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Blueprint Medicines Corporation Index to Consolidated Financial Statements

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Filed Pursuant to Rule 424(b)(4)
Registration No. 333-202938

Prospectus

8,145,834 Shares

Blueprint Medicines Corporation

Common Stock

This is an initial public offering of shares of common stock of Blueprint Medicines Corporation. All of the 8,145,834 shares of common stock are being sold by the Company.

Prior to this offering, there has been no public market for the common stock. The initial public offering price per share will be $18.00. Our common stock has been approved for listing on The NASDAQ Global Select Market under the symbol "BPMC."

See "Risk Factors" on page 12 to read about factors you should consider before buying shares of the common stock.

Neither the Securities and Exchange Commission nor any other regulatory body has approved or disapproved of these securities or passed upon the accuracy or adequacy of this prospectus. Any representation to the contrary is a criminal offense.

	Per Share	Total
Initial public offering price	$ 18.00	$ 146,625,012
Underwriting discount[(1)]	$ 1.26	$ 10,263,751
Proceeds, before expenses, to Blueprint Medicines Corporation	$ 16.74	$ 136,361,261

(1) We refer you to "Underwriting" beginning on page 157 of this prospectus for additional information regarding underwriting compensation.

To the extent that the underwriters sell more than 8,145,834 shares of common stock, the underwriters have the option to purchase up to an additional 1,221,874 shares from Blueprint Medicines Corporation at the initial price to public less the underwriting discount.

The underwriters expect to deliver the shares against payment in New York, New York on May 5, 2015.

Goldman, Sachs & Co. **Cowen and Company**

JMP Securities

Wedbush PacGrow

Prospectus dated April 29, 2015.

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Prospectus

We have not authorized anyone to provide any information or to make any representations other than those contained in this prospectus or in any free writing prospectuses we have prepared. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. This prospectus is an offer to sell only the shares offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so. The information contained in this prospectus is current only as of its date.

For investors outside of the United States: We have not, and the underwriters have not, done anything that would permit this offering or possession or distribution of this prospectus in any jurisdiction where action for that purpose is required, other than the United States. Persons outside of the United States who come into possession of this prospectus must inform themselves about, and observe any restrictions relating to, the offering of the shares of common stock and the distribution of this prospectus outside of the United States.

PROSPECTUS SUMMARY

This summary highlights information contained elsewhere in this prospectus and does not contain all of the information that you should consider in making your investment decision. Before investing in our common stock, you should carefully read this entire prospectus, including our financial statements and the related notes included elsewhere in this prospectus. You should also consider, among other things, the matters described under "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations," in each case appearing elsewhere in this prospectus. Unless otherwise stated, all references to "us," "our," "Blueprint," "Blueprint Medicines," "we," the "Company" and similar designations refer to Blueprint Medicines Corporation.

Blueprint Medicines Overview

We are a biopharmaceutical company focused on improving the lives of patients with genomically defined diseases driven by abnormal kinase activation. Our approach is to systematically and reproducibly identify kinases that are drivers of genomically defined diseases and to craft drug candidates with therapeutic windows that provide significant and durable clinical responses to patients. This integrated biology and chemistry approach enables us to drug known kinases that have been difficult to inhibit selectively and also identify, characterize and drug novel kinase targets. By focusing on genomically defined diseases, we believe that we will have a more efficient development path with a greater likelihood of success. Over the past three years, we have developed a robust small molecule drug pipeline in cancer and a rare genetic disease. One of our lead drug candidates is BLU-285, which targets KIT Exon 17 and PDGFRa D842V, abnormally active receptor tyrosine kinase mutants that are drivers of cancer and proliferative disorders. BLU-285 will initially be developed for patients with systemic mastocytosis, a myeloproliferative disorder of the mast cells, and defined subsets of patients with gastrointestinal stromal tumor, the most common sarcoma, or tumor of bone or connective tissue, of the gastrointestinal tract. Our other lead drug candidate is BLU-554, which targets FGFR4, a kinase that is aberrantly activated and is a driver of disease in a defined subset of patients with hepatocellular carcinoma, the most common type of liver cancer. Both drug candidates have demonstrated proof of concept in pre-clinical models and we expect to file Investigational New Drug applications, or INDs, in mid-2015 and initiate our Phase 1 clinical trials in mid-2015. We are also developing a drug candidate to target both RET, a receptor tyrosine kinase that can become abnormally activated when a portion of the gene that encodes RET is joined to part of another gene, and RET resistant mutants that we predict will arise from treatment with first generation therapies. We believe that our strategy will allow us to deliver transformative drugs to patients while building a fully-integrated biopharmaceutical company.

Our Focus — Highly Selective Kinase Drugs for Genomically Defined Diseases

Kinases are enzymes that function in many signaling pathways. Abnormal activation of kinases has been shown to drive several key activities of cancer cells, including growth, survival, metabolism, cell motility and angiogenesis. For many of the known kinases, there is a strong link between genetic alterations in a kinase and disease, including specific forms of cancer and rare genetic diseases. Approved kinase drugs, such as imatinib, have demonstrated significant benefit to patients, and small molecule kinase drugs achieved over $14 billion in 2013 sales. Despite this success, there is room for further improvement in kinase drug discovery and development. Many of the approved drugs are multi-kinase inhibitors that are not selective for disease drivers. This results in off-target toxicities that limit dose levels and target inhibition, thereby reducing efficacy. Further, patients who initially respond to a targeted kinase treatment often relapse due to the development of resistant mutants. Finally, as of 2014, kinase drugs approved by the U.S. Food and Drug Administration, or FDA, target less than five percent of the 518 kinases that constitute the kinome.

In addition, the function of the majority of the kinome is unknown. Taken together, this represents a substantial opportunity for developing novel and transformative drugs for cancer, rare genetic diseases and other disease areas.

Our Approach and Platform

Our approach is to systematically and reproducibly identify kinases that are drivers of genomically defined diseases and to craft drug candidates with therapeutic windows that provide significant and durable clinical responses to patients.

To capitalize on the kinase opportunity, we built a platform that integrates a novel target discovery engine and a proprietary compound library. Ou novel target discovery engine, which was developed entirely in-house under the direction of our chief scientific officer, combines our expertise in genomics, bioinformatics, and cell and structural biology to provide new insights into the biology of kinases as drivers of disease. To develop kinase drugs, we start by interrogating our proprietary compound library. Our library is a unique collection of novel small molecules rationally designed and developed entirely in-house by Blueprint Medicines' scientists as kinase inhibitors and enriched for drug-like properties. We do not owe royalties or other fees to any parties associated with our novel target discovery engine and our proprietary compound library. Another aspect of our platform is predicting resistance mutations. While treatment of patients with genomically-defined cancers with a targeted therapy typically results in a significant anti-tumor response, frequently the response is not durable due to mutations that arise in response to therapy. Through our structural and cell biology expertise, we predict mutations in kinases that render the enzyme insensitive to inhibition by an approved drug or compound in development. We have used this process of predicting resistance to inform the design of several of our next generation drugs. Using this platform, we have produced a drug pipeline of several promising drug candidates that target genomically-defined patient subsets.

As we advance our drug candidates through clinical development, we will enrich our Phase 1 trials by selecting patients most likely to respond to our drug candidates to confirm mechanistic and clinical proof of concept. We are collaborating with corporate partners to create companion diagnostics and to develop assays to measure target engagement, which is confirmation that a drug binds to its intended protein target *in vivo*, and early response We expect these approaches to enable early determination of efficacy, allowing for clear decision points in clinical trials.

Our Development Programs

We have leveraged our platform to develop a robust drug pipeline of orally available, potent and selective small molecule kinase inhibitors that target genomic drivers in several cancers and a rare genetic disease. We currently own worldwide commercial rights to all of our oncology-focused drug candidates, and have a rare genetic disease program that is the subject of our collaboration

with Alexion Pharma Holding, or Alexion. Our most advanced drug candidates are summarized in the table below.

Drug Candidates	Genomic Drivers	Initial Diseases	Stage of Development	Commercial Rights
BLU-285 (KIT Exon 17 inhibitor)	KIT D816V	SM	IND-enabling activities	Blueprint Medicines
	PDGFRa D842V	GIST	IND-enabling activities	
	KIT Exon 17 mutants	GIST	IND-enabling activities	
BLU-554 (FGFR4 inhibitor)	Aberrant FGFR4 signaling	HCC	IND-enabling activities	Blueprint Medicines
RET fusions and predicted RET resistant mutants	RET fusions*	Non-small cell lung cancer Other solid tumors	Lead optimization	Blueprint Medicines
Rare genetic disease target	Undisclosed	Rare genetic disease	Undisclosed	Alexion

* A fusion protein is encoded by a fusion gene, which is a gene in which a portion of one gene is joined to part of another gene. In the case of RET, a portion of the RET gene tha encodes the kinase domain is joined to part of another gene. RET fusion proteins are always active and are thought to be drivers in several cancers.

KIT Inhibitor Program

BLU-285 is an orally available, potent and selective inhibitor of several activating mutations of KIT that occur in Exon 17, which encodes a portio of the tyrosine kinase domain. BLU-285 also potently and selectively inhibits PDGFRa D842V. Due to the high degree of structural similarity of the kinase domains of KIT and PDGFRa, BLU-285 is able to inhibit both KIT Exon 17 mutants and the PDGFRa D842V mutant with minimal inhibition of other kinases. BLU-285 is a highly targeted therapeutic candidate for genomically-selected patients with diseases driven by these mutations, including systemic mastocytosis, or SM, and genomically-defined patient subsets within gastrointestinal stromal tumor, or GIST, which are KIT and PDGFRa mediated diseases.

Imatinib, which is an inhibitor of KIT, is approved in SM and GIST and validates this kinase as a therapeutic target in these diseases. Imatinib also inhibits PDGFRa, which is a driver of disease in a subset of GIST. However, a meaningful percentage of patients harbor mutations in KIT and PDGFRa that are not targeted by imatinib and fail to respond to treatment with the drug. We plan to initially develop BLU-285 for targeted patient populations that harbor these mutations and currently lack adequate treatments.

For SM, we demonstrated significant anti-tumor efficacy of BLU-285 in a mouse xenograft model with a mastocytoma, or mast cell tumor driven by a KIT Exon 17 mutation. For GIST, we also demonstrated significant anti-tumor efficacy with BLU-285 in an imatinib resistant patient-derived xenograft model with a KIT Exon 17 resistance mutation, which is a model believed to be highly predictive of clinical response. We have completed 28 day Good Laboratory Practice, or GLP, toxicology studies and have identified what we believe to be the dose limiting toxicity and anticipated first-in-human dose for BLU-285.

We plan to file two INDs for BLU-285, one in SM and one in GIST, in mid-2015. We plan to initiate our Phase 1 clinical trials in mid-2015. Our Phase 1 clinical trials in these indications will test the safety and tolerability of BLU-285 in multiple ascending doses with the goal of establishing a maximum tolerated dose, or MTD, or a recommended dose if the MTD is not achieved. All patients in the SM trial will be tested retrospectively for KIT D816V mutational status. Patients in the GIST trial will be tested retrospectively for both KIT Exon 17 mutations and PDGFRa D842V. Once the MTD is reached, or a recommended dose is established, we will open expansion cohorts with genomically-selected patients. We expect data to be available approximately 12 months after the start of these Phase 1 clinical trials.

FGFR4 Inhibitor Program

BLU-554 is an orally available, potent, selective and irreversible inhibitor of the kinase FGFR4. FGFR4 has historically been a challenging target to drug selectively given the closely related paralogs, proteins encoded by closely related genes, namely FGFR1-3. Aberrantly active FGFR4 signaling is a driver of disease in a subset of patients with hepatocellular carcinoma, or HCC, a disease with high unmet need and no approved genomically-targeted therapies. We plan to initially develop BLU-554 for a genomically-defined patient population within HCC with aberrantly active FGFR4 signaling.

BLU-554 has shown proof of concept in several different pre-clinical models of HCC with aberrantly active FGFR4 signaling. The administration of BLU-554 in an HCC cell-line xenograft model resulted in robust dose-dependent tumor growth inhibition. At the highest dose, BLU-554 was well-tolerated and induced complete remission in a subset of mice for at least 30 days after cessation of treatment. Further, in a patient-derived HCC xenograft model, which we believe to be highly predictive of clinical response, treatment with BLU-554 led to dose-dependent tumor growth inhibition. We have completed 28-day GLP toxicology studies and have identified what we believe to be the dose limiting toxicity and anticipated first-in-human dose for BLU-554.

IND-enabling studies are completed, and we anticipate filing our IND in mid-2015 and initiating our Phase 1 clinical trial in mid-2015. Our Phase clinical trial in patients with HCC will test the safety and tolerability of BLU-554 in multiple ascending doses with the goal of establishing an MTD or a recommended dose if the MTD is not achieved. Once the MTD is reached, or a recommended dose is established, we will open expansion cohorts wit genomically-selected patients. We expect data to be available approximately 12 months after the start of our Phase 1 clinical trial.

RET Fusion Program

Our third program targets RET fusions and predicted RET resistant mutants. By using our proprietary compound library, we have crafted drug candidates to selectively inhibit not only RET but also the RET resistant mutants. We believe we can provide a treatment that results in a more meaningful and durable clinical response by prospectively inhibiting RET and RET resistant mutants early in the treatment of the disease. Our researc suggests that RET is a driver of disease in a broad set of cancers including non-small cell lung cancer, and cancers of the thyroid, colon and breast.

Our Team

To execute on this opportunity, we assembled an experienced management team, board of directors and scientific founders who bring extensive industry experience to our company. Our management team has broad capabilities and successful track records in oncology and rare genetic diseases through previous experience at Algeta ASA, Genzyme Corporation, Millennium Pharmaceuticals, Inc., Novartis AG and Sanofi S.A. We were founded by an internationally-recognized scientific team, including Brian Druker, Nicholas Lydon and Charles Sawyers, who led the discovery and development of imatinib. The approval of imatinib revolutionized the treatment of chronic myelogenous leukemia by converting it from an aggressive and deadly cancer to a chronic, manageable disease. Our vision is to emulate the success of imatinib in a reproducible way by leveraging our platform to transforr the lives of patients while building a fully-integrated biopharmaceutical company.

Our initial investors included funds managed by Fidelity Biosciences and Third Rock Ventures. Additional blue chip investors participated in our Series B and C financings, including funds managed by (listed alphabetically) Biotechnology Value Fund, Casdin Capital, Cowen Investments,

Nextech Invest, Partner Fund Management, Perceptive Advisors, RA Capital Management, Redmile Group, Sabby Capital, and Tavistock Life Sciences.

Our Mission

Blueprint Medicines makes kinase drugs to treat patients with genomically defined diseases. Led by a team of industry innovators, Blueprint Medicines integrates a novel target discovery engine and proprietary compound library to understand the genetic blueprint of cancer and to craft highly selective therapies. This empowers Blueprint Medicines to rapidly develop patient-defined drug candidates aimed at eradicating cancer and other genomically defined diseases.

Our Principles

We maintain a culture of high integrity that embraces the following guiding principles to provide long-term benefits to patients and our stakeholders:

- ***Patients First —*** Maintaining intense focus on improving patients' lives.
- ***Thoughtfulness —*** Exploring creative approaches by daring to make well-thought-out decisions and owning the outcomes.
- ***Trust —*** Through collaboration and cooperation, building and maintaining a cohesive team that has mutual respect of different viewpoints, opinions and talents.
- ***Optimism —*** Pursuing transformative therapies that we believe will make a difference.
- ***Urgency —*** Solving complex problems rapidly, with attention and care.

Our Strategy

Our strategy was created to enable us to achieve our mission. The key tenets of our strategy include the following:

- ***Rapidly advance our lead drug candidates, BLU-285 and BLU-554, through clinical development.***
- ***Build a pipeline of kinase drugs for genomically-defined drivers of disease.***
- ***Continuously invest in our proprietary platform to ensure future growth.***
- ***Maintain the Blueprint Medicines' culture as we grow our business.***
- ***Evaluate strategic collaborations to maximize value.***

Risks Associated With Our Business

Our business is subject to a number of risks of which you should be aware before making an investment decision. These risks are discussed more fully in the "Risk Factors" section of this prospectus immediately following this prospectus summary. These risks include the following:

- We are a biopharmaceutical company with a limited operating history and have not generated any revenue from drug sales. We have incurred significant operating losses since our inception and anticipate that we will incur continued losses for the foreseeable future.
- Even if we consummate this offering, we will need to raise substantial additional funding. If we are unable to raise capital when needed, we would be forced to delay, reduce or eliminate some of our drug development programs or commercialization efforts.

- We are very early in our development efforts. All of our lead drug candidates are still in pre-clinical development. If we are unable to advance our drug candidates to clinical development, obtain regulatory approval and ultimately commercialize our drug candidates or experience significant delays in doing so, our business will be materially harmed.

- Our approach to the discovery and development of drug candidates that inhibit kinases is unproven, and we do not know whether we wil be able to develop any drugs of commercial value.

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

- Genomically defined diseases may have relatively low prevalence and it may be difficult to identify patients with the genomic driver of the disease, which may lead to delays in enrollment for our trials.

- If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals both for our drug candidates and for the related companion diagnostics, we will not be able to commercialize, or will be delayed in commercializing, our drug candidates, and our ability to generate revenue will be materially impaired.

- Our drug candidates may cause undesirable side effects that could delay or prevent their regulatory approval, limit the commercial profile of an approved label, or result in significant negative consequences following marketing approval, if any.

- The incidence and prevalence for target patient populations of our drug candidates have not been established with precision. If the market opportunities for our drug candidates are smaller than we estimate or if any approval that we obtain is based on a narrower definition of the patient population, our revenue and ability to achieve profitability will be adversely affected, possibly materially.

