a majority of the voting power of all of the then-outstanding shares of capital stock, voting as a single class, will be required to amend certain provisions of our amended and restated certificate of incorporation, including provisions relating to amending our amended and restated bylaws, the classified board, the size of our board, removal of directors, director liability, vacancies on our board, special meetings, stockholder notices, actions by written consent and exclusive jurisdiction.

Dividends

Subject to preferences that may apply to any outstanding preferred stock, holders of our common stock are entitled to receive ratably any dividends that our board of directors may declare out of funds legally available for that purpose on a non-cumulative basis.

Liquidation

In the event of our liquidation, dissolution or winding up, holders of our common stock are entitled to share ratably in all assets remaining after payment of liabilities and the liquidation preference of any outstanding preferred stock.

Rights and Preferences

Holders of our common stock have no preemptive, conversion, subscription or other rights, and there are no redemption or sinking fund provisions applicable to our common stock. The rights, preferences and privileges of the holders of our common stock are subject to and may be adversely affected by the rights of the holders of shares of any series of our preferred stock that we may designate in the future.

Preferred Stock

Immediately upon the closing of this offering, all outstanding shares of our preferred stock will convert into shares of common stock. Upon the closing of this offering, our board of directors will have the authority, without

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further action by our stockholders, to issue up to 10,000,000 shares of preferred stock in one or more series and to fix the number, rights, preferences, privileges and restrictions thereof. These rights, preferences and privileges could include dividend rights, conversion rights, voting rights, terms of redemption, liquidation preferences and sinking fund terms, and the number of shares constituting any series or the designation of such series, any or all of which may be greater than the rights of common stock. The issuance of our preferred stock could adversely affect the voting power of holders of common stock and the likelihood that such holders will receive dividend payments and payments upon liquidation. In addition, the issuance of preferred stock could have the effect of delaying, deferring or preventing a change of control or other corporate action. We have no current plan to issue any shares of preferred stock.

Stock Options

As of June 30, 2014, options to purchase an aggregate of 979,388 shares of common stock were outstanding under our 2010 Plan. In addition, options to purchase an aggregate of 306,559 shares of common stock were granted subsequent to June 30, 2014. As of June 30, 2014, 42,120 additional shares of common stock were available for future grant under our 2010 Plan and an additional 439,130 shares of common stock were reserved for future issuance under our 2010 Plan subsequent to June 30, 2014, all of which shares will cease to be available at the time our 2014 Plan becomes effective in connection with this offering. For additional information regarding the terms of this plan see the section titled Executive Compensation Employee Benefit Plans.

Stockholder Registration Rights

After the closing of this offering, certain holders of shares of our common stock, including certain holders of five percent of our capital stock and entities affiliated with certain of our directors, will be entitled to certain rights with respect to registration of such shares under the Securities Act. These shares are referred to as registrable securities. The holders of these registrable securities possess registration rights pursuant to the terms of the investor rights agreement and are described in additional detail below.

The registration of shares of our common stock pursuant to the exercise of the registration rights described below would enable the holders to trade these shares without restriction under the Securities Act when the applicable registration statement is declared effective. We will pay the registration expenses, other than underwriting discounts, selling commissions and stock transfer taxes, of the shares registered pursuant to the demand, piggyback and Form S-3 registrations described below.

Generally, in an underwritten offering, the managing underwriter, if any, has the right, subject to specified conditions, to limit the number of shares the holders may include. The demand, piggyback and Form S-3 registration rights described below will expire three years after the effective date of the registration statement, of which this prospectus forms a part, or, with respect to any particular holder, at such time that such holder can sell its shares under Rule 144 of the Securities Act during any three-month period.

Demand Registration Rights

The holders of the registrable securities will be entitled to certain demand registration rights. At any time beginning on the earlier of October 2016 or 180 days following the closing of this offering, the holders of at least 60% of the registrable securities then outstanding may make a written request that we register all or a portion of their shares, subject to certain specified exceptions. Such request for registration must cover securities the aggregate offering price of which, before payment of underwriting discounts and commissions, would exceed $50,000,000.

Piggyback Registration Rights

In connection with this offering, the holders of registrable securities were entitled to, and the necessary percentage of holders waived, their rights to notice of this offering and to include their shares of registrable securities in this offering. If we propose to register for offer and sale any of our securities under the Securities Act in another offering, either for our own account or for the account of other security holders, the holders of

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these shares will be entitled to certain piggyback registration rights allowing them to include their shares in such registration, subject to certain marketing and other limitations. As a result, whenever we propose to file a registration statement under the Securities Act, including a registration statement on Form S-3 as discussed below, other than with respect to a demand registration or a registration statement on Forms S-4 or S-8 or related to stock issued upon conversion of debt securities, the holders of these shares are entitled to notice of the registration and have the right, subject to limitations that the underwriters may impose on the number of shares included in the registration, to include their shares in the registration.

Form S-3 Registration Rights

The holders of the registrable securities will be entitled to certain Form S-3 registration rights. Any holder of these shares can make a request that we register for offer and sale their shares on Form S-3 if we are qualified to file a registration statement on Form S-3, subject to certain specified exceptions. Such request for registration on Form S-3 must cover securities the aggregate offering price of which, before payment of the underwriting discounts and commissions, equals or exceeds $5,000,000. We will not be required to effect more than two registrations on Form S-3 within any 12 month period.

Anti-Takeover Provisions of Delaware Law and Our Charter Documents

Section 203 of the Delaware General Corporation Law

We are subject to Section 203 of the Delaware General Corporation Law, which prohibits a Delaware corporation from engaging in any business combination with any interested stockholder for a period of three years after the date that such stockholder became an interested stockholder, with the following exceptions:

- before such date, the board of directors of the corporation approved either the business combination or the transaction that resulted in the stockholder becoming an interested stockholder;
- upon completion of the transaction that resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction began, excluding for purposes of determining the voting stock outstanding (but not the outstanding voting stock owned by the interested stockholder) those shares owned (1) by persons who are directors and also officers and (2) employee stock plans in which employee participants do not have the right to determine confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer; and
- on or after such date, the business combination is approved by the board of directors and authorized at an annual or special meeting of the stockholders, and not by written consent, by the affirmative vote of at least $66\,^{2}/_{3}\%$ of the outstanding voting stock that is not owned by the interested stockholder.

In general, Section 203 defines a business combination to include the following:

any merger or consolidation involving the corporation and the interested stockholder;

any sale, transfer, pledge or other disposition of 10% or more of the assets of the corporation involving the interested stockholder;

subject to certain exceptions, any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder;

any transaction involving the corporation that has the effect of increasing the proportionate share of the stock or any class or series of the corporation beneficially owned by the interested stockholder; and

the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges or other financial benefits by or through the corporation.

In general, Section 203 defines an interested stockholder as an entity or person who, together with the person s affiliates and associates, beneficially owns, or within three years prior to the time of determination of interested stockholder status owned, 15% or more of the outstanding voting stock of the corporation.

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The statute could prohibit or delay mergers or other takeover or change in control attempts and, accordingly, may discourage attempts to acquire us even though such a transaction may offer our stockholders the opportunity to sell their stock at a price above the prevailing market price.

Amended and Restated Certificate of Incorporation and Amended and Restated Bylaws

Among other things, our amended and restated certificate of incorporation and amended and restated bylaws will:

- permit our board of directors to issue up to 10,000,000 shares of preferred stock, with any rights, preferences and privileges as they may designate, including the right to approve an acquisition or other change of control;
- provide that the authorized number of directors may be changed only by resolution of our board of directors;
- provide that our board of directors will be classified into three classes of directors;
- provide that, subject to the rights of any series of preferred stock to elect directors, directors may only be removed for cause, which removal may be effected, subject to any limitation imposed by law, by the holders of at least a majority of the voting power of all of our then-outstanding shares of the capital stock entitled to vote generally at an election of directors;
- provide that all vacancies, including newly created directorships, may, except as otherwise required by law, be filled by the affirmative vote of a majority of directors then in office, even if less than a quorum;
- require that any action to be taken by our stockholders must be effected at a duly called annual or special meeting of stockholders and not be taken by written consent or electronic transmission;
- provide that stockholders seeking to present proposals before a meeting of stockholders or to nominate candidates for election as directors at a meeting of stockholders must provide advance notice in writing, and also specify requirements as to the form and content of a stockholder s notice;
- provide that special meetings of our stockholders may be called only by the chairman of our board of directors, our chief executive officer or by our board of directors pursuant to a resolution adopted by a majority of the total number of authorized directors; and
- not provide for cumulative voting rights, therefore allowing the holders of a majority of the shares of common stock entitled to vote in any election of directors to elect all of the directors standing for election, if they should so choose.

The amendment of any of these provisions would require approval by the holders of at least $66\,^{2}/_{3}\%$ of the voting power of all of our then-outstanding common stock entitled to vote generally in the election of directors, voting together as a single class.

The combination of these provisions will make it more difficult for our existing stockholders to replace our board of directors as well as for another party to obtain control of us by replacing our board of directors. Since our board of directors has the power to retain and discharge our officers, these provisions could also make it more difficult for existing stockholders or another party to effect a change in management. In addition, the authorization of undesignated preferred stock makes it possible for our board of directors to issue preferred stock with voting or other rights or preferences that could impede the success of any attempt to change our control.

These provisions are intended to enhance the likelihood of continued stability in the composition of our board of directors and its policies and to discourage coercive takeover practices and inadequate takeover bids. These provisions are also designed to reduce our vulnerability to hostile takeovers and to discourage certain tactics that may be used in proxy fights. However, such provisions could have the effect of discouraging others from making tender offers for our shares and may have the effect of delaying changes in our control or management. As a consequence, these provisions may also inhibit fluctuations in the market price of our stock

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that could result from actual or rumored takeover attempts. We believe that the benefits of these provisions, including increased protection of our potential ability to negotiate with the proponent of an unfriendly or unsolicited proposal to acquire or restructure our company, outweigh the disadvantages of discouraging takeover proposals, because negotiation of takeover proposals could result in an improvement of their terms.

Choice of Forum

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 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 certificate of incorporation or our bylaws; or any action asserting a claim against us that is governed by the internal affairs doctrine. The enforceability of similar choice of forum provisions in other companies certificates of incorporation has been challenged in legal proceedings, and it is possible that, in connection with one or more actions or proceedings described above, a court could find the choice of forum provisions contained in our certificate of incorporation to be inapplicable or unenforceable.

Listing

Our common stock has been approved for listing on the NASDAQ Global Select Market under the symbol CALA.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is American Stock Transfer & Trust Company, LLC. The transfer agent s address is 6201 15th Avenue, Brooklyn, New York 11219.

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SHARES ELIGIBLE FOR FUTURE SALE

Prior to this offering, no public market for our common stock existed, and a liquid trading market for our common stock may not develop or be sustained after this offering. Future sales of substantial amounts of our common stock in the public market, including shares issued upon exercise of outstanding options and warrants, or the anticipation of such sales, could adversely affect prevailing market prices of our common stock from time to time and could impair our future ability to raise equity capital in the future. Furthermore, because only a limited number of shares of our common stock will be available for sale shortly after this offering due to certain contractual and legal restrictions on resale described below, sales of substantial amounts of our common stock in the public market after such restrictions lapse, or the anticipation of such sales, could adversely affect the prevailing market price of our common stock and our ability to raise equity capital in the future.

Based upon the number of shares outstanding as of June 30, 2014, upon the closing of this offering, we will have outstanding an aggregate of 17,881,573 shares of our common stock, assuming no exercise of the underwriters over-allotment option and no exercise of outstanding options, after giving effect to the conversion of all outstanding shares of our preferred stock into 9,592,042 shares of common stock immediately upon the closing of this offering. All of the shares sold in this offering will be freely tradable without restrictions or further registration under the Securities Act, unless held by our affiliates, as that term is defined under Rule 144 under the Securities Act, or subject to lock-up agreements. The remaining shares of common stock outstanding upon the closing of this offering are restricted securities as defined in Rule 144. Restricted securities may be sold in the U.S. public market only if registered or if they qualify for an exemption from registration, including by reason of Rule 144 or Rule 701 under the Securities Act, which rules are summarized below. These remaining shares will generally become available for sale in the public market as follows:

- no shares will be eligible for sale in the public market on the date of this prospectus; and
- approximately 9,881,573 shares will be eligible for sale in the public market upon expiration of lock-up agreements 181 days after the date of this prospectus, subject in certain circumstances to the volume, manner of sale and other limitations of Rule 144 and Rule 701.

As of June 30, 2014, of the 979,388 shares of common stock issuable upon exercise of options outstanding, approximately 424,728 shares will be vested and eligible for sale 181 days after the date of this prospectus. In addition, approximately 40,179 shares issuable pursuant to options granted subsequent to June 30, 2014 will be vested and eligible for sale 181 days after the date of this prospectus.

We may issue shares of common stock from time to time as consideration for future acquisitions, investments or other corporate purposes. In the event that any such acquisition, investment or other transaction is significant, the number of shares of common stock that we may issue may in turn be significant. We may also grant registration rights covering those shares of common stock issued in connection with any such acquisition and investment.

In addition, the shares of common stock reserved for future issuance under our 2014 Plan and ESPP will become eligible for sale in the public market to the extent permitted by the provisions of various vesting schedules, the lock-up agreements, a registration statement under the Securities Act or an exemption from registration, including Rule 144 and Rule 701.

Rule 144

In general, persons who have beneficially owned restricted shares of our common stock for at least six months, and any affiliate of the company who owns either restricted or unrestricted shares of our common stock, are entitled to sell their securities without registration with the SEC under an exemption from registration provided by Rule 144 under the Securities Act.

In general, a person who has beneficially owned restricted shares of our common stock for at least six months would be entitled to sell their securities provided that (1) such person is not deemed to have been one of

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our affiliates at the time of, or at any time during the 90 days preceding, a sale, (2) we have been subject to the Exchange Act periodic reporting requirements for at least 90 days before the sale, and (3) we are current in our Exchange Act reporting at the time of sale.

Persons who have beneficially owned restricted shares of our common stock for at least six months, but who are our affiliates at the time of, or any time during the 90 days preceding, a sale, would be subject to additional restrictions, by which such person would be entitled to sell within any three-month period only a number of securities that does not exceed the greater of either of the following:

- 1% of the number of shares of our common stock then outstanding, which will equal approximately 178,816 shares immediately after the closing of this offering based on the number of common shares outstanding as of June 30, 2014.
- the average weekly trading volume of our common stock on the NASDAQ Global Select Market during the four calendar weeks preceding the filing of a notice on Form 144 with respect to the sale.

Such sales by affiliates must also comply with the manner of sale, current public information and notice provisions of Rule 144.

Rule 701

In general, under Rule 701 a person who purchased shares of our common stock pursuant to a written compensatory plan or contract and who is not deemed to have been one of our affiliates during the immediately preceding 90 days may sell these shares in reliance upon Rule 144, but without being required to comply with the notice, manner of sale, public information requirements or volume limitation provisions of Rule 144. Rule 701 also permits affiliates to sell their Rule 701 shares under Rule 144 without complying with the holding period requirements of Rule 144. All holders of Rule 701 shares, however, are required to wait until 90 days after the date of this prospectus before selling such shares pursuant to Rule 701. As of June 30, 2014, 208,651 shares of our outstanding common stock had been issued in reliance on Rule 701 as a result of exercises of stock options and issuance of restricted stock. However, substantially all Rule 701 shares are subject to lock-up agreements as described below and will become eligible for sale upon the expiration of the restrictions set forth in those agreements.

Form S-8 Registration Statements

We intend to file with the SEC one or more registration statements on Form S-8 under the Securities Act to register the offer and sale of shares of our common stock that are issuable pursuant to our 2010 Plan, 2014 Plan and ESPP. These registration statements will become effective immediately upon filing. Shares covered by these registration statements will then be eligible for sale in the public markets, subject to vesting restrictions, any applicable lock-up agreements described below and Rule 144 limitations applicable to affiliates.

Lock-up Agreements

We and all of our directors and executive officers and holders of substantially all of our common stock and securities exercisable for or convertible into our common stock outstanding immediately upon the closing of this offering, have agreed with the underwriters that, for a period of 180 days following the date of this prospectus, subject to certain exceptions, we and they will not, directly or indirectly, offer, sell, contract to sell, pledge, grant any option to purchase, make any short sale, or otherwise dispose of or hedge any of our shares of common stock, any options or warrants to purchase shares of our common stock, or any securities convertible into, or exchangeable for or that represent the right to receive shares of our common stock. These agreements are described in the section of this prospectus titled Underwriting.

In addition to the restrictions contained in the lock-up agreements described above, we have entered into agreements with certain security holders, including the investor rights agreement and our standard form of option agreement, that contain market stand-off provisions imposing restrictions on the ability of such security holders to offer, sell or transfer our equity securities for a period of 180 days following the date of this prospectus.

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Registration Rights

Upon the closing of this offering, the holders of 9,592,042 shares of our common stock, or their transferees, will be entitled to certain rights with respect to the registration of the offer and sale of their shares under the Securities Act. Registration of these shares under the Securities Act would result in the shares becoming freely tradable without restriction under the Securities Act immediately upon the effectiveness of the registration. See the section titled Description of Capital Stock Stockholder Registration Rights for additional information.

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MATERIAL U.S. FEDERAL INCOME AND ESTATE TAX CONSIDERATIONS FOR NON-U.S. HOLDERS OF OUR COMMON STOCK

The following summary describes the material U.S. federal income and estate tax consequences of the acquisition, ownership and disposition of our common stock acquired in this offering by Non-U.S. Holders (as defined below). This discussion does not address all aspects of U.S. federal income and estate taxes and does not deal with foreign, state and local consequences that may be relevant to Non-U.S. Holders in light of their particular circumstances, nor does it address U.S. federal tax consequences other than income and estate taxes. Special rules different from those described below may apply to certain Non-U.S. Holders that are subject to special treatment under the Internal Revenue Code of 1986, as amended, or the Code, such as financial institutions, insurance companies, tax-exempt organizations, broker-dealers and traders in securities, U.S. expatriates, controlled foreign corporations, passive foreign investment companies, corporations that accumulate earnings to avoid U.S. federal income tax, persons that hold our common stock as part of a straddle, hedge, conversion transaction, synthetic security or integrated investment or other risk reduction strategy, persons subject to the alternative minimum tax or Medicare contribution tax, partnerships and other pass-through entities, and investors in such pass-through entities. Such Non-U.S. Holders are urged to consult their own tax advisors to determine the U.S. federal, state, local and other tax consequences that may be relevant to them. Furthermore, the discussion below is based upon the provisions of the Code, and Treasury regulations, rulings and judicial decisions thereunder as of the date hereof, and such authorities may be repealed, revoked or modified, perhaps retroactively, so as to result in U.S. federal income and estate tax consequences different from those discussed below. We have not requested a ruling from the U.S. Internal Revenue Service, or IRS, with respect to the statements made and the conclusions reached in the following summary, and there can be no assurance that the IRS will agree with such statements and conclusions. This discussion assumes that the Non-U.S. Holder holds our common stock as a capital asset within the meaning of Section 1221 of the Code (generally, property held for investment).

Persons considering the purchase of our common stock pursuant to this offering should consult their own tax advisors concerning the U.S. federal income and estate tax consequences of acquiring, owning and disposing of our common stock in light of their particular situations as well as any consequences arising under the laws of any other taxing jurisdiction, including any state, local or foreign tax consequences.

For the purposes of this discussion, a Non-U.S. Holder is, for U.S. federal income tax purposes, a beneficial owner of common stock that is neither a U.S. Holder, nor a partnership (or other entity treated as a partnership for U.S. federal income tax purposes regardless of its place of organization or formation). A U.S. Holder means a beneficial owner of our common stock that is for U.S. federal income tax purposes (a) an individual who is a citizen or resident of the United States, (b) a corporation or other entity treated as a corporation created or organized in or under the laws of the United States, any state thereof or the District of Columbia, (c) an estate the income of which is subject to U.S. federal income taxation regardless of its source or (d) a trust if it (1) is subject to the primary supervision of a court within the United States and one or more U.S. persons have the authority to control all substantial decisions of the trust or (2) has a valid election in effect under applicable U.S. Treasury regulations to be treated as a U.S. person.

Distributions

Subject to the discussion below, distributions, if any, made on our common stock to a Non-U.S. Holder of our common stock to the extent made out of our current or accumulated earnings and profits (as determined under U.S. federal income tax principles) generally will constitute dividends for U.S. tax purposes and will be subject to withholding tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty. To obtain a reduced rate of withholding under a treaty, a Non-U.S. Holder generally will be required to provide us or our paying agent with a properly executed IRS Form W-8BEN, or other appropriate form, certifying the Non-U.S. Holder s entitlement to benefits under that treaty. In the case of a Non-U.S. Holder that is an entity, Treasury Regulations and the relevant tax treaty provide rules to determine whether, for purposes of

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determining the applicability of a tax treaty, dividends will be treated as paid to the entity or to those holding an interest in that entity. If a Non-U.S. Holder holds stock through a financial institution or other agent acting on the holder s behalf, the holder will be required to provide appropriate documentation to such agent. The holder s agent will then be required to provide certification to us or our paying agent, either directly or through other intermediaries. If you are eligible for a reduced rate of U.S. federal withholding tax under an income tax treaty, you may be able to obtain a refund or credit of any excess amounts withheld by timely filing an appropriate claim for a refund with the IRS.