- We may seek to establish additional collaborations, and, if we are not able to establish them on commercially reasonable terms, we may have to alter our development and commercialization plans.

- We expect to rely on third parties to conduct our clinical trials for our drug candidates. If these third parties do not successfully carry out their contractual duties, comply with regulatory requirements or meet expected deadlines, we may not be able to obtain regulatory approval for or commercialize our drug candidates and our business could be substantially harmed.

- If we are unable to adequately protect our proprietary technology or obtain and maintain patent protection for our technology and drugs o if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize technology and drugs similar or identical to ours, and our ability to successfully commercialize our technology and drugs may be impaired.

Implications of Being an Emerging Growth Company

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, and, for as long as we continue to be an "emerging growth company," we are permitted to, and intend to, rely on exemptions from certain disclosure requirements. In particular, we have provided only two years of audited financial statements and we have not included all of the executive compensation related information that would be required in this prospectus if we were not an emerging growth company. In addition, the JOBS Act provides that an "emergin growth company" can take advantage of an extended transition period for

complying with new or revised accounting standards, delaying the adoption of these accounting standards until they would apply to private companies. However, we are electing not to take advantage of such extended transition period, and as a result we will comply with new or revised accounting standards on the relevant dates on which adoption of such standards is required for non-emerging growth companies. Section 107 of the JOBS Act provides that our decision to not take advantage of the extended transition period for complying with new or revised accounting standards is irrevocable. We could be an "emerging growth company" for up to five years from completion of our initial public offering, or until the earliest of (i) the last day of the first fiscal year in which our annual gross revenues exceed $1 billion, (ii) the date that we become a "large accelerated filer" as defined in Rule 12b-2 under the Securities Exchange Act of 1934, as amended, or the Exchange Act, which would occur if the market value of our common stock that is held by non-affiliates exceeds $700 million as of the last business day of our most recently completed second fiscal quarter, or (iii) the date on which we have issued more than $1 billion in non-convertible debt during the preceding three-year period.

Corporate History and Information

We were incorporated in Delaware in October 2008 under the name ImmunoCo, Inc. In May 2010, we changed our name to Hoyle Pharmaceuticals, Inc., and in June 2011, we changed our name again to Blueprint Medicines Corporation. Our principal executive offices are located at 215 First Street, Cambridge, Massachusetts 02142, and our telephone number is (617) 374-7580. Our website address is http://www.blueprintmedicines.com. The information contained in, or that can be accessed through, our website is not part of this prospectus.

We are filing various U.S. federal trademark registrations and applications, and we own unregistered trademarks and servicemarks, including BLUEPRINT MEDICINES and our corporate logo. All other trademarks or trade names referred to in this prospectus are the property of their respective owners. Solely for convenience, the trademarks and trade names in this prospectus may be referred to without the ® and ™ symbols, but such references should not be construed as any indicator that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto. This prospectus also includes other trademarks of other persons.

THE OFFERING

Common stock offered by us	8,145,834 shares
Common stock to be outstanding after this offering	25,831,965 shares
Option to purchase additional shares	The underwriters have an option for a period of 30 days to purchase up to 1,221,874 additional shares of our common stock.
Use of proceeds	We estimate that we will receive net proceeds of approximately $133.8 million from the sale of the shares of common stock offered in this offering, or approximately $154.2 million if the underwriters exercise their option to purchase additional shares in full, based on the initial public offering price of $18.00 per share, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us. The offering is designed to provide funding for multiple proof-of-concept readouts for our drug candidates. In particular, we intend to use the net proceeds from this offering as follows: approximately $35.0 to $40.0 million to fund our two Phase 1 clinical trials for BLU-285 in SM and GIST; approximately $20.0 to $25.0 million to fund our Phase 1 clinical trial for BLU-554 in HCC, in each case, including clinical research outsourcing, drug manufacturing, companion diagnostic development and internal personnel costs; approximately $40.0 million to fund new and ongoing research activities including for our RET program and our platform with the goal of delivering one IND annually on average; and the balance for working capital and other general corporate purposes. See "Use of Proceeds" for additional information.
Risk factors	You should read carefully the "Risk Factors" beginning on page 12 and other information included in this prospectus for a discussion of factors that you should consider before deciding to invest in shares of our common stock.
NASDAQ Global Select Market symbol	"BPMC."

The number of shares of common stock to be outstanding after this offering is based on 2,218,652 shares of common stock outstanding as of December 31, 2014, including 425,279 shares of unvested restricted stock subject to repurchase by us and 166,635 stock options that were exercised prior to vesting, and the conversion of all of our outstanding shares of convertible preferred stock upon closing of this offering.

The number of shares of our common stock to be outstanding after this offering excludes the following:

- 1,335,277 shares of common stock issuable upon the exercise of outstanding stock options as of December 31, 2014 having a weighted average exercise price of $2.05 per share;

- 42,423 shares of common stock issuable upon the exercise of outstanding warrants as of December 31, 2014 having a weighted-averag exercise price of $5.89 per share;
- 572,638 shares of common stock issuable upon the exercise of stock options granted in February and March 2015 having a weighted-average exercise price of $8.92 per share and 10,000 shares issued to a former employee in March 2015;
- 1,460,084 shares of common stock reserved for future issuance under our 2015 Stock Option and Incentive Plan, or 2015 Stock Option Plan, which will become effective upon the completion of this offering; and
- 243,347 shares of common stock reserved for future issuance under our 2015 Employee Stock Purchase Plan, or 2015 ESPP, which wil become effective upon the completion of this offering.

Except as otherwise indicated, all information contained in this prospectus assumes or gives effect to:

- the automatic conversion of all of our outstanding shares of convertible preferred stock into an aggregate of 15,467,479 shares of common stock upon the completion of this offering;
- no exercise of the outstanding options or warrants described above after December 31, 2014;
- no exercise by the underwriters of their option purchase up to an additional 1,221,874 shares of our common stock in this offering;
- the adoption of our amended and restated certificate of incorporation and amended and restated by-laws, both of which we will file immediately prior to the completion of this offering; and
- a one-for-5.5 reverse stock split of our common stock effected on April 10, 2015.

SUMMARY FINANCIAL DATA

You should read the following summary financial data together with our financial statements and the related notes appearing at the end of this prospectus and the "Selected Financial Data" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" sections of this prospectus. We have derived the statement of operations data for the years ended December 31, 2013 and 2014 and the balance sheet data as of December 31, 2014 from our audited financial statements included elsewhere in this prospectus. Our historical results are not necessarily indicative of results that should be expected in the future.

	Year Ended December 31,	
	2013	2014
	(in thousands, except per share data)	
Statements of Operations Data:		
Operating expenses:		
Research and development	$ 15,928	$ 31,844
General and administrative	5,072	7,890
Total operating expenses	21,000	39,734
Other income (expense):		
Other income (expense), net	226	(98)
Interest and other expense	(138)	(453)
Total other income (expense)	88	(551)
Net loss	$ (20,912)	$ (40,285)
Convertible preferred stock dividends	(2,870)	(5,765)
Net loss applicable to common stockholders	$ (23,782)	$ (46,050)
Net loss per share applicable to common stockholders — basic and diluted(1)	$ (23.43)	$ (32.41)
Weighted-average number of common shares used in net loss per share applicable to common stockholders — basic and diluted(1)	1,015	1,421
Pro forma net loss per share applicable to common stockholders — basic and diluted (unaudited)		$ (3.07)
Pro forma weighted average number of common shares used in net loss per share applicable to common stockholders — basic and diluted (unaudited)		13,083

	As of December 31, 2014		
	Actual	Pro forma[2]	Pro forma as adjusted[3]
	(in thousands)		
Balance Sheet Data:			
Cash and cash equivalents	$ 47,240	$ 62,240	$ 196,001
Working capital[4]	41,510	52,148	185,909
Total assets	49,925	64,925	198,686
Term loan payable, net of current portion	7,338	7,338	7,338
Warrant liability	365	—	—
Convertible preferred stock	114,811	—	—
Total stockholders' (deficit) equity	(79,382)	35,794	169,555

(1) See Note 2 to the notes to our financial statements appearing elsewhere in this prospectus for further details on the calculation of basic and diluted net loss per share and pro forma basic and diluted net loss per share applicable to common stockholders.

(2) Pro forma balance sheet data give effect to the automatic conversion of all outstanding shares of our convertible preferre stock into an aggregate of 15,467,479 shares of our common stock, the conversion of our preferred stock warrants into warrants to purchase 42,423 shares of our common stock upon the completion of this offering and a $15.0 million upfron payment received in March 2015 upon execution of the agreement with Alexion Pharma Holding.

(3) Pro forma as adjusted to reflect the pro forma adjustments described in (2) above, and to further reflect the sale of share of our common stock offered in this offering, at the initial public offering price of $18.00 per share, after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.

(4) We define working capital as current assets less current liabilities.

RISK FACTORS

Investing in our common stock involves a high degree of risk. You should carefully consider the following risks and uncertainties, together with all other information in this prospectus, including our financial statements and related notes, before investing in our common stock. Any of the risk factors we describe below could adversely affect our business, financial condition or results of operations. The market price of our common stock could decline if one or more of these risks or uncertainties actually occur, causing you to lose all or part of the money you paid to buy our common stock. Additional risks that we currently do not know about or that we currently believe to be immaterial may also impair our business. Certain statements below are forward-looking statements. See "Cautionary Note Regarding Forward-Looking Statements" in this prospectus.

Risks Related to Our Financial Position and Need for Additional Capital

We are a biopharmaceutical company with a limited operating history and have not generated any revenue from drug sales. We have incurred significant operating losses since our inception and anticipate that we will incur continued losses for the foreseeable future.

We are a biopharmaceutical company with a limited operating history on which to base your investment decision. Biopharmaceutical drug development is a highly speculative undertaking and involves a substantial degree of risk. We commenced operations in April 2011. Our operations to date have been limited primarily to organizing and staffing our company, business planning, raising capital, developing our technology, identifying potential drug candidates and undertaking pre-clinical studies of our most advanced drug candidates. We have only recently identified lead drug candidates for two of our programs. We have never generated any revenue from drug sales. We have not obtained regulatory approvals for any of our drug candidates.

We have not yet demonstrated our ability to initiate or successfully complete any clinical trials, including large-scale, pivotal clinical trials, obtain regulatory approvals, manufacture a commercial scale drug, 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 drug from the time it is discovered to when it is available for treating patients. Consequently, any predictions you make about our future success or viability may not be as accurate as they could be if we had a longer operating history. In addition, as a new business, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors. We will need to transition from a company with a research focus to a company capable of supporting commercial activities. We may not be successful in such a transition.

Since inception, we have focused substantially all of our efforts and financial resources on developing our proprietary compound library, novel target discovery engine and initial drug candidates. We have funded our operations to date through proceeds from sales of convertible preferred stock and, to a lesser extent, through a loan and security agreement, or Loan and Security Agreement, that we entered into with Silicon Valley Bank in May 2013. From our inception through December 31, 2014, we had raised an aggregate of $125.1 million of gross proceeds from such transactions. As of December 31, 2014, our cash and cash equivalents and investments were $47.2 million. We have incurred net losses in each year since our inception, and we had an accumulated deficit of $82.2 million as of December 31, 2014. Our net losses were $20.9 million and $40.3 million for the years ended December 31, 2013 and 2014, respectively. Substantially all of our operating losses have resulted from costs incurred in connection with our research and development programs and from general and administrative costs associated with our operations. We expect to continue to incur significant expenses and operating losses over the next several years and for the foreseeable future. Our prior losses, combined with expected future losses, have had and will continue to have an adverse effect on our stockholders' deficit and working capital. We

expect our research and development expenses to significantly increase in connection with beginning clinical trials of our drug candidates. In addition, if we obtain marketing approval for our drug candidates, we will incur significant sales, marketing and outsourced-manufacturing expenses. Once we are a public company, we will incur additional costs associated with operating as a public company. As a result, we expect to continue to incur significant and increasing operating losses for the foreseeable future. Because of the numerous risks and uncertainties associated with developing pharmaceutical drugs, we are unable to predict the extent of any future losses or when we will become profitable, if at all. Even if we do become profitable, we may not be able to sustain or increase our profitability on a quarterly or annual basis.

Our ability to become profitable depends upon our ability to generate revenue. To date, we have not generated any revenue from our lead drug candidates, BLU-285 and BLU-554, and we do not know and do not expect to generate any revenue from the sale of drugs in the near future. We do not expect to generate significant revenue unless and until we obtain marketing approval of, and begin to sell, BLU-285, BLU-554 or one of our other drug candidates. Our ability to generate revenue depends on a number of factors, including, but not limited to, our ability to:

- initiate and successfully complete clinical trials that meet their clinical endpoints;
- initiate and successfully complete all safety studies required to obtain U.S. and foreign marketing approval for our drug candidates;
- commercialize our drug candidates, if approved, by developing a sales force or entering into additional collaborations with third parties; and
- achieve market acceptance of our drug candidates in the medical community and with third-party payors.

We expect to incur significant sales and marketing costs as we prepare to commercialize our drug candidates. Even if we initiate and successfully complete pivotal clinical trials of our drug candidates, and our drug candidates are approved for commercial sale, and despite expending these costs, our drug candidates may not be commercially successful. We may not achieve profitability soon after generating drug sales, if ever. If we are unable to generate drug revenue, we will not become profitable and may be unable to continue operations without continued funding.

Even if we consummate this offering, we will need to raise substantial additional funding. If we are unable to raise capital when needed, we would be forced to delay, reduce or eliminate some of our drug development programs or commercialization efforts.

The development of pharmaceutical drugs is capital-intensive. We are currently advancing our drug candidates through pre-clinical development and anticipate beginning clinical trials for our lead drug candidates, BLU-285 and BLU-554, in mid-2015. We expect our expenses to increase in connection with our ongoing activities, particularly as we continue the research and development of, initiate clinical trials of, and seek marketing approval for, our drug candidates. In addition, depending on the status of regulatory approval or, if we obtain marketing approval for any of our drug candidates, we expect to incur significant commercialization expenses related to drug sales, marketing, manufacturing and distribution to the extent that such sales, marketing and distribution are not the responsibility of Alexion Pharma Holding, or Alexion, or other collaborators. We may also need to raise additional funds sooner if we choose to pursue additional indications and/or geographies for our drug candidates or otherwise expand more rapidly than we presently anticipate. Furthermore, upon the closing of this offering, we expect to incur additional costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital

when needed or on attractive terms, we would be forced to delay, reduce or eliminate certain of our research and development programs or future commercialization efforts.

We expect that the net proceeds from this offering, together with our existing cash and cash equivalents, including the $15.0 million upfront payment received in March 2015 upon execution of the agreement with Alexion, will be sufficient to fund our operations through at least early 2017. Our future capital requirements will depend on and could increase significantly as a result of many factors, including:

- the scope, progress, results and costs of drug discovery, pre-clinical development, laboratory testing and clinical trials for our drug candidates;
- the scope, prioritization and number of our research and development programs;
- the success of our collaboration with Alexion;
- the costs, timing and outcome of regulatory review of our drug candidates;
- our ability to establish and maintain additional collaborations on favorable terms, if at all;
- the achievement of milestones or occurrence of other developments that trigger payments under any additional collaboration agreements we obtain;
- the extent to which we are obligated to reimburse, or entitled to reimbursement of, clinical trial costs under future collaboration agreements, if any;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;
- the extent to which we acquire or in-license other drug candidates and technologies.
- the costs of securing manufacturing arrangements for commercial production; and
- the costs of establishing or contracting for sales and marketing capabilities if we obtain regulatory clearances to market our drug candidates.

Identifying potential drug candidates and conducting pre-clinical development testing and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve drug sales. In addition, our drug candidates, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of drugs that we do not expect to be commercially available for many years, if at all. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives.

Any additional fundraising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize our drug candidates. Dislocations in the financial markets have generally made equity and debt financing more difficult to obtain, and may have a material adverse effect on our ability to meet our fundraising needs. We cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all. Moreover, the terms of any financing may adversely affect the holdings or the rights of our stockholders and the issuance of additional securities, whether equity or debt, by us, or the possibility of such issuance, may cause the market price of our shares to decline. The sale of additional equity or convertible securities would dilute all of our stockholders. The incurrence of indebtedness would result in increased fixed payment obligations and we may be required to agree to certain restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. We could also be required to seek funds through arrangements with collaborators or otherwise at an earlier stage than otherwise

would be desirable and we may be required to relinquish rights to some of our technologies or drug candidates or otherwise agree to terms unfavorable to us, any of which may have a material adverse effect on our business, operating results and prospects.

If we are unable to obtain funding on a timely basis, we may be required to significantly curtail, delay or discontinue one or more of our research or development programs or the commercialization of any drug candidate or be unable to expand our operations or otherwise capitalize on our business opportunities, as desired, which could materially affect our business, financial condition and results of operations.

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 drug candidates.

Until such time, if ever, as we can generate substantial drug revenues, we expect to finance our cash needs through a combination of private and public equity offerings, debt financings, collaborations, strategic alliances and licensing arrangements. We do not have any committed external source of funds, other than our collaboration with Alexion, which is limited in scope and duration, and funds already borrowed under the Loan and Security Agreement. To the extent that we raise additional capital through the sale of common stock or securities convertible or exchangeable into common stock, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that materially adversely affect your rights as a common stockholder. Debt financing, if available, would increase our fixed payment obligations and 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.

If we raise funds through additional collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our intellectual property, future revenue streams, research programs or drug 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 when needed, we may be required to delay, limit, reduce or terminate our drug development or future commercialization efforts or grant rights to develop and market drug candidates that we would otherwise prefer to develop and market ourselves.

If you purchase our common stock in this offering, you will incur immediate and substantial dilution in the book value of your shares.