We generally are not required to withhold tax on dividends paid to a Non-U.S. Holder that are effectively connected with the Non-U.S. Holder s conduct of a trade or business within the United States (and, if required by an applicable income tax treaty, are attributable to a permanent establishment that such holder maintains in the United States) if a properly executed IRS Form W-8ECI, stating that the dividends are so connected, is furnished to us or our paying agent (or, if stock is held through a financial institution or other agent, to such agent). In general, such effectively connected dividends will be subject to U.S. federal income tax, on a net income basis at the regular graduated rates. A corporate Non-U.S. Holder receiving effectively connected dividends may also be subject to an additional branch profits tax, which is imposed, under certain circumstances, at a rate of 30% (or such lower rate as may be specified by an applicable treaty) on the corporate Non-U.S. Holder s effectively connected earnings and profits, subject to certain adjustments.

To the extent distributions on our common stock, if any, exceed our current and accumulated earnings and profits, they will first reduce the Non-U.S. Holder s adjusted basis in our common stock, but not below zero, and then will be treated as gain to the extent of any excess, and taxed in the same manner as gain realized from a sale or other disposition of common stock as described in the next section.

Gain on Disposition of our Common Stock

Subject to the discussion below regarding backup withholding and foreign accounts, a Non-U.S. Holder generally will not be subject to U.S. federal income tax with respect to gain realized on a sale or other disposition of our common stock unless (a) the gain is effectively connected with a trade or business of such holder in the United States (and, if required by an applicable income tax treaty, is attributable to a permanent establishment that such holder maintains in the United States), (b) the Non-U.S. Holder is a nonresident alien individual and is present in the U.S. for 183 or more days in the taxable year of the disposition and certain other conditions are met or (c) we are or have been a U.S. real property holding corporation within the meaning of Code Section 897(c)(2) at any time within the shorter of the five-year period preceding such disposition or such holder s holding period. In general, we would be a U.S. real property holding corporation if interests in U.S. real estate comprised (by fair market value) at least half of our business assets. We believe that we are not, and do not anticipate becoming, a U.S. real property holding corporation. Even if we are treated as a U.S. real property holding corporation, gain realized by a Non-U.S. Holder on a disposition of our common stock will not be subject to U.S. federal income tax so long as (1) the Non-U.S. Holder owned, directly, indirectly and constructively, no more than five percent of our common stock at all times within the shorter of (i) the five-year period preceding the disposition or (ii) the holder s holding period and (2) our common stock is regularly traded on an established securities market. There can be no assurance that our common stock will qualify or will continue to qualify as regularly traded on an established securities market.

If you are a Non-U.S. Holder described in (a) above, you will be required to pay tax on the net gain derived from the sale at regular graduated U.S. federal income tax rates, and corporate Non-U.S. Holders described in (a) above may be subject to the additional branch profits tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty. If you are an individual Non-U.S. Holder described in (b) above, you will be required to pay a flat 30% tax on the gain derived from the sale, which gain may be offset by U.S. source capital losses (even though you are not considered a resident of the United States).

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Information Reporting Requirements and Backup Withholding

Generally, we must report information to the IRS with respect to any dividends we pay on our common stock including the amount of any such dividends, the name and address of the recipient, and the amount, if any, of tax withheld. A similar report is sent to the holder to whom any such dividends are paid. Pursuant to tax treaties or certain other agreements, the IRS may make its reports available to tax authorities in the recipient s country of residence.

Dividends paid by us (or our paying agents) to a Non-U.S. Holder may also be subject to U.S. backup withholding. U.S. backup withholding generally will not apply to a Non-U.S. Holder who provides a properly executed IRS Form W-8BEN or otherwise establishes an exemption.

Under current U.S. federal income tax law, U.S. information reporting and backup withholding requirements generally will apply to the proceeds of a disposition of our common stock effected by or through a U.S. office of any broker, U.S. or foreign, except that information reporting and such requirements may be avoided if the holder provides a properly executed IRS Form W-8BEN or otherwise meets documentary evidence requirements for establishing Non-U.S. Holder status or otherwise establishes an exemption. Generally, U.S. information reporting and backup withholding requirements will not apply to a payment of disposition proceeds to a Non-U.S. Holder where the transaction is effected outside the United States through a non-U.S. office of a non-U.S. broker. Information reporting and backup withholding requirements may, however, apply to a payment of disposition proceeds if the broker has actual knowledge, or reason to know, that the holder is, in fact, a U.S. person. For information reporting purposes, certain brokers with substantial U.S. ownership or operations will generally be treated in a manner similar to U.S. brokers.

Any amounts of tax withheld under the backup withholding rules may be credited against the tax liability of persons subject to backup withholding, provided that the required information is timely furnished to the IRS.

Foreign Accounts

A U.S. federal withholding tax of 30% may apply on dividends on and the gross proceeds of a disposition of our common stock paid to a foreign financial institution (as specifically defined by applicable rules) unless such institution enters into an agreement with the U.S. government to withhold on certain payments and to collect and provide to the U.S. tax authorities substantial information regarding U.S. account holders of such institution (which includes certain equity holders of such institution, as well as certain account holders that are foreign entities with U.S. owners). This U.S. federal withholding tax of 30% will also apply on dividends on and the gross proceeds of a disposition of our common stock paid to a non-financial foreign entity unless such entity provides the withholding agent with either a certification that it does not have any substantial direct or indirect U.S. owners or provides information regarding substantial direct and indirect U.S. owners of the entity. The withholding tax described above will not apply if the foreign financial institution or non-financial foreign entity otherwise qualifies for an exemption from the rules. Under certain circumstances, a Non-U.S. Holder might be eligible for refunds or credits of such taxes. Holders are encouraged to consult with their own tax advisors regarding the possible implications of these rules for their investment in our common stock.

The IRS has issued guidance providing that the withholding provisions described above will generally apply to payments of dividends made on or after July 1, 2014 and to payments of gross proceeds from a sale or other disposition of common stock on or after January 1, 2017.

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Federal Estate Tax

An individual Non-U.S. Holder who is treated as the owner of, or has made certain lifetime transfers of, an interest in our common stock will be required to include the value thereof in his or her gross estate for U.S. federal estate tax purposes, and may be subject to U.S. federal estate tax unless an applicable estate tax treaty provides otherwise, even though such individual was not a citizen or resident of the United States at the time of his or her death.

EACH PROSPECTIVE INVESTOR SHOULD CONSULT ITS OWN TAX ADVISOR REGARDING THE TAX CONSEQUENCES OF PURCHASING, HOLDING AND DISPOSING OF OUR COMMON STOCK, INCLUDING THE CONSEQUENCES OF ANY PROPOSED CHANGE IN APPLICABLE LAW.

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UNDERWRITING

Citigroup Global Markets Inc. and Leerink Partners LLC are acting as joint book-running managers of the offering and as representatives of the underwriters named below. Subject to the terms and conditions stated in the underwriting agreement dated the date of this prospectus, each underwriter named below has severally agreed to purchase, and we have agreed to sell to that underwriter, the number of shares set forth opposite the underwriter s name.

Underwriter	Number of Shares
Citigroup Global Markets Inc.	3,120,000
Leerink Partners LLC	2,560,000
Wells Fargo Securities, LLC	1,280,000
JMP Securities LLC	1,040,000
Total	8,000,000

The underwriting agreement provides that the obligations of the underwriters to purchase the shares included in this offering are subject to approval of legal matters by counsel and to other conditions. The underwriters are obligated to purchase all the shares (other than those covered by the over-allotment option described below) if they purchase any of the shares.

Shares sold by the underwriters to the public will initially be offered at the initial public offering price set forth on the cover of this prospectus. Any shares sold by the underwriters to securities dealers may be sold at a discount from the initial public offering price not to exceed $0.42 per share. If all the shares are not sold at the initial offering price, the underwriters may change the offering price and the other selling terms. The representatives have advised us that the underwriters do not intend to make sales to discretionary accounts.

If the underwriters sell more shares than the total number set forth in the table above, we have granted to the underwriters an option, exercisable for 30 days from the date of this prospectus, to purchase up to 1,200,000 additional shares at the public offering price less the underwriting discount. The underwriters may exercise the option solely for the purpose of covering over-allotments, if any, in connection with this offering. To the extent the option is exercised, each underwriter must purchase a number of additional shares approximately proportionate to that underwriter s initial purchase commitment. Any shares issued or sold under the option will be issued and sold on the same terms and conditions as the other shares that are the subject of this offering.

We, our officers and directors, and substantially all of our employees and stockholders have agreed that, for a period of 180 days from the date of this prospectus, we and they will not, without the prior written consent of Citigroup Global Markets Inc. and Leerink Partners LLC, dispose of or hedge any shares or any securities convertible into or exchangeable for our common stock. Citigroup Global Markets Inc. and Leerink Partners LLC in their sole discretion may release any of the securities subject to these lock-up agreements at any time, which, in the case of officers and directors, shall be with notice.

Prior to this offering, there has been no public market for our shares. Consequently, the initial public offering price for the shares was determined by negotiations between us and the representatives. Among the factors considered in determining the initial public offering price

were our results of operations, our current financial condition, our future prospects, our markets, the economic conditions in and future prospects for the industry in which we compete, our management, and currently prevailing general conditions in the equity securities markets, including current market valuations of publicly traded companies considered comparable to our company. We cannot assure you, however, that the price at which the shares will sell in the public market after this offering will not be lower than the initial public offering price or that an active trading market in our shares will develop and continue after this offering.

Our common stock has been approved for listing on the NASDAQ Global Select Market under the symbol CALA.

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The following table shows the underwriting discounts and commissions that we are to pay to the underwriters in connection with this offering. These amounts are shown assuming both no exercise and full exercise of the underwriters over-allotment option.

	Paid by Calithera	
	No Exercise	Full Exercise
Per share	$ 0.70	$ 0.70
Total	$ 5,600,000	$ 6,440,000

We estimate that our portion of the total expenses of this offering will be $2.7 million. We have agreed to reimburse the underwriters for expenses related to the clearing of this offering with the Financial Industry Regulatory Authority, Inc., or FINRA, in an amount up to $30,000. Such reimbursement is deemed to be underwriting compensation by FINRA.