You will suffer immediate and substantial dilution in the net tangible book value of the common stock you purchase in this offering. Based on the initial public offering price of $18.00 per share, purchasers of common stock in this offering will experience immediate dilution of $11.29 per share in net tangible book value of the common stock. In addition, investors purchasing common stock in this offering will contribute 56% of the total amount invested by stockholders since inception but will only own 32% of the shares of common stock outstanding. In the past, we issued options and other securities to acquire common stock at prices significantly below the initial public offering price. To the extent these outstanding securities are ultimately exercised, investors purchasing common stock in this offering will sustain further dilution. See "Dilution" for a more detailed description of the dilution to new investors in the offering.

Risks Related to Drug Development and Regulatory Approval

We are very early in our development efforts. All of our lead drug candidates are still in pre-clinical development. If we are unable to advance our drug candidates to clinical development, obtain regulatory approval and ultimately commercialize our drug candidates or experience significant delays in doing so, our business will be materially harmed.

We are very early in our development efforts, and all of our lead drug candidates are still in pre-clinical development. We have only recently identified lead drug candidates for two of our programs. We have invested substantially all of our efforts and financial resources in the identification and pre-clinical development of kinase inhibitors, including the development of our lead drug candidates, BLU-285 and BLU-554. Our ability to generate drug revenues, which we do not expect will occur for many years, if ever, will depend heavily on the successful development and eventual commercialization of our drug candidates, which may never occur. We currently generate no revenues from sales of any drugs, and we may never be able to develop or commercialize a marketable drug. Each of our drug candidates will require additional pre-clinical and clinical development, management of clinical, pre-clinical and manufacturing activities, regulatory approval in multiple jurisdictions, obtaining manufacturing supply, building of a commercial organization, substantial investment and significant marketing efforts before we generate any revenues from drug sales. In addition, our drug development programs contemplate the development of companion diagnostics, which are assays or tests to identify an appropriate patient population. Companion diagnostics are subject to regulation as medical devices and must themselves be approved for marketing by the U.S. Food and Drug Administration, or FDA, or certain other foreign regulatory agencies before we may commercialize our drug candidates. The success of our drug candidates will depend on several factors, including the following:

- successful completion of pre-clinical studies;
- approval of Investigational New Drug applications, or INDs, for our planned clinical trials or future clinical trials;
- successful enrollment in, and completion of, clinical trials;
- successful development of companion diagnostics for use with our drug candidates;
- receipt of regulatory approvals from applicable regulatory authorities;
- establishing commercial manufacturing capabilities or making arrangements with third-party manufacturers for clinical supply and commercial manufacturing;
- obtaining and maintaining patent and trade secret protection or regulatory exclusivity for our drug candidates;
- launching commercial sales of our drug candidates, if and when approved, whether alone or in collaboration with others;
- acceptance of the drug candidates, if and when approved, by patients, the medical community and third party payors;
- effectively competing with other therapies;
- obtaining and maintaining healthcare coverage and adequate reimbursement;
- enforcing and defending intellectual property rights and claims; and
- maintaining a continued acceptable safety profile of the drug candidates following approval.

If we do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize our drug candidates,

which would materially harm our business. If we do not receive regulatory approvals for our drug candidates, we may not be able to continue our operations.

Our approach to the discovery and development of drug candidates that inhibit kinases is unproven, and we do not know whether we will be able to develop any drugs of commercial value.

Our scientific approach focuses on using our novel target discovery engine and our proprietary compound library to identify new kinase targets in disease indications. Our focus on using our novel target discovery engine to identify potential kinase targets in disease indications may not result in the discovery and development of commercially viable drugs for these diseases. The use of our proprietary compound library may not lead to the development of commercially viable drugs. Even if we are able to develop a drug candidate that successfully targets these kinases in pre-clinical studies, we may not succeed in demonstrating safety and efficacy of the drug candidate in clinical trials.

Clinical drug development involves a lengthy and expensive process, with an uncertain outcome. We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our drug candidates.

All of our lead drug candidates are in pre-clinical development and their risk of failure is high. It is impossible to predict when or if any of our drug candidates will prove effective and safe in humans or will receive regulatory approval. Before obtaining marketing approval from regulatory authorities for the sale of any drug candidate, we must complete pre-clinical studies and then conduct extensive clinical trials to demonstrate the safety and efficacy of our drug 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 can occur at any stage of testing. The outcome of pre-clinical development testing and early clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results. Moreover, pre-clinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their drug candidates performed satisfactorily in pre-clinical studies and clinical trials have nonetheless failed to obtain marketing approval of their product candidates. Our pre-clinical studies and future clinical trials may not be successful.

We plan to commence a Phase 1 clinical trial of BLU-285 as a treatment for systemic mastocytosis, or SM, a Phase 1 clinical trial of BLU-285 as a treatment for gastrointestinal stromal tumor, or GIST, and a Phase 1 clinical trial of BLU-554 as a treatment for hepatocellular carcinoma, or HCC. Commencing each of these clinical trials is subject to finalizing the trial design based on ongoing discussions with the FDA and other regulatory authorities. For example, based on our ongoing pre-IND discussions relating to our BLU-285 program, we may be required to submit data from our ongoing 13-week toxicology studies to further support our recommended safe starting dose and define the dose limiting toxicity. In the event that the FDA requires us to submit data from such studies or we are required to satisfy other FDA requests, the start of our clinical trials for BLU-285 may be delayed. Even after we receive and incorporate guidance from these regulatory authorities, the FDA or other regulatory authorities could disagree that we have satisfied their requirements to commence our clinical trials or change their position on the acceptability of our trial designs or the clinical endpoints selected, which may require us to complete additional pre-clinical studies or clinical trials or impose stricter approval conditions than we currently expect. Successful completion of our clinical trials is a prerequisite to submitting a new drug application, or NDA, to the FDA and a Marketing Authorization Application, or MAA, in Europe for each drug candidate and, consequently, the ultimate approval and commercial marketing of BLU-285, BLU-554 and our other

drug candidates. We do not know whether any of our clinical trials will begin or be completed on schedule, if at all.

We may experience delays in completing our pre-clinical studies and initiating or completing clinical trials, and we may experience numerous unforeseen events during, or as a result of, any future clinical trials that we could conduct that could delay or prevent our ability to receive marketing approval or commercialize our drug candidates, including:

- regulators or institutional review boards, or IRBs, or ethics committees may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we may experience delays in reaching, or fail to reach, agreement on acceptable terms with prospective trial sites and prospective contract research organizations, or CROs, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- clinical trials of our drug candidates may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional pre-clinical studies or clinical trials or we may decide to abandon drug development programs;
- the number of patients required for clinical trials of our drug 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 or fail to return for post-treatment follow-up 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, or may deviate from the clinical trial protocol or drop out of the trial, which may require that we add new clinical trial sites or investigators;
- we may elect to, or regulators or IRBs or ethics committees 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 drug candidates may be greater than we anticipate;
- the supply or quality of our drug candidates or other materials necessary to conduct clinical trials of our drug candidates may be insufficient or inadequate;
- our drug candidates may have undesirable side effects or other unexpected characteristics, causing us or our investigators, regulators or IRBs or ethics committees to suspend or terminate the trials, or reports may arise from pre-clinical or clinical testing of other cancer therapies that raise safety or efficacy concerns about our drug candidates; and
- the FDA or other regulatory authorities may require us to submit additional data or impose other requirements before permitting us to initiate a clinical trial.

We could encounter delays if a clinical trial is suspended or terminated by us, by the IRBs of the institutions in which such trials are being conducted, by the Data Safety Monitoring Board, or DSMB, for such trial or by the FDA or other regulatory authorities. Such authorities may impose such a suspension or termination due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a drug, changes in governmental regulations or administrative actions or lack

of adequate funding to continue the clinical trial. Many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our drug candidates. Further, the FDA may disagree with our clinical trial design and our interpretation of data from clinical trials, or may change the requirements for approval even after it has reviewed and commented on the design for our clinical trials.

If we are required to conduct additional clinical trials or other testing of our drug candidates beyond those that we currently contemplate, if we are unable to successfully complete clinical trials of our drug 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 drug candidates;
- not obtain marketing approval at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- be subject to post-marketing testing requirements; or
- have the drug removed from the market after obtaining marketing approval.

Our drug development costs will also increase if we experience delays in testing or regulatory approvals. We do not know whether any of our clinical trials will begin as planned, will need to be restructured or will be completed on schedule, or at all. Significant pre-clinical study or clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our drug candidates or allow our competitors to bring products to market before we do and impair our ability to successfully commercialize our drug candidates and may harm our business and results of operations. Any delays in our pre-clinical or future clinical development programs may harm our business, financial condition and prospects significantly.

If we experience delays or difficulties in the enrollment of 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 drug candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or similar regulatory authorities outside the United States. In particular, because we are focused on patients with genomically defined diseases, our ability to enroll eligible patients may be limited or may result in slower enrollment than we anticipate. In addition, some of our competitors have ongoing clinical trials for drug candidates that treat the same indications as our drug candidates, and patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors' drug candidates.

Patient enrollment may be affected by other factors including:

- the severity of the disease under investigation;
- the eligibility criteria for the clinical trial in question;
- the availability of an appropriate genomic screening test;
- the perceived risks and benefits of the drug candidate under study;
- the efforts to facilitate timely enrollment in clinical trials;
- the patient referral practices of physicians;
- the ability to monitor patients adequately during and after treatment; and
- the proximity and availability of clinical trial sites for prospective patients.

Genomically defined diseases may have relatively low prevalence and it may be difficult to identify patients with the genomic driver of the disease, which may lead to delays in enrollment for our trials.

Following our general drug development strategy, we have designed our planned Phase 1 clinical trials of each of BLU-285 and BLU-554, and expect to design future trials, to include some patients with the applicable genomic alteration that causes the disease with a view to assessing possible early evidence of potential therapeutic effect. Genomically defined diseases, however, may have relatively low prevalence and it may be difficult to identify patients with the applicable genomic alteration. We intend to engage third parties to develop companion diagnostics for use in our clinical trials, but such third parties may not be successful in developing such companion diagnostics, furthering the difficulty in identifying patients with the applicable genomic alteration for our clinical trials. Our inability to enroll a sufficient number of patients with the applicable genomic alteration for our clinical trials would result in significant delays and could require us to abandon one or more clinical trials altogether. Enrollment delays in our clinical trials may result in increased development costs for our drug candidates, which would cause the value of our company to decline and limit our ability to obtain additional financing. Further, if we are unable to include patients with the applicable genomic alteration, this could compromise our ability to seek participation in FDA's expedited review and approval programs, including Breakthrough Therapy Designation and Fast Track Designation, or otherwise to seek to accelerate clinical development and regulatory timelines.

If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals both for our drug candidates and for the related companion diagnostics, we will not be able to commercialize, or will be delayed in commercializing, our drug candidates, and our ability to generate revenue will be materially impaired.

Our drug candidates and the related companion diagnostics and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale, distribution, import and export are subject to comprehensive regulation by the FDA and other regulatory agencies in the United States and by comparable authorities in other countries. Before we can commercialize any of our drug candidates, we must obtain marketing approval. We may also need marketing approval for the related companion diagnostics. We have not received approval to market any of our drug candidates or related companion diagnostics from regulatory authorities in any jurisdiction and it is possible that none of our drug candidates or any drug candidates or related companion diagnostics we may seek to develop in the future will ever obtain regulatory approval. We have only limited experience in filing and supporting the applications necessary to gain regulatory approvals and expect to rely on third-party CROs and/or regulatory consultants to assist us in this process. Securing regulatory approval requires the submission of extensive pre-clinical and clinical data and supporting information to the various regulatory authorities for each therapeutic indication to establish the drug candidate's safety and efficacy. Securing regulatory approval also requires the submission of information about the drug manufacturing process to, and inspection of manufacturing facilities by, the relevant regulatory authority. Our drug 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 regulatory approvals, both in the United States and abroad, is expensive, may take many years if additional clinical trials are required, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the drug candidates involved. 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 NDA, Pre-Market Approval, or PMA, or equivalent application types, 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 are insufficient for approval and require additional pre-clinical, clinical or other studies. Our drug candidates could be delayed in receiving, or fail to receive, regulatory approval for many reasons, including the following:

- the FDA or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical trials;
- we may be unable to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that a drug candidate is safe and effective for its proposed indication or a related companion diagnostic is suitable to identify appropriate patient populations;
- the results of clinical trials may not meet the level of statistical significance required by the FDA or comparable foreign regulatory authorities for approval;
- we may be unable to demonstrate that a drug candidate's clinical and other benefits outweigh its safety risks;
- the FDA or comparable foreign regulatory authorities may disagree with our interpretation of data from pre-clinical studies or clinical trials;
- the data collected from clinical trials of our drug candidates may not be sufficient to support the submission of an NDA or other submission or to obtain regulatory approval in the United States or elsewhere;
- the FDA or comparable foreign regulatory authorities may fail to approve the manufacturing processes or facilities of third-party manufacturers with which we contract for clinical and commercial supplies; and
- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

In addition, even if we were to obtain approval, regulatory authorities may approve any of our drug candidates for fewer or more limited indications than we request, may not approve the price we intend to charge for our drugs and related companion diagnostics, may grant approval contingent on the performance of costly post-marketing clinical trials, or may approve a drug candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that drug candidate. Any of the foregoing scenarios could materially harm the commercial prospects for our drug candidates.

If we experience delays in obtaining approval or if we fail to obtain approval of our drug candidates and related companion diagnostics, the commercial prospects for our drug candidates may be harmed and our ability to generate revenues will be materially impaired.

Our drug candidates may cause undesirable side effects that could delay or prevent their regulatory approval, limit the commercial profile of an approved label, or result in significant negative consequences following marketing approval, if any.

Undesirable side effects caused by our drug candidates could cause us to interrupt, delay or halt pre-clinical studies or could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or other regulatory authorities. While we have not yet initiated clinical trials for any of our drug candidates, as is the case with all oncology drugs, it is likely that there may be side effects

associated with their use. Results of our trials could reveal a high and unacceptable severity and prevalence of these or other side effects. In such an event, our trials could be suspended or terminated and the FDA or comparable foreign regulatory authorities could order us to cease further development of or deny approval of our drug candidates for any or all targeted indications. The drug-related side effects could affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. Any of these occurrences may harm our business, financial condition and prospects significantly.

Further, our drug candidates could cause undesirable side effects in clinical trials related to on-target toxicity. For example, the FGF19/FGFR4 signaling axis has been shown to play a role in the regulation of de novo bile acid synthesis. Modulation of this signaling axis by treatment with a small molecule FGFR4 inhibitor could lead to the clinical symptoms that were observed with administration of an FGF19 antibody. If on-target toxicity is observed, or if our drug candidates have characteristics that are unexpected, we may need to abandon their development or limit development to more narrow 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 compounds that initially showed promise in early stage testing for treating cancer have later been found to cause side effects that prevented further development of the compound.

Further, clinical trials by their nature utilize a sample of the potential patient population. With a limited number of patients and limited duration of exposure, rare and severe side effects of our drug candidates may only be uncovered with a significantly larger number of patients exposed to the drug candidate. If our drug candidates receive marketing approval and we or others identify undesirable side effects caused by such drug candidates (or any other similar drugs) after such approval, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw or limit their approval of such drug candidates;
- regulatory authorities may require the addition of labeling statements, such as a "boxed" warning or a contraindication;
- we may be required to create a medication guide outlining the risks of such side effects for distribution to patients;
- we may be required to change the way such drug candidates are distributed or administered, conduct additional clinical trials or change the labeling of the drug candidates;
- regulatory authorities may require a Risk Evaluation and Mitigation Strategy, or REMS, plan to mitigate risks, which could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools;
- we may be subject to regulatory investigations and government enforcement actions;
- we may decide to remove such drug candidates from the marketplace;
- we could be sued and held liable for injury caused to individuals exposed to or taking our drug candidates; and
- our reputation may suffer.

We believe that any of these events could prevent us from achieving or maintaining market acceptance of the affected drug candidates and could substantially increase the costs of commercializing our drug candidates, if approved, and significantly impact our ability to successfully commercialize our drug candidates and generate revenues.

A Breakthrough Therapy Designation by the FDA for our drug candidates may not lead to a faster development or regulatory review or approval process, and it does not increase the likelihood that our drug candidates will receive marketing approval.

We may seek a Breakthrough Therapy Designation for some of our drug candidates. 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 drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For drugs that have been designated as breakthrough therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens. Drugs designated as breakthrough therapies by the FDA are also eligible for accelerated approval.

Designation as a breakthrough therapy is within the discretion of the FDA. Accordingly, even if we believe one of our drug candidates meets the criteria for designation as a breakthrough therapy, the FDA may disagree and instead determine not to make such designation. In any event, the receipt of a Breakthrough Therapy Designation for a drug candidate may not result in a faster development process, review or approval compared to drugs considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our drug candidates qualify as breakthrough therapies, the FDA may later decide that the drugs no longer meet the conditions for qualification.

A Fast Track Designation by the FDA may not actually lead to a faster development or regulatory review or approval process.

We may seek Fast Track Designation for some of our drug candidates. If a drug is intended for the treatment of a serious or life-threatening condition and the drug demonstrates the potential to address unmet medical needs for this condition, the drug sponsor may apply for Fast Track Designation. The FDA has broad discretion whether or not to grant this designation, so even if we believe a particular drug candidate is eligible for this designation, we cannot assure you that the FDA would decide to grant it. Even if we do receive Fast Track Designation, we may not experience a faster development process, review or approval compared to conventional FDA procedures. The FDA may withdraw Fast Track Designation if it believes that the designation is no longer supported by data from our clinical development program.