In connection with the offering, the underwriters may purchase and sell shares in the open market. Purchases and sales in the open market may include short sales, purchases to cover short positions, which may include purchases pursuant to the over-allotment option, and stabilizing purchases.

Short sales involve secondary market sales by the underwriters of a greater number of shares than they are required to purchase in the offering.

- Covered short sales are sales of shares in an amount up to the number of shares represented by the underwriters over-allotment option.
- Naked short sales are sales of shares in an amount in excess of the number of shares represented by the underwriters over-allotment option.

Covering transactions involve purchases of shares either pursuant to the underwriters over-allotment option or in the open market in order to cover short positions.

- To close a naked short position, the underwriters must purchase shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the shares in the open market after pricing that could adversely affect investors who purchase in the offering.
- To close a covered short position, the underwriters must purchase shares in the open market or must exercise the over-allotment option. In determining the source of shares to close the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase shares through the over-allotment option.

Stabilizing transactions involve bids to purchase shares so long as the stabilizing bids do not exceed a specified maximum.

Purchases to cover short positions and stabilizing purchases, as well as other purchases by the underwriters for their own accounts, may have the effect of preventing or retarding a decline in the market price of the shares. They may also cause the price of the shares to be higher than the price that would otherwise exist in the open market in the absence of these transactions. The underwriters may conduct these transactions on the NASDAQ Global Select Market, in the over-the-counter market or otherwise. If the underwriters commence any of these transactions, they may discontinue them at any time.

Other Relationships

The underwriters are full-service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, principal

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investment, hedging, financing and brokerage activities. Certain of the underwriters and their respective affiliates may, from time to time, engage in transactions with and perform services for us in the ordinary course of their business for which they may receive customary fees and reimbursement of expenses. In the ordinary course of their various business activities, the underwriters and their respective affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (which may include bank loans and/or credit default swaps) for their own account and for the accounts of their customers and may at any time hold long and short positions in such securities and instruments. Such investments and securities activities may involve securities and/or instruments of ours or our affiliates. The underwriters and their affiliates may also make investment recommendations and/or publish or express independent research views in respect of such securities or financial instruments and may hold, or recommend to clients that they acquire, long and/or short positions in such securities and instruments.

In July 2014, entities affiliated with Leerink Partners LLC purchased an aggregate of 118,910 shares of our Series D preferred stock on the same terms as the other investors, which shares will automatically convert into 118,910 shares of our common stock immediately upon the closing of this offering. This preferred stock and the common stock into which it converts are subject to a 180-day lock-up under FINRA Rule 5110(g)(1) pursuant to which the entities affiliated with Leerink Partners LLC (or permitted assignees under the Rule) will not sell, transfer, assign, pledge or hypothecate the preferred stock or the common stock into which it converts, nor will they engage in any hedging, short sale, derivative, put or call transaction that would result in the effective economic disposition of the preferred stock or the common stock into which it converts for a period of 180 days immediately following the date of effectiveness, except as provided in FINRA Rule 5110(g)(2).

We have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act, or to contribute to payments the underwriters may be required to make because of any of those liabilities.

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 that had submitted indications of interest have agreed to purchase 1,650,000 shares of our common stock in this offering at the initial public offering price. The underwriters will receive the same discount from the 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.

Notice to Prospective Investors in the European Economic Area

In relation to each member state of the European Economic Area that has implemented the Prospectus Directive (each, a relevant member state), with effect from and including the date on which the Prospectus Directive is implemented in that relevant member state (the relevant implementation date), an offer of shares described in this prospectus may not be made to the public in that relevant member state other than:

to any legal entity which is a qualified investor as defined in the Prospectus Directive;

to fewer than 100 or, if the relevant member state has implemented the relevant provision of the 2010 PD Amending Directive, 150 natural or legal persons (other than qualified investors as defined in the Prospectus Directive), as permitted under the Prospectus Directive, subject to obtaining the prior consent of the relevant Dealer or Dealers nominated by us for any such offer; or

in any other circumstances falling within Article 3(2) of the Prospectus Directive,

provided that no such offer of shares shall require us or any underwriter to publish a prospectus pursuant to Article 3 of the Prospectus Directive.

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For purposes of this provision, the expression an offer of securities to the public in any relevant member state means the communication in any form and by any means of sufficient information on the terms of the offer and the shares to be offered so as to enable an investor to decide to purchase or subscribe for the shares, as the expression may be varied in that member state by any measure implementing the Prospectus Directive in that member state, and the expression Prospectus Directive means Directive 2003/71/EC (and amendments thereto, including the 2010 PD Amending Directive, to the extent implemented in the relevant member state) and includes any relevant implementing measure in the relevant member state. The expression 2010 PD Amending Directive means Directive 2010/73/EU.

The sellers of the shares have not authorized and do not authorize the making of any offer of shares through any financial intermediary on their behalf, other than offers made by the underwriters with a view to the final placement of the shares as contemplated in this prospectus. Accordingly, no purchaser of the shares, other than the underwriters, is authorized to make any further offer of the shares on behalf of the sellers or the underwriters.

Notice to Prospective Investors in the United Kingdom

This prospectus is only being distributed to, and is only directed at, persons in the United Kingdom that are qualified investors within the meaning of Article 2(1)(e) of the Prospectus Directive that are also (i) investment professionals falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005 (the Order) or (ii) high net worth entities, and other persons to whom it may lawfully be communicated, falling within Article 49(2)(a) to (d) of the Order (each such person being referred to as a relevant person). This prospectus and its contents are confidential and should not be distributed, published or reproduced (in whole or in part) or disclosed by recipients to any other persons in the United Kingdom. Any person in the United Kingdom that is not a relevant person should not act or rely on this document or any of its contents.

Notice to Prospective Investors in France

Neither this prospectus nor any other offering material relating to the shares described in this prospectus has been submitted to the clearance procedures of the *Autorité des Marchés Financiers* or of the competent authority of another member state of the European Economic Area and notified to the *Autorité des Marchés Financiers*. The shares have not been offered or sold and will not be offered or sold, directly or indirectly, to the public in France. Neither this prospectus nor any other offering material relating to the shares has been or will be:

- released, issued, distributed or caused to be released, issued or distributed to the public in France; or
- used in connection with any offer for subscription or sale of the shares to the public in France.

Such offers, sales and distributions will be made in France only:

- to qualified investors (*investisseurs qualifiés*) and/or to a restricted circle of investors (*cercle restreint d investisseurs*), in each case investing for their own account, all as defined in, and in accordance with articles L.411-2, D.411-1, D.411-2, D.734-1, D.744-1,

D.754-1 and D.764-1 of the French *Code monétaire et financier*;

to investment services providers authorized to engage in portfolio management on behalf of third parties; or

in a transaction that, in accordance with article L.411-2-II-1°-or-2°-or 3° of the French *Code monétaire et financier* and article 211-2 of the General Regulations (*Règlement Général*) of the *Autorité des Marchés Financiers*, does not constitute a public offer (*appel public à l épargne*).

The shares may be resold directly or indirectly, only in compliance with articles L.411-1, L.411-2, L.412-1 and L.621-8 through L.621-8-3 of the French *Code monétaire et financier*.

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Notice to Prospective Investors in Australia

No prospectus or other disclosure document (as defined in the Corporations Act 2001 (Cth) of Australia (Corporations Act)) in relation to the common stock has been or will be lodged with the Australian Securities & Investments Commission (ASIC). This document has not been lodged with ASIC and is only directed to certain categories of exempt persons. Accordingly, if you receive this document in Australia:

(a) you confirm and warrant that you are either:

(i) a sophisticated investor under section 708(8)(a) or (b) of the Corporations Act;

(ii) a sophisticated investor under section 708(8)(c) or (d) of the Corporations Act and that you have provided an accountant s certificate to us which complies with the requirements of section 708(8)(c)(i) or (ii) of the Corporations Act and related regulations before the offer has been made;

(iii) a person associated with the company under section 708(12) of the Corporations Act; or

(iv) a professional investor within the meaning of section 708(11)(a) or (b) of the Corporations Act, and to the extent that you are unable to confirm or warrant that you are an exempt sophisticated investor, associated person or professional investor under the Corporations Act any offer made to you under this document is void and incapable of acceptance; and

(b) you warrant and agree that you will not offer any of the common stock for resale in Australia within 12 months of that common stock being issued unless any such resale offer is exempt from the requirement to issue a disclosure document under section 708 of the Corporations Act.

Notice to Prospective Investors in Hong Kong

The shares may not be offered or sold in Hong Kong by means of any document other than (i) in circumstances which do not constitute an offer to the public within the meaning of the Companies Ordinance (Cap. 32, Laws of Hong Kong), or (ii) to professional investors within the meaning of the Securities and Futures Ordinance (Cap. 571, Laws of Hong Kong) and any rules made thereunder, or (iii) in other circumstances which do not result in the document being a prospectus within the meaning of the Companies Ordinance (Cap. 32, Laws of Hong Kong) and no advertisement, invitation or document relating to the shares may be issued or may be in the possession of any person for the purpose of issue (in each case whether in Hong Kong or elsewhere), which is directed at, or the contents of which are likely to be accessed or read by, the public in Hong Kong (except if permitted to do so under the laws of Hong Kong) other than with respect to shares which are or are intended to be disposed of only to persons outside Hong Kong or only to professional investors within the meaning of the Securities and Futures Ordinance (Cap. 571, Laws of Hong Kong) and any rules made thereunder.

Notice to Prospective Investors in Japan

The shares offered in this prospectus have not been and will not be registered under the Financial Instruments and Exchange Law of Japan. The shares have not been offered or sold and will not be offered or sold, directly or indirectly, in Japan or to or for the account of any resident of Japan (including any corporation or other entity organized under the laws of Japan), except (i) pursuant to an exemption from the registration requirements of the Financial Instruments and Exchange Law and (ii) in compliance with any other applicable requirements of Japanese law.

Notice to Prospective Investors in Singapore

This prospectus has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the shares may not be circulated or distributed, nor may the shares be

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offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (i) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore (the SFA), (ii) to a relevant person pursuant to Section 275(1), or any person pursuant to Section 275(1A), and in accordance with the conditions specified in Section 275 of the SFA or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA, in each case subject to compliance with conditions set forth in the SFA.