We may seek Orphan Drug Designation for some of our drug candidates, and we may be unsuccessful or may be unable to maintain the benefits associated with Orphan Drug Designation, including the potential for market exclusivity.

As part of our business strategy, we may seek Orphan Drug Designation for our drug candidates, and we may be unsuccessful. Regulatory authorities in some jurisdictions, including the United States and Europe, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a drug as an orphan drug if it is a drug intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals annually in the United States, or a patient population greater than 200,000 in the United States where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the United States. In the United States, Orphan Drug Designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers.

Similarly, in Europe, the European Commission grants Orphan Drug Designation after receiving the opinion of the European Medicines Agency's, or EMA, Committee for Orphan Medicinal Products on an Orphan Drug Designation application. Orphan Drug Designation is intended to promote the development of drugs that are intended for the diagnosis, prevention or treatment of life-threatening or chronically debilitating conditions affecting not more than 5 in 10,000 persons in Europe and for which no satisfactory method of diagnosis, prevention, or treatment has been authorized (or the product would be a significant benefit to those affected). Additionally, designation is granted for drugs intended for the diagnosis, prevention, or treatment of a life-threatening, seriously debilitating or serious and chronic condition and when, without incentives, it is unlikely that sales of the drug in Europe would be sufficient to justify the necessary investment in developing the drug. In Europe, Orphan Drug Designation entitles a party to financial incentives such as reduction of fees or fee waivers.

Generally, if a drug with an Orphan Drug Designation subsequently receives the first marketing approval for the indication for which it has such designation, the drug is entitled to a period of marketing exclusivity, which precludes the EMA or the FDA from approving another marketing application for the same drug and indication for that time period, except in limited circumstances. The applicable period is seven years in the United States and ten years in Europe. The European exclusivity period can be reduced to six years if a drug no longer meets the criteria for Orphan Drug Designation or if the drug is sufficiently profitable so that market exclusivity is no longer justified.

Even if we obtain orphan drug exclusivity for a drug, that exclusivity may not effectively protect the drug from competition because different drugs can be approved for the same condition. Even after an orphan drug is approved, the FDA can subsequently approve the same drug for the same condition if the FDA concludes that the later drug is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care. In addition, a designated orphan drug may not receive orphan drug exclusivity if it is approved for a use that is broader than the indication for which it received orphan designation. Moreover, orphan drug exclusive marketing rights in the United States may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition. Orphan Drug Designation neither shortens the development time or regulatory review time of a drug nor gives the drug any advantage in the regulatory review or approval process. While we intend to seek Orphan Drug Designation for our drug candidates, we may never receive such designations. Even if we do receive such designations, there is no guarantee that we will enjoy the benefits of those designations.

Even if we receive regulatory approval for any of our drug candidates, we will be subject to ongoing obligations and continued regulatory review, which may result in significant additional expense. Additionally, our drug candidates, if approved, could be subject to labeling and other restrictions and market withdrawal and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our drugs.

If the FDA or a comparable foreign regulatory authority approves any of our drug candidates, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion and recordkeeping for the drug will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with current Good Manufacturing Practices, or cGMPs, and Good Clinical Practices, or GCPs, for any clinical trials that we conduct post-approval. Any regulatory approvals that we receive for our drug candidates may also be subject to limitations on the approved indicated uses for which the drug may be marketed or to the conditions of approval, or contain requirements for potentially costly

post-marketing testing, including Phase 4 clinical trials, and surveillance to monitor the safety and efficacy of the drug. Later discovery of previously unknown problems with a drug, including adverse events of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things:

- restrictions on the marketing or manufacturing of the drug, withdrawal of the drug from the market, or voluntary drug recalls;
- fines, warning letters or holds on clinical trials;
- refusal by the FDA to approve pending applications or supplements to approved applications filed by us, or suspension or revocation of drug license approvals;
- drug seizure or detention, or refusal to permit the import or export of drugs; and
- injunctions or the imposition of civil or criminal penalties.

The FDA's policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our drug candidates. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained, which would adversely affect our business, prospects and ability to achieve or sustain profitability.

We may not be successful in our efforts to use and expand our development platform to build a pipeline of drug candidates.

A key element of our strategy is to use our novel target discovery engine to identify kinases that are drivers in genomically defined diseases with high unmet medical need in order to build a pipeline of drug candidates. Although our research and development efforts to date have resulted in a pipeline of drug candidates, we may not be able to continue to identify novel kinase drivers and develop drug candidates. Even if we are successful in continuing to build our pipeline, the potential drug candidates that we identify may not be suitable for clinical development. For example, they may be shown to have harmful side effects or other characteristics that indicate that they are unlikely to be drugs that will receive marketing approval and achieve market acceptance. If we do not successfully develop and commercialize drug candidates based upon our approach, we will not be able to obtain drug revenues in future periods, which likely would result in significant harm to our financial position and adversely affect our stock price.

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

Because we have limited financial and managerial resources, we focus on research programs and drug candidates that we identify for specific indications. As a result, we may forego or delay pursuit of opportunities with other drug 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 drugs or profitable market opportunities. Our spending on current and future research and development programs and drug candidates for specific indications may not yield any commercially viable drugs. If we do not accurately evaluate the commercial potential or target market for a particular drug candidate, we may relinquish valuable rights to that drug 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 drug candidate.

Risks Related to Commercialization

The incidence and prevalence for target patient populations of our drug candidates have not been established with precision. If the market opportunities for our drug candidates are smaller than we estimate or if any approval that we obtain is based on a narrower definition of the patient population, our revenue and ability to achieve profitability will be adversely affected, possibly materially.

The precise incidence and prevalence for SM, GIST and HCC are unknown. Our projections of both the number of people who have these diseases, as well as the subset of people with these diseases who have the potential to benefit from treatment with our drug candidates, are based on estimates. We estimate that there are approximately: (i) 4,500 addressable patients with advanced forms of SM and approximately 16,000 addressable patients with indolent SM in the United States, France, Germany, Italy, Spain, the United Kingdom and Japan, or the Major Markets; (ii) 500 addressable patients with PDGFRa D842V-driven, unresectable or metastatic GIST in the Major Markets and approximately 20,000 addressable patients in the Major Markets with unresectable or metastatic frontline GIST; and (iii) 18,000 first line and 6,000 second line addressable HCC patients with aberrantly active FGFR4, signaling in the Major Markets.

The total addressable market opportunity for BLU-285 for the treatment of patients with SM and GIST and BLU-554 for the treatment of HCC patients with aberrantly active FGFR4 signaling will ultimately depend upon, among other things, the diagnosis criteria included in the final label for each of BLU-285 and BLU-554, if our drug candidates are approved for sale for these indications, acceptance by the medical community and patient access, drug pricing and reimbursement. The number of patients in the Major Markets and elsewhere may turn out to be lower than expected, patients may not be otherwise amenable to treatment with our drugs, or new patients may become increasingly difficult to identify or gain access to, all of which would adversely affect our results of operations and our business.

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

The development and commercialization of new drugs is highly competitive. We face competition with respect to our current drug candidates, and will face competition with respect to any drug 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 drugs or are pursuing the development of therapies in the field of kinase inhibition for cancer and other diseases. Some of these competitive drugs 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.

Specifically, there are a large number of companies developing or marketing treatments for cancer, including many major pharmaceutical and biotechnology companies. If BLU-285 receives marketing approval for advanced SM, GIST and/or for patients with GIST with the PDGFRa D842V mutation, it may face competition from other drug candidates in development for these indications, including drug candidates in development from AB Science S.A., Plexxikon Inc., a wholly-owned subsidiary of Daiichi Sankyo Company, Limited, Deciphera Pharmaceuticals, LLC, Novartis AG, AROG Pharmaceuticals, Inc. and ARIAD Pharmaceuticals, Inc. Further, if BLU-554 receives marketing approval for patients with HCC with FGF19 overexpression, it will face competition from

sorafenib, the only approved systemic medical therapy for HCC. In addition, we are aware of potentially competitive drug candidates in development by AstraZeneca plc, Bayer AG, Johnson & Johnson, Novartis AG, Taiho Pharmaceutical Co., Ltd. and Xoma Ltd.

Many of the companies against which we are competing or against which we may compete in the future have significantly greater financial resources and expertise in research and development, manufacturing, pre-clinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved drugs 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. Smaller or early stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. 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.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize drugs that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any drugs that we or our collaborators may develop. Our competitors also may obtain FDA or other regulatory approval for their drugs more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we or our collaborators are able to enter the market. The key competitive factors affecting the success of all of our drug candidates, if approved, are likely to be their efficacy, safety, convenience, price, the effectiveness of companion diagnostics in guiding the use of related drugs, the level of generic competition and the availability of reimbursement from government and other third-party payors.

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

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

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

Although we maintain product liability insurance coverage, it may not be adequate to cover all liabilities that we may incur. We anticipate that we will need to increase our insurance coverage when we begin clinical trials and if we successfully commercialize any drug candidate. 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 or our collaborators are unable to successfully develop and commercialize companion diagnostics for our drug candidates, or experience significant delays in doing so we may not realize the full commercial potential of our drug candidates.

Because we are focused on precision medicine, in which predictive biomarkers will be used to identify the right patients for our drug candidates, we believe that our success may depend, in part, on the development and commercialization of companion diagnostics. There has been limited success to date industrywide in developing and commercializing these types of companion diagnostics. To be successful, we need to address a number of scientific, technical and logistical challenges. We have not yet initiated development and commercialization of companion diagnostics. We have little experience in the development and commercialization of diagnostics and may not be successful in developing and commercializing appropriate diagnostics to pair with any of our drug candidates that receive marketing approval. Companion diagnostics are subject to regulation by the FDA and similar regulatory authorities outside the United States as medical devices and require separate regulatory approval prior to commercialization. Given our limited experience in developing and commercializing diagnostics, we expect to rely in part or in whole on third parties for their design, manufacture and commercialization. We and our collaborators may encounter difficulties in developing and obtaining approval for the companion diagnostics, including issues relating to selectivity/specificity, analytical validation, reproducibility, or clinical validation. Any delay or failure by us or our collaborators to develop or obtain regulatory approval of the companion diagnostics could delay or prevent approval of our drug candidates. If we, or any third parties that we engage to assist us, are unable to successfully develop and commercialize companion diagnostics for our drug candidates, or experience delays in doing so:

- the development of our drug candidates may be adversely affected if we are unable to appropriately select patients for enrollment in our clinical trials;
- our drug candidates may not receive marketing approval if safe and effective use of a therapeutic drug candidate depends on an *in vitro* diagnostic; and
- we may not realize the full commercial potential of any drug candidates that receive marketing approval if, among other reasons, we are unable to appropriately select patients who are likely to benefit from therapy with our drugs.

As a result, our business would be harmed, possibly materially.

In addition, third party collaborators may encounter production difficulties that could constrain the supply of the companion diagnostics, and both they and we may have difficulties gaining acceptance of the use of the companion diagnostics in the clinical community. If such companion diagnostics fail to gain market acceptance, it would have an adverse effect on our ability to derive revenues from sales of our drug candidates, if approved. In addition, the diagnostic company with whom we contract may decide to discontinue selling or manufacturing the companion diagnostic that we anticipate using in connection with development and commercialization of our drug candidates or our relationship with such diagnostic company may otherwise terminate. We may not be able to enter into arrangements with another diagnostic company to obtain supplies of an alternative diagnostic test for use in connection with the development and commercialization of our drug candidates or do so on commercially reasonable terms, which could adversely affect and/or delay the development or commercialization of our drug candidates.

Even if we are able to commercialize any drug candidates, such drugs may become subject to unfavorable pricing regulations or third-party coverage and reimbursement policies, which would harm our business.

The regulations that govern regulatory approvals, pricing and reimbursement for new drugs vary widely from country to country. 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 approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a drug candidate in a particular country, but then be subject to price regulations that delay our commercial launch of the drug candidate, possibly for lengthy time periods, and negatively impact the revenues we are able to generate from the sale of the drug candidate in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more drug candidates, even if our drug candidates obtain marketing approval.

Our ability to commercialize any drug candidates successfully also will depend in part on the extent to which coverage and reimbursement for these drug candidates and related treatments will be available from government authorities, 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 primary 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 reimbursement for particular drugs. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for drugs. We cannot be sure that coverage will be available for any drug candidate that we commercialize and, if coverage is available, the level of reimbursement. Reimbursement may impact the demand for, or the price of, any drug 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 drug candidate for which we obtain marketing approval.

There may be significant delays in obtaining reimbursement for newly approved drugs, and coverage may be more limited than the purposes for which the drug is approved by the FDA or similar regulatory authorities outside the United States. Moreover, eligibility for reimbursement does not imply that any drug 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 clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs and 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 policy and payment limitations in setting their own reimbursement policies. Our inability to promptly obtain coverage and profitable payment rates from both government-funded and private payors for any approved drugs that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize drugs and our overall financial condition.

Healthcare legislative reform measures may have a material adverse effect on our business and results of operations.

In the United States, there have been and continue to be a number of legislative initiatives to contain healthcare costs. For example, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or the Affordable Care Act, was passed, which substantially changes the way health care is financed by both governmental and private insurers, and significantly impacts the U.S. pharmaceutical industry. The Affordable Care Act, among other things, subjects biologic products to potential competition by lower-cost biosimilars, addresses a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected, increases the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extends the rebate program to individuals enrolled in Medicaid managed care organizations, establishes annual fees and taxes on manufacturers of certain branded prescription drugs, and a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D.

In addition, other legislative changes have been proposed and adopted in the United States since the Affordable Care Act was enacted. On August 2, 2011, the Budget Control Act of 2011 among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers of 2% per fiscal year. These reductions went into effect on April 1, 2013 and, due to subsequent legislative amendments to the statute, will remain in effect through 2024 unless additional Congressional action is taken. On January 2, 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several types of providers.

Moreover, payment methodologies may be subject to changes in healthcare legislation and regulatory initiatives. For example, the Middle Class Tax Relief and Job Creation Act of 2012 required that the Centers for Medicare & Medicaid Services, the agency responsible for administering the Medicare program, or CMS, reduce the Medicare clinical laboratory fee schedule by 2% in 2013, which served as a base for 2014 and subsequent years. In addition, effective January 1, 2014, CMS also began bundling the Medicare payments for certain laboratory tests ordered while a patient received services in a hospital outpatient setting. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our drug candidates or companion diagnostics or additional pricing pressures.

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

We do not currently have a sales or marketing infrastructure and have limited experience in the sale, marketing or distribution of drugs. To achieve commercial success for any approved drug candidate for which we retain sales and marketing responsibilities, we must build our sales, marketing, managerial, and other non-technical capabilities or make arrangements with third parties to perform these services. In the future, we may choose to build a focused sales and marketing

infrastructure to sell, or participate in sales activities with our collaborators for, some of our drug candidates if and when they are approved.

There are risks involved with both establishing our own sales and marketing capabilities and 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 drug launch. If the commercial launch of a drug 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 drug 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 drugs;
- the lack of complementary drugs to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; 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 drug revenues or the profitability of these drug revenues to us are likely to be lower than if we were to market and sell any drug candidates that we develop ourselves. In addition, we may not be successful in entering into arrangements with third parties to sell and market our drug candidates or may be unable to do so on terms that are favorable to us. We likely will 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 drug candidates 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 drug candidates. Further, our business, results of operations, financial condition and prospects will be materially adversely affected.

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, exclusion from government healthcare programs, contractual damages, reputational harm and diminished profits and future earnings.

Although we do not currently have any drugs on the market, once we begin commercializing our drug candidates, we will be subject to additional healthcare statutory and regulatory requirements and enforcement by the federal government and the states and foreign governments in which we conduct our business. Healthcare providers, physicians and third-party payors play a primary role in the recommendation and prescription of any drug 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 drug candidates for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations, include the following:

- the federal 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. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;

- the federal False Claims Act imposes criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government. In addition, the government may assert that a claim including items and services resulting from a violation of the federal Anti-Kickback Statute constitutes a false of fraudulent claim for purposes of the False Claims Act;

- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program, or 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; similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;

- the federal physician payment transparency requirements, sometimes referred to as the "Sunshine Act" under the Affordable Care Act require manufacturers of drugs, devices, biologics and medical supplies that are reimbursable under Medicare, Medicaid, or the Children's Health Insurance Program to report to the Department of Health and Human Services information related to physician payments and other transfers of value and the ownership and investment interests of such physicians and their immediate family members;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 and its implementing regulations, which also imposes obligations on certain covered entity healthcare providers, health plans, and healthcare clearinghouses as well as their business associates that perform certain services involving the use or disclosure of individually identifiable health information, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information; and

- analogous state laws and regulations, such as state anti-kickback and false claims laws that 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, and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Ensuring that our future business arrangements with third parties comply with applicable healthcare laws and regulations could involve substantial costs. It is possible that governmental authorities will conclude that our business practices do 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, including anticipated activities to be conducted by our sales team, were to be 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 is 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.

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

Our future profitability may depend, in part, on our ability to commercialize our drug candidates in foreign markets for which we may rely on collaboration with third parties. We are not permitted to market or promote any of our drug candidates before we receive regulatory approval from the applicable regulatory authority in that foreign market, and we may never receive such regulatory approval for any of our drug candidates. To obtain separate regulatory approval in many other countries we must comply with numerous and varying regulatory requirements of such countries regarding safety and efficacy and governing, among other things, clinical trials and commercial sales, pricing and distribution of our drug candidates, and we cannot predict success in these jurisdictions. If we obtain approval of our drug candidates and ultimately commercialize our drug candidates in foreign markets, we would be subject to additional risks and uncertainties, including:

- our customers' ability to obtain reimbursement for our drug candidates in foreign markets;
- our inability to directly control commercial activities because we are relying on third parties;
- the burden of complying with complex and changing foreign regulatory, tax, accounting and legal requirements;
- different medical practices and customs in foreign countries affecting acceptance in the marketplace;
- import or export licensing requirements;
- longer accounts receivable collection times;
- longer lead times for shipping;
- language barriers for technical training;
- reduced protection of intellectual property rights in some foreign countries;
- the existence of additional potentially relevant third-party intellectual property rights;
- foreign currency exchange rate fluctuations; and
- the interpretation of contractual provisions governed by foreign laws in the event of a contract dispute.