Where the shares are subscribed or purchased under Section 275 of the SFA by a relevant person which is:

a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or

a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary of the trust is an individual who is an accredited investor,

shares, debentures and units of shares and debentures of that corporation or the beneficiaries rights and interest (howsoever described) in that trust shall not be transferred within six months after that corporation or that trust has acquired the shares pursuant to an offer made under Section 275 of the SFA except:

to an institutional investor (for corporations, under Section 274 of the SFA) or to a relevant person defined in Section 275(2) of the SFA, or to any person pursuant to an offer that is made on terms that such shares, debentures and units of shares and debentures of that corporation or such rights and interest in that trust are acquired at a consideration of not less than $0.2 million (or its equivalent in a foreign currency) for each transaction, whether such amount is to be paid for in cash or by exchange of securities or other assets, and further for corporations, in accordance with the conditions specified in Section 275 of the SFA;

where no consideration is or will be given for the transfer; or

where the transfer is by operation of law.

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LEGAL MATTERS

The validity of the shares of common stock offered hereby will be passed upon for us by Cooley LLP, Palo Alto, California. As of the date of this prospectus, GC&H Investments, LLC and GC&H Investments, entities comprised of partners and associates of Cooley LLP, beneficially own an aggregate of 8,917 shares of our preferred stock, all of which will be converted into 8,917 shares of common stock upon the closing of this offering. Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C., Boston, Massachusetts is acting as counsel to the underwriters.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our financial statements at December 31, 2012 and 2013, and for each of the two years in the period ended December 31, 2013, as set forth in their report. We have included our financial statements in the prospectus and elsewhere in the registration statement in reliance on Ernst & Young LLP s report, given on their authority as experts in accounting and auditing.

WHERE CAN YOU FIND ADDITIONAL INFORMATION

We have filed with the SEC a registration statement on Form S-1 under the Securities Act with respect to the shares of common stock being offered by this prospectus. This prospectus does not contain all of the information in the registration statement and its exhibits. For further information about us and the common stock offered by this prospectus, we refer you to the registration statement and its exhibits. Statements contained in this prospectus as to the contents of any contract or any other document referred to are not necessarily complete, and in each instance, we refer you to the copy of the contract or other document filed as an exhibit to the registration statement. Each of these statements is qualified in all respects by this reference.

You can read our SEC filings, including the registration statement, over the Internet at the SEC s website at http://www.sec.gov. You may also read and copy any document we file with the SEC at its public reference facilities at 100 F Street, NE, Washington, D.C. 20549. You may also obtain copies of these documents at prescribed rates by writing to the Public Reference Section of the SEC at 100 F Street, NE, Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the operation of the public reference facilities.

Upon the closing of this offering, we will be subject to the information reporting requirements of the Exchange Act, and we will file reports, proxy statements and other information with the SEC. These reports, proxy statements and other information will be available for inspection and copying at the public reference room and web site of the SEC referred to above. We also maintain a website at www.calithera.com, at which you may access these materials free of charge as soon as reasonably practicable after they are electronically filed with, or furnished to, the SEC. The information contained on, or that can be accessed through, our website is not a part of this prospectus. Investors should not rely on any such information in deciding whether to purchase our common stock. We have included our website address in this prospectus solely as an inactive textual reference.

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CALITHERA BIOSCIENCES, INC.

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REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Board of Directors and Stockholders of

Calithera Biosciences, Inc.

We have audited the accompanying balance sheets of Calithera Biosciences, Inc. (the Company) as of December 31, 2012 and 2013, and the related statements of operations and comprehensive loss, convertible preferred stock and stockholders deficit, and cash flows for each of the two years in the period ended December 31, 2013. These financial statements are the responsibility of the Company s management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. We were not engaged to perform an audit of the Company s internal control over financial reporting. Our audits included consideration of internal control over financial reporting as a basis for designing audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the Company s internal control over financial reporting. Accordingly, we express no such opinion. An audit also includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of the Company at December 31, 2012 and 2013, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2013 in conformity with U.S. generally accepted accounting principles.

/s/ Ernst & Young LLP

Redwood City, California

July 25, 2014, except for the last paragraph in Note 1, as to which the date is September 19, 2014

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CALITHERA BIOSCIENCES, INC.

BALANCE SHEETS

(in thousands, except per share amounts)

	December 31, 2012	December 31, 2013
Assets		
Current assets:		
Cash and cash equivalents	$ 2,205	$ 33,820
Prepaid expenses and other current assets	67	349
Total current assets	2,272	34,169
Restricted cash	107	116
Property and equipment, net	681	559
Total assets	$ 3,060	$ 34,844
Liabilities, Convertible Preferred Stock and Stockholders Deficit		
Current liabilities:		
Accounts payable	$ 25	$ 150
Accrued liabilities	884	1,194
Total current liabilities	909	1,344
Deferred rent		31
Total liabilities	909	1,375
Commitments and contingencies (Note 8)		
Convertible preferred stock, $0.0001 par value: 4,019 and 7,757 shares authorized as of December 31, 2012 and 2013; 1,704 and 7,689 shares issued and outstanding as of December 31, 2012 and 2013; aggregate liquidation preference of $55,450 as of December 31, 2013	10,722	54,282
Stockholders deficit:		
Common stock, $0.0001 par value, 5,208 and 9,896 shares authorized as of December 31, 2012 and 2013; 58 and 161 shares issued and outstanding as of December 31, 2012 and 2013		1
Additional paid-in capital	9,194	9,328
Accumulated deficit	(17,765)	(30,142)
Total stockholders deficit	(8,571)	(20,813)
Total liabilities, convertible preferred stock and stockholders deficit	$ 3,060	$ 34,844

See accompanying notes.

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CALITHERA BIOSCIENCES, INC.

STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS

(in thousands, except per share amounts)

	Year Ended December 31,	
	2012	2013
Operating expenses:		
Research and development	$ 6,558	$ 9,900
General and administrative	1,417	2,478
Total operating expenses	7,975	12,378
Loss from operations	(7,975)	(12,378)
Other income		1
Net loss and comprehensive loss	(7,975)	(12,377)
Gain on extinguishment of convertible preferred stock	2,889	
Net loss attributable to common stockholders	$ (5,086)	$ (12,377)
Net loss per share attributable to common stockholders, basic and diluted	$ (366.13)	$ (131.53)
Shares used in computing net loss per share attributable to common stockholders, basic and diluted	14	94
Pro forma net loss per share attributable to common stockholders, basic and diluted (unaudited)		$ (3.03)
Shares used in computing pro forma net loss per share attributable to common stockholders, basic and diluted (unaudited)		4,083

See accompanying notes.

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CALITHERA BIOSCIENCES, INC.

STATEMENTS OF CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS DEFICIT

(in thousands, except per share amounts)

	Convertible Preferred Stock		Common Stock		Additional Paid-In Capital	Accumulated Deficit	Total Stockholders Deficit
	Shares	Amount	Shares	Amount			
Balance at December 31, 2011	875	$ 7,689	10	$	$ 6,230	$ (9,790)	$ (3,560)
Issuance of Series B convertible preferred stock for cash at $4.77 per share in May 2012, net of $15 in issuance costs	838	3,985					
Extinguishment of convertible preferred stock and related conversion to common stock	(428)	(2,930)	43		41		41
Gain on extinguishment of convertible preferred stock					2,889		2,889
Issuance of Series C convertible preferred stock for cash at $4.77 per share in December 2012, net of $22 in issuance costs	419	1,978					
Vesting of common stock issued to founders			3				
Exercise of stock options			2		3		3
Stock-based compensation expense					31		31
Net loss						(7,975)	(7,975)
Balance at December 31, 2012	1,704	10,722	58		9,194	(17,765)	(8,571)
Issuance of Series C convertible preferred stock for cash at $4.77 per share in April 2013, net of $24 in issuance costs	1,823	8,676					
Issuance of Series D convertible preferred stock for cash at $8.41 per share in October 2013, net of $115 in issuance costs	4,162	34,884					
Vesting of common stock issued to founders			3				
Exercise of stock options			100	1	64		65
Stock-based compensation expense					70		70
Net loss						(12,377)	(12,377)
Balance at December 31, 2013	7,689	$ 54,282	161	$ 1	$ 9,328	$ (30,142)	$ (20,813)

See accompanying notes.

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CALITHERA BIOSCIENCES, INC.

STATEMENTS OF CASH FLOWS

(in thousands)

	Year Ended December 31,	
	2012	**2013**
Cash Flows From Operating Activities		
Net loss	$ (7,975)	$ (12,377)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	269	281
Stock-based compensation	31	70
Loss on disposal of property and equipment	7	5
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	(9)	(282)
Accounts payable	25	125
Accrued liabilities	675	310
Deferred rent	(13)	31
Net cash used in operating activities	(6,990)	(11,837)
Cash Flows From Investing Activities		
Purchase of property and equipment	(49)	(164)
Increase in restricted cash		(9)
Net cash used in investing activities	(49)	(173)
Cash Flows From Financing Activities		
Proceeds from issuance of convertible preferred stock, net of issuance costs	5,963	43,560
Proceeds from issuance of common stock	3	65
Net cash provided by financing activities	5,966	43,625
Net increase (decrease) in cash and cash equivalents	(1,073)	31,615
Cash and cash equivalents at beginning of period	3,278	2,205
Cash and cash equivalents at end of period	$ 2,205	$ 33,820
Supplemental Disclosures of Non-Cash Investing and Financing Information:		
Conversion of convertible preferred stock to common stock	$ 41	$
Gain on extinguishment of convertible preferred stock	$ 2,889	$

See accompanying notes.

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CALITHERA BIOSCIENCES, INC.

NOTES TO FINANCIAL STATEMENTS

1. Organization and Basis of Presentation

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

Liquidity

In the course of its development activities, the Company has sustained operating losses and expects such losses to continue over the next several years. The Company s ultimate success depends on the outcome of its research and development activities. The Company has incurred net losses from operations since inception and has an accumulated deficit of $30.1 million as of December 31, 2013. In July 2014, the Company issued 1,902,583 shares of Series D convertible preferred stock for $16.0 million in net proceeds (see Note 11). The Company intends to raise additional capital through the issuance of additional equity, and potentially through strategic alliances with partner companies. However, if such financing is not available at adequate levels, the Company will need to reevaluate its operating plans. Management believes that the currently available resources will provide sufficient funds to enable the Company to meet its operating plan for at least the next twelve months. However, if the Company s anticipated operating results are not achieved in future periods, management believes that planned expenditures may need to be reduced in order to extend the time period over which the then-available resources would be able to fund the Company s operations.

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

2. Summary of Significant Accounting Policies

Use of Estimates

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

Cash and Cash Equivalents

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

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Restricted Cash

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

Concentration of Credit Risk

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

Property and Equipment

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

The useful lives of the property and equipment are as follows:

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

Impairment of Long-Lived Assets

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

Accrued Research and Development Costs

The Company accrues for estimated costs of research and development activities conducted by third-party service providers, which include the conduct of preclinical studies and clinical trials, and contract manufacturing activities. The Company records the estimated costs of research and development activities based upon the estimated amount of services provided but not yet invoiced, and include these costs in accrued liabilities in the balance sheets and within research and development expense in the statements of operations and comprehensive loss. These costs are a significant component of the Company s research and development expenses. The Company accrues for these costs based on factors such as estimates of the work completed and in accordance with agreements established with its third-party service providers. The Company makes significant judgments and estimates in determining the accrued liabilities balance in each reporting period. As actual costs become

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known, the Company adjusts its accrued liabilities. The Company has not experienced any material differences between accrued costs and actual costs incurred. However, the status and timing of actual services performed, number of patients enrolled, and the rate of patient enrollments may vary from the Company s estimates, resulting in adjustments to expense in future periods. Changes in these estimates that result in material changes to the Company s accruals could materially affect the Company s results of operations.

Research and Development Costs

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

Deferred Rent

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

Convertible Preferred Stock

The Company records all shares of convertible preferred stock net of offering costs on the dates of issuance, which represents the carrying value. Upon certain change-in-control events that are outside the control of the Company, including liquidation, sale or transfer of control of the Company, holders of the convertible preferred stock can cause redemption for cash. Accordingly, the convertible preferred stock shares are considered contingently redeemable, and therefore classified as temporary equity on the balance sheets instead of within stockholders deficit. The Company has not adjusted the carrying value of the convertible preferred stock to their redemption values, since it is uncertain whether or when, a redemption event will occur.

Stock-Based Compensation

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

Income Taxes

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

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The Company recognizes benefits of uncertain tax positions if it is more likely than not that such positions will be sustained upon examination based solely on their technical merits, as the largest amount of benefit that is more likely than not to be realized upon the ultimate settlement. The Company s policy is to recognize interest and penalties related to the underpayment of income taxes as a component of income tax expense or benefit. To date, there have been no interest or penalties charged in relation to the unrecognized tax benefits.

Net Loss per Share Attributable to Common Stockholders

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

Unaudited Pro Forma Net Loss per Share Attributable to Common Stockholders

Unaudited pro forma basic and diluted net loss per share attributable to common stockholders has been computed to give effect to the conversion of the shares of convertible preferred stock into common stock as if such conversion had occurred as of January 1, 2013 or the original date of issuance, if later. The unaudited pro forma net loss per share attributable to common stockholders does not include the shares expected to be sold and related proceeds to be received from an initial public offering.

Recent Accounting Pronouncements

In June 2014, the Financial Accounting Standards Board issued Accounting Standards Update (ASU) 2014-10, *Development Stage Entities (Topic 915): Elimination of Certain Financial Reporting Requirements, Including an Amendment to Variable Interest Entities Guidance in Topic 810, Consolidation.* ASU 2014-10 simplifies the accounting guidance by removing all incremental financial reporting requirements for development stage entities. The amendments related to the elimination of the inception-to-date information and other disclosure requirement of Topic 915 should be applied retrospectively, and are effective for annual reporting periods beginning after December 15, 2014, and interim periods therein. The Company has elected to early adopt this guidance as of January 1, 2012.

3. Fair Value Measurements

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

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

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

Level 2 Inputs are observable, unadjusted quoted prices in active markets for similar assets or liabilities, unadjusted quoted prices for identical or similar assets or liabilities in markets that are not active, or other

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inputs that are observable or can be corroborated by observable market data for substantially the full term of the related assets or liabilities; and

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

The Company s financial instruments consist only of Level 1 assets, which are highly liquid money market funds. As of December 31, 2012 and 2013, the Company had $107,000 and $116,000 in money market funds that are included in restricted cash on the balance sheets.

4. Balance Sheet Components

Property and Equipment, Net

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

	December 31,	
	2012	2013
Research and development equipment	$ 1,116	$ 1,137
Furniture and office equipment	30	52
Computer equipment	97	156
Software	36	38
Leasehold improvements	12	47
Total property and equipment	1,291	1,430
Less: accumulated depreciation and amortization	(610)	(871)
Property and equipment, net	$ 681	$ 559

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

Accrued Liabilities

Accrued liabilities consist of the following (in thousands):

	December 31, 2012	December 31, 2013
Accrued bonus and payroll expenses	$ 758	$ 934
Accrued professional and consulting services	108	127
Accrued clinical and manufacturing expenses	15	107
Other	3	26
Total accrued liabilities	$ 884	$ 1,194

5. Convertible Preferred Stock and Stockholders Deficit

Convertible Preferred Stock

Under the Company s Amended and Restated Certificate of Incorporation, the Company is authorized to issue two classes of shares: convertible preferred and common stock.

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As of December 31, 2012, convertible preferred stock consisted of the following (in thousands, except share amounts):

	Shares Authorized	Shares Outstanding	Carrying Values	Liquidation Preference
Series A	36,665	27,497	$ 2,786	$ 3,750
Series B	1,676,727	1,257,543	5,958	6,000
Series C	2,305,499	419,181	1,978	2,000
Total	4,018,891	1,704,221	$ 10,722	$ 11,750

As of December 31, 2013, convertible preferred stock consisted of the following (in thousands, except share amounts):

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

Significant provisions of the convertible preferred stock are as follows:

Dividends When, as and if declared by the Company s Board of Directors, the holders of the Series A convertible preferred stock (Series A), the Series B convertible preferred stock (Series B), the Series C convertible preferred stock (Series C), the Series D convertible preferred stock (Series D), collectively referred to as Preferred Stock, are entitled to receive non-cumulative dividends, out of any assets legally available, prior and in preference to the declaration or payment of any dividend on the common stock or other securities and rights convertible of the Company, at the rate equal to 8% of the respective original issue price. The original issue price per share for Series B is $4.77, for Series C is $4.77, and for Series D is $8.41. In 2011, in conjunction with the issuance of Series B, the Company adjusted the original issue price per share for Series A from $272.74 to $136.37. There have been no dividends declared as of December 31, 2013.

Liquidation In the event of any liquidation, dissolution, or winding up of the Company, either voluntary or involuntary, the holders of Series A, Series B, Series C, and Series D are entitled to receive, on a pari passu basis, prior and in preference to any distribution of any of the assets of the Company to the holders of common stock by reason of their ownership thereof, an amount per share equal to respective original issue price for each outstanding share of Series A, Series B, Series C and Series D (subject to adjustment for recapitalizations) and an amount equal to all declared but unpaid dividends on such shares. If available assets are insufficient to pay the full liquidation preference, the available assets will be distributed ratably among the holders of preferred stock. If there are excess assets to be allocated on liquidation beyond what is described above, holders of preferred stock and common stock will share in such assets on an as-converted basis.

Voting Each holder of shares of Preferred Stock is entitled to the number of votes equal to the number of shares of common stock into which such shares of Preferred Stock could be converted and has voting rights and powers equal to the voting rights and powers of the common stock, and shall vote together with the common stock as a single class on an as-converted basis on all matters as to which holders of common stock have the right to vote.

For as long as at least 10,000,000 shares of Preferred Stock (subject to adjustment for any stock split or other similar event affecting the Preferred Stock after the filing date thereof) remain outstanding, the Company may not, either directly or indirectly by amendment, merger, consolidation or otherwise, make modifications to

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the terms of the Preferred Stock or take certain other specified actions without the written or affirmative vote of the holders of at least 60% of the then outstanding shares of Preferred Stock (voting together as a single class on an as-converted basis), given in writing or by vote at a meeting, consenting or voting (as the case may be).

Conversion Each share of preferred stock, at the option of the holder, is convertible into common stock determined by dividing the original issue price of the respective Preferred Stock, as applicable, by the conversion price applicable to such share in effect on the date the certificate is surrendered for conversion, subject to certain provisions for adjustment of the conversion price. Conversion of each share of Preferred Stock is automatic upon the closing of a firm commitment underwritten public offering with aggregate gross proceeds of not less than $50.0 million (before deduction of underwriting discounts and commissions) or the agreement or written consent of holders of at least 60% of the then-outstanding shares of Preferred Stock.

Extinguishment of Preferred Stock

In 2011, the liquidation preference of the Series A was reduced from $272.74 per share to $136.37 per share in conjunction with the issuance of Series B. The Company has accounted for the amendment to the liquidation preference of the Series A as an extinguishment of the initial Series A and establishment of an adjusted Series A due to the significance of the change in the fair value. The Company recorded a gain of $6.2 million within stockholders deficit equal to the difference between the fair value of the adjusted Series A and the carrying amount of the initial Series A extinguished.

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

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

Common Stock

Common stockholders are entitled to dividends when, as and if declared by the Board of Directors, subject to the prior rights of the preferred stockholders. As of December 31, 2013, no dividends had been declared by the Board of Directors.

As of December 31, 2013, the Company had reserved shares of common stock for issuance as follows:

Convertible preferred stock outstanding	7,689,459
Options issued and outstanding	864,830
Options available for future grants	263,428
Total	8,817,717

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Restricted Stock

In March 2010, the Company entered into a restricted stock purchase agreement with two founders of the Company. The individuals purchased a total of 17,416 shares of common stock for a total purchase price of $836. These agreements contain a repurchase option that gives the Company an irrevocable option for a period of ninety days after the individual s employment is terminated either voluntarily or involuntarily to repurchase the unvested restricted stock at a price that is the lower of the original price per share paid by the founder for such stock or the fair value as of the date of such repurchase. The restricted stock vested and the repurchase option lapsed over 48 months measured from the date that the first share of Series A was issued, which was June 17, 2010. As of December 31, 2012 and 2013, 3,973 and 1,146 of these shares, respectively, remained subject to repurchase.

6. Stock Option Plan

In 2010, the Company adopted the 2010 Equity Incentive Plan (the 2010 Plan). Under the Plan, shares of the Company s common stock have been reserved for the issuance of stock options to employees, directors, and consultants under terms and provisions established by the Board of Directors. A total of 1,230,298 shares were reserved for issuance under the 2010 Plan at December 31, 2013, of which 263,428 shares are available for future grant. Under the terms of the 2010 Plan, options may be granted at an exercise price not less than fair market value. For employees holding more than 10% of the voting rights of all classes of stock, the exercise prices for incentive and nonstatutory stock options may not be less than 110% of fair market value, as determined by the Board of Directors. The terms of options granted under the 2010 Plan may not exceed ten years. The vesting schedule of newly issued option grants is typically four years.