Foreign sales of our drug candidates could also be adversely affected by the imposition of governmental controls, political and economic instability, trade restrictions and changes in tariffs.

Governments outside the United States tend to impose strict price controls, which may adversely affect our revenues, if any.

In some countries, particularly the countries in Europe, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a drug. To obtain reimbursement or pricing approval in some countries, we may be required to

conduct a clinical trial that compares the cost-effectiveness of our drug candidate to other available therapies. If reimbursement of our drugs is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be harmed, possibly materially.

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 have a material adverse effect on the success of 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 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, hazardous or radioactive materials.

Risks Related to Our Dependence on Third Parties

We may seek to establish additional collaborations, and, if we are not able 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 drug candidates will require substantial additional cash to fund expenses. For some of our drug candidates, we may decide to collaborate with additional pharmaceutical and biotechnology companies for the development and potential commercialization of those drug 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 drug candidate, the costs and complexities of manufacturing and delivering such drug candidate to patients, the potential of competing drugs, 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 drug candidates or technologies 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 drug candidate. The terms of any additional collaborations or other arrangements that we may establish may not be favorable to us.

We may also be restricted under existing collaboration agreements from entering into future agreements on certain terms with potential collaborators. 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.

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

In addition, our collaboration with Alexion and any future collaborations that we enter into may not be successful. The success of our collaboration arrangements will depend heavily on the efforts and activities of our collaborators. Collaborators generally have significant discretion in determining the efforts and resources that they will apply to these collaborations. Disagreements between parties to a collaboration arrangement regarding clinical development and commercialization matters can lead to delays in the development process or commercializing the applicable drug candidate and, in some cases, termination of the collaboration arrangement. These disagreements can be difficult to resolve if neither of the parties has final decision-making authority. Collaborations with pharmaceutical or biotechnology companies and other third parties often are terminated or allowed to expire by the other party. Any such termination or expiration would adversely affect us financially and could harm our business reputation.

We expect to rely on third parties to conduct our clinical trials for our drug candidates. If these third parties do not successfully carry out their contractual duties, comply with regulatory requirements or meet expected deadlines, we may not be able to obtain regulatory approval for or commercialize our drug candidates and our business could be substantially harmed.

We do not have the ability to independently conduct clinical trials. We expect to rely on medical institutions, clinical investigators, contract laboratories and other third parties, such as CROs, to conduct or otherwise support clinical trials for our drug candidates. We expect to rely heavily on these parties for execution of clinical trials for our drug candidates and control only certain aspects of their activities. Nevertheless, we will be responsible for ensuring that each of our clinical trials is conducted in accordance with the applicable protocol, legal and regulatory requirements and scientific standards, and our reliance on CROs will not relieve us of our regulatory responsibilities. For any violations of laws and regulations during the conduct of our clinical trials, we could be subject to warning letters or enforcement action that may include civil penalties up to and including criminal prosecution.

We and our CROs will be required to comply with regulations, including GCPs, for conducting, monitoring, recording and reporting the results of clinical trials to ensure that the data and results are scientifically credible and accurate, and that the trial patients are adequately informed of the potential risks of participating in clinical trials and their rights are protected. These regulations are enforced by the FDA, the Competent Authorities of the Member States of the European Economic Area and comparable foreign regulatory authorities for any drugs in clinical development. The FDA enforces GCP regulations through periodic inspections of clinical trial sponsors, principal investigators and trial sites. If we or our CROs fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our

marketing applications. We cannot assure you that, upon inspection, the FDA will determine that any of our future clinical trials will comply with GCPs. In addition, our clinical trials must be conducted with drug candidates produced under cGMPs regulations. Our failure or the failure of our CROs to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process and could also subject us to enforcement action. We also are required to register ongoing clinical trials and post the results of completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within certain timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

Although we intend to design the clinical trials for our drug candidates, CROs will conduct all of the clinical trials. As a result, many important aspects of our development programs, including their conduct and timing, will be outside of our direct control. Our reliance on third parties to conduct future clinical trials will also result in less direct control over the management of data developed through clinical trials than would be the case if we were relying entirely upon our own staff. Communicating with outside parties can also be challenging, potentially leading to mistakes as well as difficulties in coordinating activities. Outside parties may:

- have staffing difficulties;
- fail to comply with contractual obligations;
- experience regulatory compliance issues;
- undergo changes in priorities or become financially distressed; or
- form relationships with other entities, some of which may be our competitors.

These factors may materially adversely affect the willingness or ability of third parties to conduct our clinical trials and may subject us to unexpected cost increases that are beyond our control. If the CROs do not perform clinical trials in a satisfactory manner, breach their obligations to us or fail to comply with regulatory requirements, the development, regulatory approval and commercialization of our drug candidates may be delayed, we may not be able to obtain regulatory approval and commercialize our drug candidates, or our development program materially and irreversibly harmed. If we are unable to rely on clinical data collected by our CROs, we could be required to repeat, extend the duration of, or increase the size of any clinical trials we conduct and this could significantly delay commercialization and require significantly greater expenditures.

If any of our relationships with these third-party CROs terminate, we may not be able to enter into arrangements with alternative CROs. If CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols, regulatory requirements or for other reasons, any clinical trials such CROs are associated with may be extended, delayed or terminated, and we may not be able to obtain regulatory approval for or successfully commercialize our drug candidates. As a result, we believe that our financial results and the commercial prospects for our drug candidates in the subject indication would be harmed, our costs could increase and our ability to generate revenue could be delayed.

We contract with third parties for the manufacture of our drug candidates for pre-clinical development and expect to continue to do so for clinical testing and commercialization. This reliance on third parties increases the risk that we will not have sufficient quantities of our drug candidates or drugs or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.

We do not currently own or operate, nor do we have any plans to establish in the future, any manufacturing facilities or personnel. We rely, and expect to continue to rely, on third parties for the

manufacture of our drug candidates for pre-clinical development and clinical testing, as well as for the commercial manufacture of our drugs if any of our drug candidates receive marketing approval. This reliance on third parties increases the risk that we will not have sufficient quantities of our drug candidates or drugs or such quantities at an acceptable cost or quality, which could delay, prevent or impair our development or commercialization efforts.

The facilities used by our contract manufacturers to manufacture our drug candidates must be approved by the FDA pursuant to inspections that will be conducted after we submit our marketing applications to the FDA. We do not control the manufacturing process of, and will be completely dependent on, our contract manufacturers for compliance with cGMPs in connection with the manufacture of our drug candidates. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or others, they will not be able to secure and/or maintain regulatory approval for their manufacturing facilities. In addition, we have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or a comparable foreign regulatory authority does not approve these facilities for the manufacture of our drug candidates or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market our drug candidates, if approved. Further, our failure, or the failure of our third party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of drug candidates or drugs, if approved, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect our business and supplies of our drug candidates.

We may be unable to establish any 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;
- the possible misappropriation of our proprietary information, including our trade secrets and know-how; and
- the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us.

Our drug candidates and any drugs that we may develop may compete with other drug candidates and approved drugs for access to manufacturing facilities. There are a limited number of manufacturers that operate under cGMP regulations 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. If our current contract manufacturers cannot perform as agreed, we may be required to replace such manufacturers. Although we believe that there are several potential alternative manufacturers who could manufacture our drug 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 drug candidates or drugs may adversely affect our future profit margins and our ability to commercialize any drugs that receive marketing approval on a timely and competitive basis.

The third parties upon whom we rely for the supply of the active pharmaceutical ingredient, drug product and drug substance used in our lead drug candidates are our sole source of supply, and the loss of any of these suppliers could significantly harm our business.

The active pharmaceutical ingredients, or API, drug product and drug substance used in our lead drug candidates are supplied to us from single-source suppliers. Our ability to successfully develop our drug candidates, and to ultimately supply our commercial drugs in quantities sufficient to meet the market demand, depends in part on our ability to obtain the API, drug product and drug substance for these drugs in accordance with regulatory requirements and in sufficient quantities for commercialization and clinical testing. We do not currently have arrangements in place for a redundant or second-source supply of any such API, drug product or drug substance in the event any of our current suppliers of such API, drug product and drug substance cease their operations for any reason.

For all of our drug candidates, we intend to identify and qualify additional manufacturers to provide such API, drug product and drug substance prior to submission of an NDA to the FDA and/or an MAA to the EMA. We are not certain, however, that our single-source suppliers will be able to meet our demand for their products, either because of the nature of our agreements with those suppliers, our limited experience with those suppliers or our relative importance as a customer to those suppliers. It may be difficult for us to assess their ability to timely meet our demand in the future based on past performance. While our suppliers have generally met our demand for their products on a timely basis in the past, they may subordinate our needs in the future to their other customers.

Establishing additional or replacement suppliers for the API, drug product and drug substance used in our drug candidates, if required, may not be accomplished quickly. If we are able to find a replacement supplier, such replacement supplier would need to be qualified and may require additional regulatory approval, which could result in further delay. While we seek to maintain adequate inventory of the API, drug product and drug substance used in our drug candidates, any interruption or delay in the supply of components or materials, or our inability to obtain such API, drug product and drug substance from alternate sources at acceptable prices in a timely manner could impede, delay, limit or prevent our development efforts, which could harm our business, results of operations, financial condition and prospects.

Risks Related to Intellectual Property

If we are unable to adequately protect our proprietary technology or obtain and maintain patent protection for our technology and drugs or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize technology and drugs similar or identical to ours, and our ability to successfully commercialize our technology and drugs may be impaired.

Our commercial success depends in part on our ability to obtain and maintain proprietary or intellectual property protection in the United States and other countries for our drug candidates, including BLU-285 and BLU-554, and our core technologies, including our novel target discovery engine and our proprietary compound library and other know-how. We seek to protect our proprietary and intellectual property position by, among other methods, filing patent applications in the United States and abroad related to our proprietary technology, inventions and improvements that are important to the development and implementation of our business. We also rely on trade secrets, know-how and continuing technological innovation to develop and maintain our proprietary and intellectual property position.

We own a patent and patent applications that relate to BLU-285 and BLU-554 as composition of matter. We also own applications relating to composition of matter for KIT Exon 17 inhibitors with

different compound families, composition of matter for FGFR4 inhibitors with multiple compound families, and composition of matter for inhibitors of the predicted RET resistant mutants, as well as methods of use for these novel compounds. The issued patent directed to BLU-554 composition of matter is expected to expire in 2033, and any patents issuing from our pending patent applications are projected to expire between 2034 and 2036.

As of March 31, 2015, we owned four pending U.S. patent applications, nine pending foreign patent applications and three pending Patent Cooperation Treaty, or PCT, patent applications that relate to our KIT Exon 17 program. Any U.S. or ex-U.S. patents issuing from the pending applications covering BLU-285 will have a statutory expiration date of October 2034. Patent term adjustments or patent term extensions could result in later expiration dates.

As of March 31, 2015, we owned one issued U.S. patent, three pending U.S. patent applications, 32 foreign patent applications corresponding to two of these pending U.S. applications, and two pending PCT patent applications that relate to our FGFR4 program. Each of the U.S. and ex-U.S. patent issuing from the pending applications covering BLU-554 will have a statutory expiration date of July 2033, December 2033, or October 2034. Patent term adjustments or patent term extensions could result in later expiration dates.

As of March 31, 2015, we owned one pending U.S. patent application that relates to our RET program.

The intellectual property portfolio directed to our platform includes patent applications directed to novel gene fusions and the uses of these fusions for detecting and treating conditions implicated with these fusions. As of March 31, 2015, we owned eight pending U.S. patent applications and two PCT patent applications related to our platform.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation.

The degree of patent protection we require to successfully commercialize our drug candidates may be unavailable or severely limited in some cases and may not adequately protect our rights or permit us to gain or keep any competitive advantage. We cannot provide any assurances that any of our patents have, or that any of our pending patent applications that mature into issued patents will include, claims with a scope sufficient to protect BLU-285, BLU-554 or our other drug candidates. In addition, the laws of foreign countries may not protect our rights to the same extent as the laws of the United States. Furthermore, patents have a limited lifespan. In the United States, the natural expiration of a patent is generally twenty years after it is filed. Various extensions may be available; however, the life of a patent, and the protection it affords, is limited. Given the amount of time required for the development, testing and regulatory review of new drug candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our owned and licensed patent portfolio may not provide us with adequate and continuing patent protection sufficient to exclude others from commercializing drugs similar or identical to our drug candidates, including generic versions of such drugs.

Other parties have developed technologies that may be related or competitive to our own, and such parties may have filed or may file patent applications, or may have received or may receive patents, claiming inventions that may overlap or conflict with those claimed in our own patent applications or issued patents, with respect to either the same methods or formulations or the same subject matter, in either case that we may rely upon to dominate our patent position in the market. Publications of 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. Therefore, we cannot know with certainty whether

we were the first to make the inventions claimed in our owned or licensed patents or pending patent applications, or that we were the first to file for patent protection of such inventions. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights cannot be predicted with any certainty.

In addition, the patent prosecution process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. Further, with respect to most of the pending patent applications covering our drug candidates, prosecution has yet to commence. Patent prosecution is a lengthy process, during which the scope of the claims initially submitted for examination by the U.S. Patent and Trademark Office, or USPTO, have been significantly narrowed by the time they issue, if at all. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Moreover, in some circumstances, we do not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology that we license from third parties. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business.

Even if we acquire patent protection that we expect should enable us to maintain such competitive advantage, third parties may challenge the validity, enforceability or scope thereof, which may result in such patents being narrowed, invalidated or held unenforceable. The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our owned and licensed patents may be challenged in the courts or patent offices in the United States and abroad. For example, we may be subject to a third-party submission of prior art to the USPTO challenging the priority of an invention claimed within one of our patents, which submissions may also be made prior to a patent's issuance, precluding the granting of any of our pending patent applications. We may become involved in opposition, derivation, reexamination, *inter partes* review, post-grant review or interference proceedings challenging our patent rights or the patent rights of others from whom we have obtained licenses to such rights. Competitors may claim that they invented the inventions claimed in our issued patents or patent applications prior to us, or may file patent applications before we do. Competitors may also claim that we are infringing on their patents and that we therefore cannot practice our technology as claimed under our patents, if issued. Competitors may also contest our patents, if issued, by showing the patent examiner that the invention was not original, was not novel or was obvious. In litigation, a competitor could claim that our patents, if issued, are not valid for a number of reasons. If a court agrees, we would lose our rights to those challenged patents.

In addition, we may in the future be subject to claims by our former employees or consultants asserting an ownership right in our patents or patent applications, as a result of the work they performed on our behalf. Although we generally require all of our employees, consultants and advisors and any other third parties who have access to our proprietary know-how, information or technology to assign or grant similar rights to their inventions to us, we cannot be certain that we have executed such agreements with all parties who may have contributed to our intellectual property, nor can we be certain that our agreements with such parties will be upheld in the face of a potential challenge, or that they will not be breached, for which we may not have an adequate remedy.

An adverse determination in any such submission or proceeding may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and drugs, without payment to us, or could limit the duration of the patent protection covering our technology and drug candidates. Such challenges may also result in our inability to manufacture or commercialize our drug candidates without

infringing third party patent rights. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future drug candidates.

Even if they are unchallenged, our issued patents and our pending patents, if issued, may not provide us with any meaningful protection or prevent competitors from designing around our patent claims to circumvent our owned or licensed patents by developing similar or alternative technologies or drugs in a non-infringing manner. For example, a third party may develop a competitive drug that provides benefits similar to one or more of our drug candidates but that has a different composition that falls outside the scope of our patent protection. If the patent protection provided by the patents and patent applications we hold or pursue with respect to our drug candidates is not sufficiently broad to impede such competition, our ability to successfully commercialize our drug candidates could be negatively affected, which would harm our business.

Third parties may initiate legal proceedings alleging that we are infringing their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business.

Our commercial success depends upon our ability and the ability of our collaborators to develop, manufacture, market and sell our drug candidates and use our proprietary technologies without infringing the proprietary rights and intellectual property of third parties. The biotechnology and pharmaceutical industries are characterized by extensive and frequent litigation regarding patents and other intellectual property rights. We may in the future become party to, or threatened with, adversarial proceedings or litigation regarding intellectual property rights with respect to our drug candidates and technology, including interference proceedings before the USPTO. Our competitors or other third parties may assert infringement claims against us, alleging that our drugs are covered by their patents. Given the vast number of patents in our field of technology, we cannot be certain that we do not infringe existing patents or that we will not infringe patents that may be granted in the future. Many companies have filed, and continue to file, patent applications related to kinase inhibitors. Some of these patent applications have already been allowed or issued, and others may issue in the future. Since this area is competitive and of strong interest to pharmaceutical and biotechnology companies, there will likely be additional patent applications filed and additional patents granted in the future, as well as additional research and development programs expected in the future. Furthermore, because patent applications can take many years to issue and may be confidential for 18 months or more after filing, and because pending patent claims can be revised before issuance, there may be applications now pending which may later result in issued patents that may be infringed by the manufacture, use or sale of our drug candidates. If a patent holder believes our drug or drug candidate infringes on its patent, the patent holder may sue us even if we have received patent protection for our technology. Moreover, we may face patent infringement claims from non-practicing entities that have no relevant drug revenue and against whom our own patent portfolio may thus have no deterrent effect.