The following summarizes option activity under the 2010 Plan (in thousands, except share and price per option data):

	Shares Available for Grant	Number of Options	Weighted-Average Exercise Price Per Option	Aggregate Intrinsic Value
Balance as of December 31, 2011	20,757	134,781	$ 1.08	
Shares reserved	136,482			
Options granted	(127,452)	127,452	$ 0.48	
Options exercised		(1,765)	$ 1.46	
Options canceled	15,540	(15,540)	$ 0.92	
Balance as of December 31, 2012	45,327	244,928	$ 0.77	
Shares reserved	938,276			
Options granted	(725,161)	725,161	$ 1.99	
Options exercised		(100,273)	$ 0.64	
Options canceled	4,986	(4,986)	$ 1.05	
Balance Outstanding as of December 31, 2013	263,428	864,830	$ 1.80	$ 769
Exercisable as of December 31, 2013		58,458	$ 1.56	$ 102
Vested and expected to vest as of December 31, 2013			$ 1.81	$ 725

The aggregate intrinsic values of options outstanding, exercisable, vested and expected to vest were calculated as the difference between the exercise price of the options and the estimated fair value of the Company s common stock, as determined by the Board of Directors, as of December 31, 2013.

The total fair value of options that vested during the years ended December 31, 2012 and 2013 was $32,000 and $60,000, respectively.

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As of December 31, 2013, the weighted-average remaining contractual life was 8.6 years and 9.5 years for exercisable options and vested and expected to vest options, respectively.

Stock-Based Compensation Expense

Total stock-based compensation recognized was as follows (in thousands):

	Year Ended December 31,	
	2012	2013
Research and development	$ 21	$ 47
General and administrative	10	23
Total stock-based compensation expense	$ 31	$ 70

The weighted-average fair value per share of employee options granted during the years ended December 31, 2012 and 2013 were $0.48 and $1.44, respectively. As of December 31, 2013, the total unrecognized compensation expense related to unvested options, net of estimated forfeitures, was $1.1 million, which the Company expects to recognize over an estimated weighted average period of 3.7 years.

The fair value of the shares of common stock underlying stock options has historically been determined by the Company s Board of Directors. Because there has been no public market for the Company s common stock, the Board of Directors has determined fair value of the common stock at the time of grant of the option by considering a number of objective and subjective factors including important developments in the Company s operations, valuations performed by an independent third party, sales of convertible preferred stock, actual operating results and financial performance, the conditions in the biotechnology industry and the economy in general, the stock price performance and volatility of comparable public companies, and the lack of liquidity of the Company s common stock, among other factors.

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

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

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

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

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

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

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

	Year Ended December 31,	
	2012	2013
Expected term (in years)	5.9	6.3
Volatility	79.8%	87.1 96.0%
Risk-free interest rate	0.9%	1.1 1.9%
Dividend yield		

7. Income Taxes

No provision for income taxes was recorded for the years ended December 31, 2012 and 2013. The Company has incurred net operating losses for all the periods presented. The Company has not reflected any benefit of such net operating loss carryforwards in the accompanying financial statements. The Company has established a full valuation allowance against its deferred tax assets due to the uncertainty surrounding the realization of such assets.

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

	Year Ended December 31,	
	2012	2013
Federal statutory income tax rate	34.0%	34.0%
State income taxes, net of federal benefit	5.8	5.8
Federal and state tax credits	1.2	3.8
Change in valuation allowance	(41.0)	(43.6)
	0.0%	0.0%

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

	December 31,	
	2012	2013
Deferred tax assets:		
Net operating loss carryforwards	$ 6,804	$ 11,584
Tax credits	451	963
Accrued liabilities	302	384
Others	71	91
Gross deferred tax assets	7,628	13,022
Valuation allowance	(7,628)	(13,022)

Net deferred tax assets	$	$

Due to the Company s lack of earnings history, the deferred tax assets have been fully offset by a valuation allowance as of December 31, 2012 and 2013. The valuation allowance increased by $3.3 million and $5.4 million during the years ended December 31, 2012 and 2013, respectively.

As of December 31, 2013, the Company 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.

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As of December 31, 2013, the Company 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.

Uncertain Tax Positions

A reconciliation of the Company s unrecognized tax benefits for the years ended December 31, 2012 and 2013 is as follows (in thousands):

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

The Company does not expect the unrecognized tax benefits to change significantly over the next 12 months.

Interest and penalties are zero, and the Company s policy is to account for interest and penalties in tax expense on the statement of operations and comprehensive loss. The Company files income tax returns in the U.S. federal and California tax jurisdictions. All periods since inception are subject to examination by U.S. federal and California tax jurisdictions.

8. Commitments and Contingencies

Facilities

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

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

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

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Future aggregate minimum lease payments under the noncancelable operating leases as of December 31, 2013 (in thousands):

Year ending December 31,	Amounts
2014	$ 716
2015	960
2016	960
2017	880
Total	$ 3,516

Rent expense under operating leases was $782,000 and $866,000 for the years ended December 31, 2012 and 2013, respectively.

Indemnifications

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

9. Net Loss per Common Share and Unaudited Pro Forma Net Loss per Common Share

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

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

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The Company has presented unaudited pro forma basic and diluted net loss per common share, which has been computed to give effect to the conversion of all shares of convertible preferred stock into shares of common stock as if such conversion had occurred as of the beginning of the period presented. The following table sets forth the computation of the Company s pro forma basic and diluted net loss per common share (in thousands, except per share amounts):

	Year Ended December 31, 2013 (unaudited)
Net loss used in computing pro forma per share attributable to common stockholders, basic and diluted	$ (12,377)
Shares used in computing net loss per share attributable to common stockholders, basic and diluted	94
Pro forma adjustments to reflect assumed conversion of convertible preferred stock	3,989
Shares used in computing pro forma net loss per share attributable to common stockholders, basic and diluted	4,083
Pro forma net loss per share attributable to common stockholders, basic and diluted	$ (3.03)

10. Related Party Transactions

The spouse of the Company s Chief Executive Officer is the founder of a management consulting firm that provided services to the Company. For the years ended December 31, 2012 and 2013, the Company recognized $41,000 and $62,000, respectively, paid to this management consulting firm, for consulting services which were primarily included in research and development expenses in the statements of operations and comprehensive loss. As of December 31, 2012 and 2013, the Company had an outstanding liability to the management consulting firm of $20,000 and nil, respectively.

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

11. Subsequent Events

The Company has evaluated subsequent events occurring after December 31, 2013 up to July 25, 2014, the date the financial statements were available to be issued.

Series D Convertible Preferred Stock

In July 2014, the Company issued 1,902,583 shares of Series D at a price of $8.41 per share for aggregate net proceeds of $16.0 million.

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CALITHERA BIOSCIENCES, INC.

CONDENSED BALANCE SHEETS

(in thousands, except per share amounts)

	December 31, 2013	June 30, 2014 (unaudited)	Pro Forma Stockholders Equity as of June 30, 2014 (unaudited)
Assets			
Current assets:			
Cash and cash equivalents	$ 33,820	$ 27,750	
Prepaid expenses and other current assets	349	1,497	
Total current assets	34,169	29,247	
Restricted cash	116	46	
Property and equipment, net	559	753	
Other assets		609	
Total assets	$ 34,844	$ 30,655	
Liabilities, Convertible Preferred Stock and Stockholders Deficit			
Current liabilities:			
Accounts payable	$ 150	$ 1,037	
Accrued liabilities	1,194	2,082	
Funds received in advance for preferred stock financing		3,000	
Total current liabilities	1,344	6,119	
Deferred rent	31	297	
Total liabilities	1,375	6,416	
Commitments and contingencies			
Convertible preferred stock, $0.0001 par value, 7,757 and 11,340 shares authorized as of December 31, 2013 and June 30, 2014 (unaudited); 7,689 shares issued and outstanding as of December 31, 2013 and June 30, 2014 (unaudited); no shares authorized, issued and outstanding, pro forma (unaudited); aggregate liquidation preference of $55,450 as of June 30, 2014 (unaudited)	54,282	54,282	$
Stockholders deficit:			
Common stock, $0.0001 par value, 9,896 and 13,438 shares authorized as of December 31, 2013 and June 30, 2014 (unaudited); 161 and 290 shares issued and outstanding as of December 31, 2013 and June 30, 2014 (unaudited); 7,979 shares issued and outstanding, pro forma (unaudited)	1	1	1
Additional paid-in capital	9,328	9,738	64,020
Accumulated deficit	(30,142)	(39,782)	(39,782)

Total stockholders (deficit) equity	(20,813)	(30,043)	$ 24,239
Total liabilities and stockholders deficit	$ 34,844	$ 30,655	

See accompanying notes.

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CALITHERA BIOSCIENCES, INC.

CONDENSED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS

(Unaudited)

(in thousands, except per share amounts)

	Six Months Ended June 30,	
	2013	**2014**
Operating expenses:		
Research and development	$ 4,069	$ 7,501
General and administrative	903	2,141
Total operating expenses	4,972	9,642
Loss from operations	(4,972)	(9,642)
Other income		2
Net loss and comprehensive loss	$ (4,972)	$ (9,640)
Net loss per share attributable to common stock holders, basic and diluted	$ (84.62)	$ (47.14)
Weighted average common shares used to compute net loss per share attributable to common stockholders, basic and diluted	59	205
Pro forma net loss per share attributable to common stockholders, basic and diluted		$ (1.22)
Shares used in computing pro forma net loss per share attributable to common stockholders, basic and diluted		7,894

See accompanying notes.

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CALITHERA BIOSCIENCES, INC.

CONDENSED STATEMENTS OF CASH FLOWS

(Unaudited)

(in thousands)

	Six Month Ended June 30,	
	2013	**2014**
Cash Flows From Operating Activities		
Net loss	$ (4,972)	$ (9,640)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	138	155
Stock-based compensation	22	211
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	(27)	(1,148)
Other assets		(609)
Accounts payable	64	736
Accrued liabilities	71	848
Deferred rent		344
Net cash used in operating activities	(4,704)	(9,103)
Cash Flows From Investing Activities		
Purchase of property and equipment	(82)	(182)
Change in restricted cash	(8)	70
Net cash used in investing activities	(90)	(112)
Cash Flows From Financing Activities		
Net proceeds from issuance of convertible preferred stock	8,676	
Fund received in advance for the Series D convertible preferred stock financing		3,000
Proceeds from stock option exercises		145
Net cash provided by financing activities	8,676	3,145
Net increase (decrease) in cash and cash equivalents	3,882	(6,070)
Cash and cash equivalents at beginning of period	2,205	33,820
Cash and cash equivalents at end of period	$ 6,086	$ 27,750
Supplemental Disclosure of Non-Cash Investing and Financing Information:		
Services settled through the issuance of common stock	$	$ 55
Unpaid amounts related to purchase of property and equipment	$	$ 168

See accompanying notes.

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CALITHERA BIOSCIENCES, INC.

NOTES TO UNAUDITED INTERIM CONDENSED FINANCIAL STATEMENTS

1. Organization and Basis of Presentation

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

Liquidity

The Company has incurred net losses from operations since inception and had an accumulated deficit of $39.8 million as of June 30, 2014. The Company had cash and cash equivalents of $27.8 million as of June 30, 2014. In July 2014, the Company issued 1,902,583 shares of Series D convertible preferred stock for $16.0 million in net proceeds (see Note 8). Management believes that the currently available resources will provide sufficient funds to enable the Company to meet its operating plan for at least the next twelve months. However, if the Company s anticipated operating results are not achieved in future periods, management believes that planned expenditures may need to be reduced in order to extend the time period over which the then-available resources would be able to fund the Company s operations.

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

2. Summary of Significant Accounting Policies

Unaudited Interim Financial Information

The interim condensed balance sheet as of June 30, 2014, and the statements of operations and comprehensive loss, and cash flows for the six months ended June 30, 2013 and 2014 are unaudited. The unaudited interim financial statements have been prepared on the same basis as the annual financial statements and reflect, in the opinion of management, all adjustments of a normal and recurring nature that are necessary for the fair presentation of the Company s financial position as of June 30, 2014 and its results of operations and cash flows for the six months ended

June 30, 2013 and 2014. The financial data and the other information disclosed in these notes to financial statements related to the six-month periods are also unaudited. The results of operations for the six months ended June 30, 2014 are not necessarily indicative of the results to be expected for the year ending December 31, 2014 or for any other future annual or interim period. The balance sheet as of December 31, 2013 included herein was derived from the audited financial statements as of that date. These financial statements should be read in conjunction with the Company s audited financial statements included elsewhere in this prospectus.

Unaudited Pro Forma Stockholder s Equity

In August 2014, the Company s Board of Directors authorized management of the Company to file a registration statement with the Securities and Exchange Commission for the Company to sell shares of its common stock to the public. The unaudited pro forma stockholders equity as of June 30, 2014 presents the Company s stockholders equity as though all the Company s outstanding convertible preferred stock had

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converted into shares of common stock upon the completion of an initial public offering (IPO) of the Company s common stock.

Use of Estimates

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

Cash and Cash Equivalents

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

Accrued Research and Development Costs

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

Deferred Offering Costs

Deferred offering costs, consisting of legal, accounting, printer and filing fees related to the IPO are capitalized. The deferred offering costs will be offset against proceeds from the IPO upon the effectiveness of the offering. In the event the offering is terminated, all capitalized deferred offering costs will be expensed. As of June 30, 2014, $609,000 of deferred offering costs were capitalized, which are included in other assets in the accompanying condensed balance sheets. No amounts were deferred as of December 31, 2013.

Net Loss per Share Attributable to Common Stockholders

Basic net loss per share attributable to common stockholders is calculated by dividing the net loss attributable to common stockholders by the weighted average number of shares of common stock outstanding during the period without consideration of common stock equivalents. Since the Company was in a loss position for all periods presented, basic net loss per share attributable to common stockholders is the same as diluted net

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

Pro Forma Net Loss per Share Attributable to Common Stockholders

Pro forma basic and diluted net loss per share attributable to common stockholders has been computed to give effect to the conversion of the shares of convertible preferred stock into common stock as if such conversion had occurred at the beginning of the period. The pro forma net loss per share attributable to common stockholders does not include the shares expected to be sold and related proceeds to be received from an initial public offering.

Recent Accounting Pronouncements

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

3. Fair Value Measurements

Fair value accounting is applied for all financial assets and liabilities that are recognized or disclosed at fair value in the financial statements on a recurring basis (at least annually). Financial instruments include cash and cash equivalents, accounts payable and accrued liabilities that approximate fair value due to their relatively short maturities. Assets and liabilities recorded at fair value on a recurring basis in the balance sheets are categorized based upon the level of judgment associated with the inputs used to measure their fair values. Fair value is defined as the exchange price that would be received for an asset or an exit price that would be paid to transfer a liability in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. The authoritative guidance on fair value measurements establishes a three-tier fair value hierarchy for disclosure of fair value measurements as follows:

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

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

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

The Company s financial instruments consist only of Level 1 assets, which are highly liquid money market funds. At December 31, 2013 and June 30, 2014, the Company had $116,000 and $46,000 in money market funds that are included in restricted cash on the balance sheets.

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4. Accrued Liabilities

Accrued liabilities consist of the following (in thousands):

	December 31, 2013	June 30, 2014
Accrued bonus and payroll expenses	$ 934	$ 808
Accrued professional and consulting services	127	508
Accrued clinical and manufacturing expenses	107	611
Deferred rent current		78
Other	26	77
Total accrued liabilities	$ 1,194	$ 2,082

5. Stock Based Compensation

Stock Incentive Plan

In 2010, the Company adopted the 2010 Equity Incentive Plan (2010 Plan). A total of 1,230,297 shares were reserved for issuance under the 2010 Plan as of June 30, 2014, of which 42,120 shares were available for future grant. A summary of stock option activity under the 2010 Plan is as follows (in thousands, except share data and contractual term amounts):

	Options Outstanding			
	Number of Shares Underlying Outstanding Options	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term (Years)	Aggregate Intrinsic Value
Outstanding December 31, 2013	864,829	$ 1.80		$ 769
Options granted	240,605	$ 2.64		
Options exercised	(106,691)	$ 1.36		
Options canceled	(19,297)	$ 1.20		
Outstanding June 30, 2014	979,446	$ 2.07	9.20	$ 3,173
Exercisable June 30, 2014	81,953	$ 2.18	8.65	$ 282
Vested and expected to vest June 30, 2014	939,515	$ 2.07	9.20	$ 3,040

The aggregate intrinsic values of options outstanding, vested and exercisable and vested and expected to vest were calculated as the difference between the exercise price of the options and the estimated fair value of the Company s common stock as determined by the Company s Board of Directors as of June 30, 2014. For the six months ended June 30, 2013 and 2014, the total intrinsic value of options exercised was nil and $418,000, respectively.

The weighted-average grant-date fair value of options granted during the six months ended June 30, 2013 and 2014 was $0.48 and $3.84 per share, respectively. The total estimated fair value of options vested during the six months ended June 30, 2013 and 2014 was $0.48 and $1.44 per share, respectively.

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Stock-Based Compensation

Total stock-based compensation recognized was as follows (in thousands):

	Six Months Ended June 30,	
	2013	2014
Research and development	$ 15	$ 103
General and administrative	7	108
Total stock-based compensation	$ 22	$ 211

As of June 30, 2014, the total unrecognized compensation expense related to unvested options, net of estimated forfeitures, was $1.8 million, which the Company expects to recognize over an estimated weighted-average period of 3.5 years.

The fair value of the shares of common stock underlying stock options has historically been determined by the Company s Board of Directors. Because there has been no public market for the Company s common stock, the Board of Directors has determined fair value of the common stock at the time of grant of the option by considering a number of objective and subjective factors including important developments in the Company s operations, valuations performed by an independent third party, sales of convertible preferred stock, actual operating results and financial performance, the conditions in the biotechnology industry and the economy in general, the stock price performance and volatility of comparable public companies, and the lack of liquidity of the Company s common stock, among other factors.

In each of the periods presented, the exercise price per share for each stock option was the same as the fair value of the Company s common stock on the date of grant as determined by the Company s Board of Directors, other than with respect to stock options to purchase an aggregate of 190,814 shares of common stock granted in April and May 2014. The Company subsequently performed a reassessment of the fair value of the common stock underlying the stock options granted in April and May 2014, and for financial reporting purposes reassessed the fair value of these grants from $2.64 per share to $5.28 per share and recognized $27,000 of additional stock-based compensation expense during the six months ended June 30, 2014.

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

	Six Months Ended June 30,	
	2013	2014
Expected term (in years)	6.25 years	5.99 - 6.25 years
Volatility	87.1%	95.4 - 96.4%
Risk-free interest rate	1.16%	1.89 - 2.00%
Expected dividend rate	%	%

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6. Net Loss and Pro Forma Net Loss per Share Attributable to Common Stockholders

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

	June 30,	
	2013	2014
Convertible preferred stock	3,528	7,689
Options to purchase common stock	503	979
Common stock subject to repurchase	2	
Total	4,033	8,668

In contemplation of the IPO, the Company has presented the pro forma basic and diluted net loss per share attributable to common stockholders, which has been computed to give effect to the conversion of all series of convertible preferred stock into shares of common stock as though the conversion had occurred as of the beginning of the period. The following table sets forth the computation of the Company s pro forma basic and diluted net loss per share attributable to commons stockholders (in thousands, except the per share amount):

	Six Months Ended June 30, 2014
Net loss used in computing pro forma net loss per share attributable to common stockholders, basic and diluted	$ (9,640)
Shares used in computing net loss per share attributable to common stockholders, basic and diluted	205
Pro forma adjustments to reflect assumed conversion of convertible preferred stock	7,689
Shares used in computing pro forma net loss per share attributable to common stockholders, basic and diluted	7,894
Pro forma net loss per share attributable to common stockholders, basic and diluted	$ (1.22)

7. Related Party Transactions

The spouse of the Company s Chief Executive Officer was the founder of a management consulting firm that provided services to the Company until he was hired as an employee in April 2013. For the six months ended June 30, 2013, the Company recognized expense of $62,000, for consulting services which were primarily included in the research and development expenses in the statement of operations and comprehensive loss. As of December 31, 2013, the Company had no outstanding liability to this management consulting firm.

The spouse of one of the Company s executive officers is a consultant who provides accounting services for the Company. For the six months ended June 30, 2013 and 2014, the Company recognized expense of $25,000 and $61,000, respectively, for consulting services within the general and administrative expense in the statements of operations and comprehensive loss. As of December 31, 2013 and June 30, 2014, the Company had an outstanding liability to the spouse of $12,000 and nil, respectively.

8. Subsequent Events

The Company has evaluated subsequent events occurring after December 31, 2013 up to July 25, 2014, the date the financial statements were available to be issued.

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Series D Convertible Preferred Stock

In July 2014, the Company issued 1,902,583 shares of Series D convertible preferred stock at a price of $8.41 per share for aggregate net proceeds of $16.0 million.

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8,000,000 Shares

Common Stock

PROSPECTUS

October 1, 2014

Citigroup **Leerink Partners**

Wells Fargo Securities **JMP Securities**