If we are found to infringe a third party's intellectual property rights, we could be required to obtain a license from such third party to continue developing and marketing our drug candidates and technology. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain such a license, it could be granted on non-exclusive terms, thereby providing our competitors and other third parties access to the same technologies licensed to us. Without such a license, we could be forced, including by court order, to cease developing and commercializing the infringing technology or drug candidates. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees if we are found to have willfully infringed such third-party patent rights. A finding of infringement could

prevent us from commercializing our drug candidates or force us to cease some of our business operations, which could materially harm our business.

We may become involved in lawsuits to protect or enforce our patents and other intellectual property rights, which could be expensive, time consuming and unsuccessful.

Competitors and other third parties may infringe, misappropriate or otherwise violate our patents and other intellectual property rights. To counter infringement or unauthorized use, we may be required to file infringement claims. A court may disagree with our allegations, however, and may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the third-party technology in question. Further, such third parties could counterclaim that we infringe their intellectual property or that a patent we have asserted against them is invalid or unenforceable. In patent litigation in the United States, defendant counterclaims challenging the validity, enforceability or scope of asserted patents are commonplace. In addition, third parties may initiate legal proceedings against us to assert such challenges to our intellectual property rights. The outcome of any such proceeding is generally unpredictable. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness or non-enablement. Patents may be unenforceable if someone connected with prosecution of the patent withheld relevant information from the USPTO or made a misleading statement during prosecution. It is possible that prior art of which we and the patent examiner were unaware during prosecution exists, which could render our patents invalid. Moreover, it is also possible that prior art may exist that we are aware of but do not believe is relevant to our current or future patents, but that could nevertheless be determined to render our patents invalid.

An adverse result in any litigation proceeding could put one or more of our patents at risk of being invalidated or interpreted narrowly. If a defendant were to prevail on a legal assertion of invalidity or unenforceability of our patents covering one of our drug candidates, we would lose at least part, and perhaps all, of the patent protection covering such drug candidate. Competing drugs may also be sold in other countries in which our patent coverage might not exist or be as strong. If we lose a foreign patent lawsuit, alleging our infringement of a competitor's patents, we could be prevented from marketing our drugs in one or more foreign countries. Any of these outcomes would have a materially adverse effect on our business.

Intellectual property litigation could cause us to spend substantial resources and distract our personnel from their normal responsibilities.

Litigation or other legal proceedings relating to intellectual property claims, with or without merit, is unpredictable and generally expensive and time consuming and is likely to divert significant resources from our core business, including distracting our technical and management personnel from their normal responsibilities. 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. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities.

We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and more mature and developed intellectual property portfolios. Accordingly, despite our efforts, we may not

be able to prevent third parties from infringing upon or misappropriating or from successfully challenging our intellectual property rights. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace.

Obtaining and maintaining patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. In addition, periodic maintenance fees on issued patents often must be paid to the USPTO and foreign patent agencies over the lifetime of the patent. While an unintentional lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. If we fail to maintain the patents and patent applications covering our drugs or procedures, we may not be able to stop a competitor from marketing drugs that are the same as or similar to our drug candidates, which would have a material adverse effect on our business.

We may not be able to effectively enforce our intellectual property rights throughout the world.

Filing, prosecuting and defending patents on our drug candidates in all countries throughout the world would be prohibitively expensive. The requirements for patentability may differ in certain countries, particularly in developing countries. Moreover, our ability to protect and enforce our intellectual property rights may be adversely affected by unforeseen changes in foreign intellectual property laws. Additionally, the patent laws of some foreign countries do not afford intellectual property protection to the same extent as the laws of the United States. Many companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions. The legal systems of some countries, particularly developing countries, do not favor the enforcement of patents and other intellectual property rights. This could make it difficult for us to stop the infringement of our patents or the misappropriation of our other intellectual property rights. For example, many foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own drugs and, further, may export otherwise infringing drugs to territories where we have patent protection, if our ability to enforce our patents to stop infringing activities is inadequate. These drugs may compete with our drug candidates, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Proceedings to enforce our patent rights in foreign jurisdictions, whether or not successful, could result in substantial costs and divert our efforts and resources from other aspects of our business. Furthermore, while we intend to protect our intellectual property rights in the major markets for our drug candidates, we cannot ensure that we will be able to initiate or maintain similar efforts in all jurisdictions in which we may wish to market our drug candidates. Accordingly, our efforts to protect our intellectual property rights in such countries may be inadequate.

Changes to the patent law in the United States and other jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our drug candidates.

As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involve both technological and legal complexity and is therefore costly, time consuming and inherently uncertain. Recent patent reform legislation in the United States and other countries, including the Leahy-Smith America Invents Act, or Leahy-Smith Act, signed into law on September 16, 2011, could increase those uncertainties and costs. The Leahy-Smith Act includes a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications are prosecuted, redefine prior art and provide more efficient and cost-effective avenues for competitors to challenge the validity of patents. In addition, the Leahy-Smith Act has transformed the U.S. patent system into a "first to file" system. The first-to-file provisions, however, only became effective on March 16, 2013. Accordingly, it is not yet clear what, if any, impact the Leahy-Smith Act will have on the operation of our business. However, the Leahy-Smith Act and its implementation could make it more difficult to obtain patent protection for our inventions and increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could harm our business, results of operations and financial condition.

The U.S. Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. Additionally, there have been recent proposals for additional changes to the patent laws of the United States and other countries that, if adopted, could impact our ability to obtain patent protection for our proprietary technology or our ability to enforce our proprietary technology. Depending on future actions by the U.S. Congress, the U.S. courts, the USPTO and the relevant law-making bodies in other countries, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

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

In addition to the protection afforded by patents, we rely upon unpatented trade secret protection, unpatented know-how and continuing technological innovation to develop and maintain our competitive position. With respect to the building of our proprietary compound library, we consider trade secrets and know-how to be our primary intellectual property. We seek to protect our proprietary technology and processes, in part, by entering into confidentiality agreements with our collaborators, scientific advisors, employees and consultants, and invention assignment agreements with our consultants and employees. We may not be able to prevent the unauthorized disclosure or use of our technical know-how or other trade secrets by the parties to these agreements, however, despite the existence generally of confidentiality agreements and other contractual restrictions. Monitoring unauthorized uses and disclosures is difficult, and we do not know whether the steps we have taken to protect our proprietary technologies will be effective. If any of the collaborators, scientific advisors, employees and consultants who are parties to these agreements breaches or violates the terms of any of these agreements, we may not have adequate remedies for any such breach or violation, and we could lose our trade secrets as a result. Enforcing a claim that a third party illegally obtained and is using our trade secrets, like patent litigation, is expensive and time consuming, and the outcome is unpredictable. In addition, courts outside the United States are sometimes less willing to protect trade secrets.

Our trade secrets could otherwise become known or be independently discovered by our competitors. Competitors could purchase our drug candidates and attempt to replicate some or all

of the competitive advantages we derive from our development efforts, willfully infringe our intellectual property rights, design around our protected technology or develop their own competitive technologies that fall outside of our intellectual property rights. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us. If our trade secrets are not adequately protected so as to protect our market against competitors' drugs, our competitive position could be adversely affected, as could our business.

We may be subject to damages resulting from claims that we or our employees have wrongfully used or disclosed alleged trade secrets of our competitors or are in breach of non-competition or non-solicitation agreements with our competitors.

We could in the future be subject to claims that we or our employees have inadvertently or otherwise used or disclosed alleged trade secrets or other proprietary information of former employers or competitors. Although we try to ensure that our employees and consultants do not use the intellectual property, proprietary information, know-how or trade secrets of others in their work for us, we may in the future be subject to claims that we caused an employee to breach the terms of his or her non-competition or non-solicitation agreement, or that we or these individuals have, inadvertently or otherwise, used or disclosed the alleged trade secrets or other proprietary information of a former employer or competitor. Litigation may be necessary to defend against these claims. Even if we are successful in defending against these claims, litigation could result in substantial costs and could be a distraction to management. If our defenses to these claims fail, in addition to requiring us to pay monetary damages, a court could prohibit us from using technologies or features that are essential to our drug candidates, if such technologies or features are found to incorporate or be derived from the trade secrets or other proprietary information of the former employers. An inability to incorporate such technologies or features would have a material adverse effect on our business, and may prevent us from successfully commercializing our drug candidates. In addition, we may lose valuable intellectual property rights or personnel as a result of such claims. Moreover, any such litigation or the threat thereof may adversely affect our ability to hire employees or contract with independent sales representatives. A loss of key personnel or their work product could hamper or prevent our ability to commercialize our drug candidates, which would have an adverse effect on our business, results of operations and financial condition.

Risks Related to Employee Matters, Managing Growth and Other Risks Related to Our Business

Our future success depends on our ability to retain key executives and to attract, retain and motivate qualified personnel.

We are highly dependent on the research and development, clinical and business development expertise of Jeffrey W. Albers, our President and Chief Executive Officer, Anthony L. Boral, our Senior Vice President, Clinical Development, Kyle D. Kuvalanka, our Chief Business Officer, and Christoph Lengauer, our Chief Scientific Officer, as well as the other principal members of our management, scientific and clinical team. Although we have entered into employment letter agreements with our executive officers, each of them may terminate their employment with us at any time. We do not maintain "key person" insurance for any of our executives or other employees. 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. If we are unable to continue to attract and retain high quality personnel, our ability to pursue our growth strategy will be limited.

Recruiting and retaining qualified scientific, clinical, manufacturing and sales and marketing personnel will also be critical to our success. The loss of the services of our executive officers or other key employees could impede the achievement of our research, development and commercialization objectives and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval of and commercialize drugs. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these key 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. Failure to succeed in clinical trials may make it more challenging to recruit and retain qualified scientific personnel.

We will need to develop and expand our company, and we may encounter difficulties in managing this development and expansion, which could disrupt our operations.

As of March 31, 2015 we had 60 full-time employees, and in connection with becoming a public company, we expect to increase our number of employees and the scope of our operations. To manage our anticipated development and expansion, 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. Also, our management may need to divert a disproportionate amount of its attention away from its day-to-day activities and devote a substantial amount of time to managing these development activities. Due to our limited resources, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. This may result in weaknesses in our infrastructure, give rise to operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees. The physical expansion of our operations may lead to significant costs and may divert financial resources from other projects, such as the development of our drug candidates. If our management is unable to effectively manage our expected development and expansion, our expenses may increase more than expected, our ability to generate or increase our revenue could be reduced and we may not be able to implement our business strategy. Our future financial performance and our ability to commercialize our drug candidates, if approved, and compete effectively will depend, in part, on our ability to effectively manage the future development and expansion of our company.

Unfavorable global economic conditions could adversely affect our business, financial condition or results of operations.

Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets. For example, the global financial crisis caused extreme volatility and disruptions in the capital and credit markets. A severe or prolonged economic downturn, such as the global financial crisis, could result in a variety of risks to our business, including, weakened demand for our drug candidates and our ability to raise additional capital when needed on acceptable terms, if at all. A weak or declining economy could also strain our suppliers, possibly resulting in supply disruption, or cause our customers to delay making payments for our services. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business.

We or the third parties upon whom we depend may be adversely affected by earthquakes or other natural disasters and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.

Earthquakes or other natural disasters could severely disrupt our operations, and have a material adverse effect on our business, results of operations, financial condition and prospects. If a natural disaster, power outage or other event occurred that prevented us from using all or a significant portion of our headquarters, that damaged critical infrastructure, such as the manufacturing facilities of our third-party contract manufacturers, or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. The disaster recovery and business continuity plans we have in place may prove inadequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which, could have a material adverse effect on our business.

Our internal computer systems, or those of our third-party CROs or other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our drug candidates' development programs.

Despite the implementation of security measures, our internal computer systems and those of our third-party CROs and other contractors and consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. While we have not experienced any such system failure, accident, or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our programs. For example, the loss of clinical trial data for our drug candidates could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach results in a loss of or damage to our data or applications or other data or applications relating to our technology or drug candidates, or inappropriate disclosure of confidential or proprietary information, we could incur liabilities and the further development of our drug candidates could be delayed.

Our employees, principal investigators, CROs and consultants may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements and insider trading.

We are exposed to the risk that our employees, principal investigators, CROs and consultants may engage in fraudulent conduct or other illegal activity. Misconduct by these parties could include intentional, reckless and/or negligent conduct or disclosure of unauthorized activities to us that violate the regulations of the FDA and other regulatory authorities, including those laws requiring the reporting of true, complete and accurate information to such authorities; healthcare fraud and abuse laws and regulations in the United States and abroad; or laws that require the reporting of financial information or data accurately. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Activities subject to these laws also involve the improper use of information obtained in the course of clinical trials or creating fraudulent data in our pre-clinical studies or clinical trials, which could result in regulatory sanctions and cause serious harm to our reputation. We intend to adopt, prior to the completion of this offering, a code of conduct applicable to all of our employees, but it is not always possible to identify and deter misconduct by employees and other third parties, and the

precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. Additionally, we are subject to the risk that a person could allege such fraud or other misconduct, even if none occurred. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of civil, criminal and administrative penalties, damages, monetary fines, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

We may acquire businesses or drugs, or form strategic alliances, in the future, and we may not realize the benefits of such acquisitions.

We may acquire additional businesses or drugs, form strategic alliances or create joint ventures with third parties that we believe will complement or augment our existing business. If we acquire businesses with promising markets or technologies, we may not be able to realize the benefit of acquiring such businesses if we are unable to successfully integrate them with our existing operations and company culture. We may encounter numerous difficulties in developing, manufacturing and marketing any new drugs resulting from a strategic alliance or acquisition that delay or prevent us from realizing their expected benefits or enhancing our business. We cannot assure you that, following any such acquisition, we will achieve the expected synergies to justify the transaction.

Risks Related to Our Common Stock and This Offering

We will incur increased costs as a result of operating as a public company, and our management will be required to devote substantial time to new compliance initiatives.

As a public company, and particularly after we are no longer an "emerging growth company," we will incur significant legal, accounting and other expenses that we did not incur as a private company. In addition, the Sarbanes-Oxley Act of 2002 and rules subsequently implemented by the Securities and Exchange Commission and NASDAQ have imposed various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel will need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will increase our legal and financial compliance costs and will make some activities more time-consuming and costly. For example, we expect that these rules and regulations may make it more difficult and more expensive for us to obtain director and officer liability insurance.

Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404, we will be required to furnish a report by our management on our internal control over financial reporting, including an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. However, while we remain an emerging growth company, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404 within the prescribed period, we will be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for

internal control over financial reporting. Despite our efforts, there is a risk that neither we nor our independent registered public accounting firm will be able to conclude within the prescribed timeframe that our internal control over financial reporting is effective as required by Section 404. This could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

The price of our common stock may be volatile and fluctuate substantially, which could result in substantial losses for purchasers of our common stock in this offering.

Our stock price is likely to be volatile. The stock market in general and the market for biopharmaceutical companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, you may not be able to sell your 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 drugs or technologies;
- results of clinical trials of our drug 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 drug candidates or clinical development programs;
- the results of our efforts to discover, develop, acquire or in-license additional drug candidates or drugs;
- 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;
- 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.

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

Prior to this offering, there has been no public market for shares of our common stock. Although our common stock has been approved for listing on The NASDAQ Global Select Market, an active trading market for our shares may never develop or be sustained following this offering. The initial public offering price of our common stock was determined through negotiations between us and the underwriters. This initial public offering price may not be indicative of the market price of our common stock after this offering. In the absence of an active trading market for our common stock, investors may not be able to sell their common stock at or above the initial public offering price or at the time that they would like to sell.

If securities analysts do not publish research or reports about our business or if they publish negative evaluations of our stock, the price of our stock could decline.

The trading market for our common stock will rely in part on the research and reports that industry or financial analysts publish about us or our business. We may never obtain research coverage by industry or financial analysts. If no or few analysts commence coverage of us, the trading price of our stock would likely decrease. Even if we do obtain analyst coverage, if one or more of the analysts covering our business downgrade their evaluations of our stock, the price of our stock could decline. If one or more of these analysts cease to cover our stock, we could lose visibility in the market for our stock, which in turn could cause our stock price to decline.

Our executive officers, directors, principal stockholders and their affiliates will continue to exercise significant influence over our company after this offering, which will limit your ability to influence corporate matters and could delay or prevent a change in corporate control.

Immediately following the completion of this offering, and disregarding any shares of common stock that they purchase in this offering, the existing holdings of our executive officers, directors, principal stockholders and their affiliates, including investment funds affiliated with Third Rock Ventures and entities affiliated with Fidelity Biosciences Corp., or Fidelity, will represent beneficial ownership, in the aggregate, of approximately 41% of our outstanding common stock, assuming no exercise of the underwriters' option to acquire additional common stock in this offering and assuming we issue the number of shares of common stock as set forth on the cover page of this prospectus. As a result, these stockholders, if they act together, will be able to influence our management and affairs and the outcome of matters submitted to our stockholders for approval, including the election of directors and any sale, merger, consolidation, or sale of all or substantially all of our assets. These stockholders acquired their shares of common stock for substantially less than the price of the shares of common stock being acquired in this offering, and these stockholders may have interests, with respect to their common stock, that are different from those of investors in this offering and the concentration of voting power among these stockholders may have an adverse effect on the price of our common stock. In addition, this concentration of ownership might adversely affect the market price of our common stock by:

- delaying, deferring or preventing a change of control of us;
- impeding a merger, consolidation, takeover or other business combination involving us; or
- discouraging a potential acquirer from making a tender offer or otherwise attempting to obtain control of us.

See "Principal Stockholders" in this prospectus for more information regarding the ownership of our outstanding common stock by our executive officers, directors, principal stockholders and their affiliates.

Anti-takeover provisions in our charter documents and under Delaware law could make an acquisition of us, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.

Provisions in our amended and restated certificate of incorporation and amended and restated by-laws may delay or prevent an acquisition of us or a change in our management. These provisions include a classified board of directors, a prohibition on actions by written consent of our stockholders and the ability of our board of directors to issue preferred stock without stockholder approval. In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which limits the ability of stockholders owning in excess of 15% of our outstanding voting stock to merge or combine with us. Although

we believe these provisions collectively provide for an opportunity to obtain greater value for stockholders by requiring potential acquirors to negotiate with our board of directors, they would apply even if an offer rejected by our board were considered beneficial by some stockholders. In addition, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors, which is responsible for appointing the members of our management.

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

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 other legal restrictions on resale discussed in this prospectus lapse, the market price of our common stock could decline. Based upon the number of shares of common stock, on an as-converted basis, outstanding as of December 31, 2014, upon the completion of this offering, we will have outstanding a total of 25,831,965 shares of common stock, assuming no exercise of the underwriters' option to purchase an additional 1,221,874 shares. Of these shares, as of the date of this prospectus, approximately 8,145,834 shares of our common stock, plus any shares sold upon exercise of the underwriters' option to purchase additional shares, will be freely tradable, without restriction, in the public market immediately following this offering, assuming that current stockholders do not purchase shares in this offering. The representatives of the underwriters, however, may, in their sole discretion, permit our officers, directors and other stockholders who are subject to these lock-up agreements to sell shares prior to the expiration of the lock-up agreements.

The lock-up agreements pertaining to this offering will expire 180 days from the date of this prospectus. After the lock-up agreements expire, based upon the number of shares of common stock, on an as-converted basis, outstanding as of December 31, 2014, up to an additional 13,294,402 shares of common stock will be eligible for sale in the public market, approximately 11% of which shares are held by directors, executive officers and other affiliates and will be subject to certain limitations of Rule 144 under the Securities Act of 1933, as amended, or the Securities Act.

Upon completion of this offering, 3,081,131 shares of common stock that are either subject to outstanding options, reserved for future issuance under our equity incentive plans or subject to outstanding warrants will become eligible for sale in the public market to the extent permitted by the provisions of various vesting schedules, the lock-up agreements and Rule 144 and Rule 701 under the Securities Act. If these additional shares of common stock are sold, or if it is perceived that they will be sold, in the public market, the market price of our common stock could decline.

After this offering, the holders of approximately 15,467,479 shares of our common stock will be entitled to rights with respect to the registration of their shares under the Securities Act, subject to the lock-up agreements described above. Registration of these shares under the Securities Act would result in the shares becoming freely tradable without restriction under the Securities Act, except for shares purchased by affiliates. Any sales of securities by these stockholders could have a material adverse effect on the market our common stock.

We have broad discretion in how we use the proceeds of this offering and may not use these proceeds effectively, which could affect our results of operations and cause our stock price to decline.

We will have considerable discretion in the application of the net proceeds of this offering. We intend to use the net proceeds from this offering to fund our Phase 1 clinical trials of BLU-285 in SM and GIST, our Phase 1 clinical trial of BLU-554 in HCC, in each case, including drug

manufacturing, companion diagnostic development and internal personnel and costs, and to fund new and ongoing research activities including for our RET program, working capital and other general corporate purposes, which may include funding for the hiring of additional personnel, capital expenditures and the costs of operating as a public company. As a result, investors will be relying upon management's judgment with only limited information about our specific intentions for the use of the balance of the net proceeds of this offering. We may use the net proceeds for purposes that do not yield a significant return or any return at all for our stockholders. In addition, pending their use, we may invest the net proceeds from this offering in a manner that does not produce income or that loses value.

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

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. We will remain an emerging growth company until the earlier of (i) the last day of the fiscal year in which we have total annual gross revenues of $1 billion or more; (ii) the last day of the fiscal year following the fifth anniversary of the date of the completion of this offering; (iii) the date on which we have issued more than $1 billion in nonconvertible debt during the previous three years; or (iv) the date on which we are deemed to be a large accelerated filer under the rules of the Securities and Exchange Commission, which means the market value of our common stock that is held by non-affiliates exceeds $700 million as of the prior June 30th. For so long as we remain an emerging growth company, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include:

- not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002;
- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements;
- providing only two years of audited financial statements in addition to any required unaudited interim financial statements and a correspondingly reduced "Management's Discussion and Analysis of Financial Condition and Results of Operations" disclosure;
- reduced disclosure obligations regarding executive compensation; 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. In this prospectus, we have not included all of the executive compensation-related information that would be required if we were not an emerging growth company.

We may choose to take advantage of some, but not all, of the available exemptions. We have taken advantage of reduced reporting burdens in this prospectus. In particular, we have provided only two years of audited financial statements and have not included all of the executive compensation information that would be required if we were not an emerging growth company. We cannot predict whether investors will find our common stock less attractive if we rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This allows an emerging growth company to delay the adoption of certain accounting standards until those

standards would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this exemption from new or revised accounting standards and, therefore, we will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

Because we do not anticipate paying any cash dividends on our capital stock in the foreseeable future, capital appreciation, if any, will be your sole source of gain.

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. Additionally, under the Loan and Security Agreement, we are currently restricted from paying cash dividends, and we expect these restrictions to continue in the future. In addition, the terms of any future debt agreements may preclude us from paying dividends. As a result, capital appreciation, if any, of our common stock will be your sole source of gain for the foreseeable future.

Our ability to utilize our net operating loss carryforwards and certain other tax attributes may be limited.

Under Section 382 of the Internal Revenue Code of 1986, as amended, if a corporation undergoes an "ownership change" (generally defined as a greater than 50% change (by value) in the ownership of its equity over a three year period), the corporation's ability to use its pre-change net operating loss carryforwards and certain other pre-change tax attributes to offset its post-change income may be limited. We may have experienced such ownership changes in the past, and we may experience ownership changes in the future as a result of this offering or subsequent shifts in our stock ownership, some of which are outside the Company's control. As of December 31, 2014, we had federal net operating loss carryforwards of approximately $78.1 million, and our ability to utilize those net operating loss carryforwards could be limited by an "ownership change" as described above, which could result in increased tax liability to the Company.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

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

- our use of the net proceeds from this offering;
- the accuracy of our estimates regarding expenses, future revenues and capital requirements;
- the initiation, timing, progress and results of our pre-clinical studies and clinical trials, and our research and development programs;
- our ability to retain the continued service of our key professional and to identify, hire and retain additional qualified professionals;
- our ability to advance drug candidates into, and successfully complete, clinical trials;
- the number of patients with the genomically defined diseases that our drug candidates are targeting;
- the timing or likelihood of regulatory filing and approvals;
- the commercialization of our drug candidates, if approved;
- the pricing and reimbursement of our drug candidates, if approved;
- the implementation of our business model, strategic plans for our business, drug candidates and technology;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our drug candidates and technology;
- estimates of our expenses, future revenues, capital requirements and our needs for additional financing;
- the potential benefits of our existing collaboration with Alexion Pharma Holding and our ability to enter into other strategic arrangements;
- our ability to maintain and establish collaborations or obtain additional grant funding;
- our financial performance;
- developments relating to our competitors and our industry; and
- other risks and uncertainties, including those listed under the caption "Risk Factors."

Any forward-looking statements in this prospectus reflect our current views with respect to future events or to our future financial performance and involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by these forward-looking statements. Important factors that may cause actual results to differ materially from current expectations include, among other things, those listed under "Risk Factors" and elsewhere in this prospectus. Given these uncertainties, you should not place undue reliance on these forward-looking statements. Except as required by law, we assume no

obligation to update or revise these forward-looking statements for any reason, even if new information becomes available in the future.

This prospectus also contains estimates, projections and other information concerning our industry, our business, and the markets for certain diseases, including data regarding the estimated size of those markets, and the incidence and prevalence of certain medical conditions. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances reflected in this information. Unless otherwise expressly stated, we obtained this industry, business, market and other data from reports, research surveys, studies and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data and similar sources.

USE OF PROCEEDS

We estimate that we will receive net proceeds of approximately $133.8 million from the sale of the shares of common stock offered in this offering, or approximately $154.2 million if the underwriters exercise their option to purchase additional shares in full, based on the initial public offering price of $18.00 per share, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us.

The principal purposes of this offering are to increase our financial flexibility, create a public market for our common stock and to facilitate our access to the public equity markets. The offering is designed to provide funding through multiple proof-of-concept readouts for our drug candidates. In particular, we currently expect to use the net proceeds from this offering as follows:

- approximately $35.0 to 40.0 million for our two Phase 1 clinical trials of BLU-285 in SM and GIST, including clinical research outsourcing, drug manufacturing, companion diagnostic development and internal personnel costs;
- approximately $20.0 to 25.0 million for our Phase 1 clinical trial of BLU-554 in HCC, including clinical research outsourcing, drug manufacturing, companion diagnostic development and internal personnel costs; and
- approximately $40.0 million for new and ongoing research activities, including for our RET program and our platform with the goal of delivering one IND annually on average.

We expect to use the remainder of the net proceeds from this offering for working capital and other general corporate purposes, which may include funding for the hiring of additional personnel, capital expenditures and the costs of operating as a public company.

We believe the net proceeds from this offering, together with our existing cash and cash equivalents, including the $15.0 million upfront payment received in March 2015 upon execution of the agreement with Alexion, will be sufficient to fund our Phase 1 clinical trials of BLU-285 in SM and GIST and of BLU-554 in HCC.

Based on our current plans, we believe our cash and cash equivalents, including the $15.0 million upfront payment received in March 2015 upon execution of the agreement with Alexion, together with the net proceeds to us from this offering, will be sufficient to fund our operations through at least early 2017.

Although we currently anticipate that we will use the net proceeds from this offering as described above, there may be circumstances where a reallocation of funds is necessary. The amounts and timing of our actual expenditures will depend upon numerous factors, including our sales and marketing and commercialization efforts, demand for our drugs, our operating costs and the other factors described under "Risk Factors" in this prospectus. Accordingly, our management will have flexibility in applying the net proceeds from this offering. An investor will not have the opportunity to evaluate the economic, financial or other information on which we base our decisions on how to use the proceeds.

Although we may use a portion of the net proceeds of this offering for the acquisition or licensing, as the case may be, of additional technologies, other assets or businesses, or for other strategic investments or opportunities, we have no current understandings, agreements or commitments to do so.

Pending our use of the net proceeds from this offering, we intend to invest the net proceeds in a variety of capital preservation investments, including short-term, investment-grade, interest-bearing instruments and U.S. government securities.

DIVIDEND POLICY

We have never declared or paid cash dividends on our capital stock. We currently 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. In addition, pursuant to our loan and security agreement with Silicon Valley Bank, we are prohibited from paying cash dividends without the prior written consent of Silicon Valley Bank. Moreover, the terms of any future debt agreements may preclude us from paying dividends. Any future determination to pay dividends will be made at the discretion of our board of directors and will depend on various factors, including applicable laws, our results of operations, financial condition, future prospects and any other factors deemed relevant by our board of directors. Investors should not purchase our common stock with the expectation of receiving cash dividend.

CAPITALIZATION

The following table sets forth our cash and cash equivalents and capitalization as of December 31, 2014:

- on an actual basis;
- on a pro forma basis to reflect the conversion of all outstanding shares of our convertible preferred stock into an aggregate of 15,467,479 shares of common stock, the conversion of our preferred stock warrants into warrants to purchase 42,423 shares of our common stock prior to the completion of this offering and a $15.0 million upfront payment received in March 2015 upon execution of the agreement with Alexion Pharma Holding; and
- on a pro forma as adjusted basis to additionally reflect the issuance and sale by us of shares of our common stock in this offering, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us, at the initial public offering price of $18.00 per share.

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 December 31, 2014		
(in thousands, except share and per share data)	**Actual**	**Pro forma**	**Pro forma as adjusted**
Cash and cash equivalents	$ 47,240	$ 62,240	$ 196,001
Term loan payable, net of current portion	7,338	7,338	7,338
Warrant to purchase convertible preferred stock	365	—	—
Series A convertible preferred stock, $0.001 par value: 40,150,000 shares authorized, 40,000,000 shares issued and outstanding, actual; no shares authorized, issued or outstanding, pro forma and pro forma as adjusted	39,958	—	—
Series B convertible preferred stock, $0.001 par value: 20,999,996 shares authorized, 20,916,663 shares issued and outstanding, actual; no shares authorized, issued or outstanding, pro forma and pro forma as adjusted	24,985	—	—
Series C convertible preferred stock, $0.001 par value: 24,154,589 shares authorized, 24,154,589 shares issued and outstanding, actual; no shares authorized, issued or outstanding, pro forma and pro forma as adjusted	49,868	—	—
Common stock, $0.001 par value; 110,000,000 shares authorized; 2,218,652, shares issued and 1,626,738 shares outstanding, actual; 110,000,000 shares authorized, pro forma; 17,686,131 shares issued and 17,094,217 outstanding, pro forma; 110,000,000 shares authorized, pro forma as adjusted; 25,831,965 shares issued and 25,240,051 shares outstanding, pro forma as adjusted;	2	17	25
Additional paid-in capital	2,822	117,983	251,736
Accumulated deficit	(82,206)	(82,206)	(82,206)
Total stockholders' (deficit) equity	(79,382)	35,794	169,555
Total capitalization	$ 43,132	$ 43,132	$ 176,893

The number of shares of common stock to be outstanding after this offering is based on 2,218,652 shares of common stock outstanding as of December 31, 2014, including 425,279 shares of unvested restricted stock subject to repurchase by us and 166,635 stock options that were exercised prior to vesting, and the conversion of all of our outstanding shares of convertible preferred stock upon closing of this offering.

The number of shares of our common stock to be outstanding after this offering excludes the following:

- 1,335,277 shares of common stock issuable upon the exercise of outstanding stock options as of December 31, 2014 having a weighted-average exercise price of $2.05 per share;
- 42,423 shares of common stock issuable upon the exercise of outstanding warrants as of December 31, 2014 having a weighted-average exercise price of $5.89 per share;
- 572,638 shares of common stock issuable upon the exercise of stock options granted in February and March 2015 having a weighted-average exercise price of $8.92 per share and 10,000 shares issued to a former employee in March 2015;
- 1,460,084 shares of common stock reserved for future issuance under our 2015 Stock Option Plan, which will become effective upon the completion of this offering; and
- 243,347 shares of common stock reserved for future issuance under our 2015 ESPP, which will become effective upon the completion of this offering.

DILUTION

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

As of December 31, 2014 we had a historical net tangible book value of $35.7 million, or $2.09 per share of common stock, taking into account the expected conversion of our outstanding convertible preferred stock into common stock prior to the completion of this offering. Without giving effect to the conversion of our outstanding convertible preferred stock into common stock, we had a historical net tangible book value of $(79.5) million, or $(48.86) per share of common stock, as of December 31, 2014. Historical net tangible book value per share is equal to our total tangible assets, excluding deferred costs, less total liabilities, including convertible preferred stock, divided by the number of outstanding shares of our common stock (excluding 425,279 shares of unvested restricted stock subject to repurchase by us and 166,635 stock options that were exercised prior to vesting). Investors participating in this offering will incur immediate and substantial dilution. After giving effect to (1) the conversion of all of our convertible preferred stock into 15,467,479 shares of common stock prior to the completion of this offering and (2) the sale of 8,145,834 shares of common stock in this offering, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us, at the initial public offering price of $18.00 per share, our pro forma as adjusted net tangible book value as of December 31, 2014 would have been approximately $169.4 million, or approximately $6.71 per share of common stock. This represents an immediate increase in pro forma as adjusted net tangible book value of $4.62 per share to our existing stockholders and an immediate dilution of $11.29 per share to investors participating in this offering.

The following table illustrates this per share dilution:

Initial public offering price per share		$ 18.00
Historical net tangible book value per share as of December 31, 2014	$ (48.86)	
Increase attributable to the conversion of outstanding convertible preferred stock and reclassification of convertible preferred stock warrants	50.95	
Pro forma net tangible book value per share as of December 31, 2014	2.09	
Increase in net tangible book value per share attributable to new investors	4.62	
Pro forma net tangible book value per share after this offering		6.71
Dilution per share to new investors		$ 11.29

If the underwriters exercise their option to purchase additional shares in full, pro forma as adjusted net tangible book value as of December 31, 2014 will increase to $189.9 million, or $7.18 per share, representing an increase to existing stockholders of $5.09 per share, and there will be an immediate dilution of $10.82 per share to new investors.

The following table summarizes, on a pro forma as adjusted basis as of December 31, 2014, the differences between the number of shares of common stock purchased from us, the total consideration and the average price per share paid by existing stockholders (giving effect to the conversion of all of our convertible preferred stock into 15,467,479 shares of common stock prior to the completion of this offering) and by investors participating in this offering, after deducting the

underwriting discounts and commissions and estimated offering expenses, at the initial public offering price of $18.00 per share.

	Shares Purchased		Total Consideration		Average
	Number	Percent	Amount	Percent	Price / Share
Existing stockholders	17,686,131	68%	$ 115,495,933	44%	$ 6.53
New investors	8,145,834	32%	146,625,012	56%	$ 18.00
Total	25,831,965	100%	$ 262,120,945	100%	$ 10.15

The table above assumes no exercise of the underwriters' option to purchase additional shares in this offering. If the underwriters' option to purchase additional shares is exercised in full, the number of shares of our common stock held by existing stockholders would be reduced to 65% of the total number of shares of our common stock outstanding after this offering, and the number of shares of common stock held by new investors participating in the offering would be increased to 35% of the total number of shares of our common stock outstanding after this offering.

The number of shares of common stock to be outstanding after this offering is based on 2,218,652 shares of common stock outstanding as of December 31, 2014, including 425,279 shares of unvested restricted stock subject to repurchase by us and 166,635 stock options that were exercised prior to vesting, and the conversion of all of our outstanding shares of convertible preferred stock upon closing of this offering.

The number of shares of our common stock to be outstanding after this offering excludes the following:

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- 572,638 shares of common stock issuable upon the exercise of stock options granted in February and March 2015 having a weighted-average exercise price of $8.92 per share and 10,000 shares issued to a former employee in March 2015;
- 1,460,084 shares of common stock reserved for future issuance under our 2015 Stock Option Plan, which will become effective upon the completion of this offering; and
- 243,347 shares of common stock reserved for future issuance under our 2015 ESPP, which will become effective upon the completion of this offering.

Furthermore, we may choose to raise additional capital through the sale of equity or convertible debt securities due to market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. New investors will experience further dilution if any of our outstanding options or warrants are exercised, new options are issued and exercised under our equity incentive plans or we issue additional shares of common stock, other equity securities or convertible debt securities in the future.

SELECTED FINANCIAL DATA

You should read the following selected financial data together with our financial statements and the related notes appearing at the end of this prospectus and the "Management's Discussion and Analysis of Financial Condition and Results of Operations" section of this prospectus. We have derived the statement of operations data for the years ended December 31, 2013 and 2014 and the balance sheet data as of December 31, 2013 and 2014 from our audited financial statements included elsewhere in this prospectus. Our historical results are not necessarily indicative of the results that should be expected in the future.

	Year Ended December 31,	
	2013	2014
	(in thousands, except per share data)	
Statements of Operations Data:		
Operating expenses:		
Research and development	$ 15,928	$ 31,844
General and administrative	5,072	7,890
Total operating expenses	21,000	$ 39,734
Other income (expense):		
Other income (expense), net	226	(98)
Interest and other expense	(138)	(453)
Total other income (expense)	88	(551)
Net loss	$ (20,912)	$ (40,285)
Convertible preferred stock dividends	(2,870)	(5,765)
Net loss applicable to common stockholders	$ (23,782)	$ (46,050)
Net loss per share applicable to common stockholders — basic and diluted(1)	$ (23.43)	$ (32.41)
Weighted-average number of common shares used in net loss per share applicable to common stockholders — basic and diluted(1)	1,015	1,421
Pro forma net loss per share applicable to common stockholders — basic and diluted (unaudited)		$ (3.07)
Pro forma weighted average number of common shares used in net loss per share applicable to common stockholders — basic and diluted (unaudited)		13,083

	As of December 31,	
	2013	2014
	(in thousands)	
Balance Sheet Data:		
Cash and cash equivalents	$ 1,987	$ 47,240
Working capital(2)	(705)	41,510
Total assets	4,135	49,925
Term loan payable, net of current portion	2,155	7,338
Warrant liability	119	365
Convertible preferred stock	39,958	114,811
Total stockholders' (deficit) equity	(41,454)	(79,382)

(1) See Note 2 to the notes to our financial statements appearing elsewhere in this prospectus for further details on the calculation of basic and diluted net loss per share and pro forma basic and diluted net loss per share applicable to common stockholders.

(2) We define working capital as current assets less current liabilities.

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

You should read the following discussion and analysis of our financial condition and results of operations together with our financial statements and related notes appearing in this prospectus. Some of the information contained in this discussion and analysis or set forth elsewhere in this prospectus, including information with respect to our plans and strategy for our business and related financing, includes forward-looking statements that involve risks and uncertainties. As a result of many factors, including those factors set forth in the "Risk Factors" section of this prospectus, our actual results could differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

We are a biopharmaceutical company focused on improving the lives of patients with genomically defined diseases driven by abnormal kinase activation. Our approach is to systematically and reproducibly identify kinases that are drivers of genomically defined diseases and to craft drug candidates with therapeutic windows that provide significant and durable clinical responses to patients. This integrated biology and chemistry approach enables us to drug known kinases that have been difficult to inhibit selectively and also identify, characterize and drug novel kinase targets. By focusing on genomically defined diseases, we believe that we will have a more efficient development path with a greater likelihood of success. Over the past three years, we have developed a robust small molecule drug pipeline in cancer and a rare genetic disease. One of our lead drug candidates is BLU-285, which targets KIT Exon 17 and PDGFRa D842V, abnormally active receptor tyrosine kinase mutants that are drivers of cancer and proliferative disorders. BLU-285 will initially be developed for patients with systemic mastocytosis, a myeloproliferative disorder of the mast cells, and defined subsets of patients with gastrointestinal stromal tumor, the most common sarcoma, or tumor of bone or connective tissue, of the gastrointestinal tract. Our other lead drug candidate is BLU-554, which targets FGFR4, a kinase that is aberrantly activated and is a driver of disease in a defined subset of patients with hepatocellular carcinoma, the most common type of liver cancer. Both drug candidates have demonstrated proof of concept in pre-clinical models and we expect to file Investigational New Drug applications, or INDs, in mid-2015 and initiate our Phase 1 clinical trials in mid-2015. We are also developing a drug candidate to target both RET, a receptor tyrosine kinase that can become abnormally activated when a portion of the gene that encodes RET is joined to part of another gene, and RET resistant mutants that we predict will arise from treatment with first generation therapies. We believe that our strategy will allow us to deliver transformative drugs to patients while building a fully-integrated biopharmaceutical company.

Since inception, our operations have focused on organizing and staffing our company, business planning, raising capital, establishing our intellectual property, building our platform including our proprietary compound library and new target discovery engine, identifying kinase drug targets and potential drug candidates, producing drug substance and drug product material for use in pre-clinical studies, and conducting pre-clinical studies, including Good Laboratory Practice, or GLP, toxicology studies. We expect to begin conducting clinical trials in mid-2015. We do not have any drugs approved for sale and have not generated any revenue from drug sales. We have funded our operations primarily through private placements of our convertible preferred stock and debt financing. From inception through December 31, 2014, we have raised an aggregate of $125.1 million of gross proceeds to fund our operations, of which $115.1 million was from the issuance of convertible preferred stock and $10.0 million was from a debt financing.

Since inception, we have incurred significant operating losses. Our net losses were $20.9 million and $40.3 million for the years ended December 31, 2013 and 2014, respectively. As of December 31, 2014, we had an accumulated deficit of $82.2 million. We expect to continue to

incur significant expenses and operating losses over the next several years. We anticipate that our expenses will increase significantly in connection with our ongoing activities, as we:

- continue IND enabling activities and commence the planned clinical development activities for our lead drug candidates BLU-285 and BLU-554;
- continue to discover, validate and develop additional drug candidates;
- maintain, expand and protect our intellectual property portfolio;
- hire additional research, development and business personnel; and
- incur additional costs associated with operating as a public company upon the closing of this offering.

Financial Operations Overview

Revenue

To date, we have not generated any revenue from drug sales and do not expect to generate any revenue from the sale of drugs in the near future. As of December 31, 2014, we had not generated any revenue from collaboration agreements, research fees, or license fees. In March 2015, we executed a research, development and commercialization agreement with Alexion Pharma Holding, or Alexion. The terms of this arrangement contain multiple deliverables. We evaluate multiple-element arrangements to determine (1) the deliverables included in the arrangement and (2) whether the deliverables represent separate units of accounting or whether they must be accounted for as a combined unit of accounting. We recognize arrangement consideration allocated to each unit of accounting when all of the revenue recognition criteria in Financial Accounting Standards Board, or FASB, Accounting Standards Codification, or ASC, Topic 605 *Revenue Recognition*, or ASC 605 are satisfied for that unit of accounting.

In the future, we will seek to generate revenue from a combination of drug sales and additional strategic relationships we may enter into.

Expenses

Research and Development Expenses

Research and development expenses consist primarily of costs incurred for our research activities, including our drug discovery efforts, and the development of our drug candidates, which include:

- employee-related expenses including salaries, benefits, and stock-based compensation expense;
- expenses incurred under agreements with third parties that conduct research and development, pre-clinical activities and manufacturing on our behalf;
- the cost of consultants;
- the cost of lab supplies and acquiring, developing, and manufacturing pre-clinical study materials; and
- facilities, depreciation, and other expenses, which include direct and allocated expenses for rent and maintenance of facilities, insurance, and other operating costs.

Research and development costs are expensed as incurred. Costs for certain activities are recognized based on an evaluation of the progress to completion of specific tasks. Nonrefundable advance payments for goods or services to be received 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.

The successful development of our drug candidates is highly uncertain. As such, at this time, we cannot reasonably estimate or know the nature, timing and estimated costs of the efforts that will be necessary to complete the remainder of the development of these drug candidates. We are also unable to predict when, if ever, material net cash inflows will commence from our drug candidates. This is due to the numerous risks and uncertainties associated with developing drugs, including the uncertainty of:

- establishing an appropriate safety profile with IND-enabling toxicology studies;
- successful enrollment in, and completion of clinical trials;
- 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 regulatory exclusivity for our drug candidates;
- commercializing the drug candidates, if and when approved, whether alone or in collaboration with others; and
- continued acceptable safety profile of the drugs following approval.

A change in the outcome of any of these variables with respect to the development of any of our drug candidates would significantly change the costs and timing associated with the development of that drug candidate.

Research and development activities are central to our business model. Drug candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials. We expect research and development costs to increase significantly for the foreseeable future as our drug candidate development programs progress. However, we do not believe that it is possible at this time to accurately project total program-specific expenses through commercialization. There are numerous factors associated with the successful commercialization of any of our drug candidates, including future trial design and various regulatory requirements, many of which cannot be determined with accuracy at this time based on our stage of development. Additionally, future commercial and regulatory factors beyond our control will impact our clinical development programs and plans.

A significant portion of our research and development costs have been external costs, which we track on a program-by-program basis following nomination as a development candidate. Our internal research and development costs are primarily personnel-related costs, depreciation and other indirect costs. We do not track our internal research and development expenses on a program-by-program basis as they are deployed across multiple projects under development. The following table summarizes our external research and development expenses, by program following nomination as a development candidate, for the year ended December 31, 2014. Pre-development candidate expenses, unallocated costs and internal research and development costs have been

classified separately. We had not yet nominated any development candidates for the year ended December 31, 2013.

	Year Ended December 31, 2014 (in thousands)
BLU-285 external costs	$ 5,290
BLU-554 external costs	3,437
Pre-development candidate expenses and unallocated costs	13,855
Internal research and development costs	9,262
	$ 31,844

General and Administrative Expenses

General and administrative expenses consist primarily of salaries and other related costs, including stock-based compensation, for personnel in executive, finance, accounting, business development, legal and human resources functions. Stock-based compensation includes expense associated with stock-based awards issued to non-employees, including directors for non-board related services. Other significant costs include facility costs not otherwise included in research and development expenses, legal fees relating to patent and corporate matters and fees for accounting and consulting services.

We anticipate that our general and administrative expenses will increase in the future to support continued research and development activities, including the initiation of our clinical trials and increased costs of operating as a public company. These increases will likely include increased costs related to the hiring of additional personnel and fees to outside consultants, among other expenses. We also anticipate increased expenses associated with being a public company, including costs for audit, legal, regulatory and tax-related services, director and officer insurance premiums and investor relations costs.

Other Income (Expense)

Other income (expense) consists primarily of interest expense on amounts outstanding under a loan and security agreement, or Loan and Security Agreement, that we entered into with Silicon Valley Bank in May 2013, amortization of debt discount and the re-measurement gain or loss associated with the change in the fair value of the convertible preferred stock warrant liability.

Critical Accounting Policies and Estimates

Our management's discussion and analysis of our financial condition and results of operations are based on our financial statements, which have been prepared in accordance with U.S. generally accepted accounting principles. The preparation of these financial statements requires us to make judgments and estimates that affect the reported amounts of assets, liabilities, revenues, and expenses and the disclosure of contingent assets and liabilities in our financial statements. We base our estimates on historical experience, known trends and events, and various other factors that are believed to be reasonable under the circumstances. Actual results may differ from these estimates under different assumptions or conditions. On an ongoing basis, we evaluate our judgments and estimates in light of changes in circumstances, facts and experience. The effects of material revisions in estimates, if any, will be reflected in the financial statements prospectively from the date of change in estimates.

While our significant accounting policies are described in more detail in the notes to our financial statements appearing elsewhere in this prospectus, we believe the following accounting policies used in the preparation of our financial statements require the most significant judgments and estimates.

Accrued Research and Development Expenses

As part of the process of preparing our financial statements, we are required to estimate our accrued expenses as of each balance sheet date. This process involves reviewing open contracts and purchase orders, communicating with our personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of the actual cost. The majority of our service providers invoice us monthly in arrears for services performed or when contractual milestones are met. We make estimates of our accrued expenses as of each balance sheet date based on facts and circumstances known to us at that time. We periodically confirm the accuracy of our estimates with the service providers and make adjustments if necessary. The significant estimates in our accrued research and development expenses include the costs incurred for services performed by our vendors in connection with research and development activities for which we have not yet been invoiced.

We base our expenses related to research and development activities on our estimates of the services received and efforts expended pursuant to quotes and contracts with vendors that conduct research and development on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the research and development expense. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrual or prepaid accordingly. Non-refundable advance payments for goods and services that will be used in future research and development activities are expensed when the activity has been performed or when the goods have been received rather than when the payment is made.

Although we do not expect our estimates to be materially different from amounts actually incurred, if our estimates of the status and timing of services performed differ from the actual status and timing of services performed, it could result in us reporting amounts that are too high or too low in any particular period. To date, there have been no material differences between our estimates of such expenses and the amounts actually incurred.

Stock-based Compensation

We expense the fair value of employee stock awards, net of estimated forfeitures, adjusted to reflect actual forfeitures, over the requisite service period, which is typically the vesting period. Compensation cost for restricted stock awards issued to employees is measured using the grant date intrinsic value of the award, net of estimated forfeitures, and is adjusted to reflect actual forfeitures. We estimate the fair value of options granted to employees at the date of grant using the Black-Scholes option-pricing model that requires management to apply judgment and make estimates, including:

- expected volatility, which is calculated based on reported volatility data for a representative group of publicly traded companies for which historical information is available. Since we are privately held as of the date of these financial statements, we do not have relevant historical data to support our expected volatility. As such, we have used an average of

expected volatility based on the volatilities of a representative group of publicly traded biopharmaceutical companies. For purposes of identifying representative companies, we considered characteristics such as number of product candidates in early stages of product development, area of therapeutic focus, length of trading history, similar vesting provisions and a similar percentage of stock options that were in-the-money. The expected volatility was determined using an average of the historical volatilities of the representative group of companies for a period equal to the expected term of the option grant. We intend to consistently apply this process using the same representative companies until a sufficient amount of historical information regarding the volatility of our own share price becomes available or until circumstances change, such that the identified entities are no longer representative companies. In the latter case, more suitable, similar entities whose share prices are publicly available would be utilized in the calculation;

- risk-free interest rate, which is based on the U.S. Treasury yield curve in effect at the time of grant commensurate with the expected life assumption;

- expected term, which we calculate using the simplified method, as prescribed by the Securities and Exchange Commission Staff Accounting Bulletin No. 107, *Share-Based Payment,* as we have insufficient historical information regarding our stock options to provide a basis for an estimate;

- fair value of the underlying common shares, which is determined using the option-pricing method, or OPM, or a hybrid of the probability-weighted expected return method, or PWERM, and the OPM, and was approved by our board of directors; and

- dividend yield, which is zero based on the fact that we never paid cash dividends and do not expect to pay any cash dividends in the foreseeable future.

We have computed the fair value of stock options at the date of grant using the following weighted-average assumptions:

	Year Ended December 31, 2013	Year Ended December 31, 2014
Risk-free interest rate	1.70% - 2.84%	1.70% - 2.14%
Expected dividend yield	0.00%	0.00%
Expected term (years)	6.1	6.1
Expected stock price volatility	88.96%	92.99%

Stock-based awards issued to non-employees, including directors for non-board related services, are accounted for based on the fair value of such services received or of the intrinsic value of equity instruments issued, whichever is more reliably measured. These stock-based awards are revalued at each vesting date and period-end. Stock-based awards subject to service-based vesting conditions are expensed on a straight-line basis over the vesting period. In accordance with the Accounting Standards Codification, or ASC, 718, stock-based awards subject to both performance-and service-based vesting conditions are recognized using an accelerated attribution model.

The amount of stock-based compensation expense recognized during a period is based on the value of the portion of the awards that are expected to vest. Forfeitures are estimated at the time of grant and revised, if necessary, in subsequent periods if actual forfeitures differ from those estimates. The term "forfeitures" is distinct from "cancellations" or "expirations" and represents only the unvested portion of the surrendered option. We evaluate our forfeiture rate at each reporting period. Ultimately, the actual expense recognized over the vesting period will be for only those options that vest.

Common Stock Valuation

The following table presents the grant dates, numbers of underlying shares of common stock and the per share exercise prices of stock options granted between January 1, 2014 and the date of this prospectus, along with the fair value per share utilized to calculate stock-based compensation expense:

Date of Issuance	Type of Award	Number of Shares	Exercise Price of Award per Share(1)	Fair Value of Common Stock per Share on Grant Date	Per Share Estimated Fair Value of Award(2)(3)
3/6/14	Options	96,906	$ 1.87	$ 1.87	$ 1.43
5/6/14	Options	71,817	$ 1.87	$ 1.87	$ 1.43
7/30/14	Options	595,142	$ 1.87	$ 4.24(4)	$ 3.58
8/18/14	Options	351,331	$ 1.87	$ 4.24(4)	$ 3.63
10/8/14	Options	47,272	$ 1.87	$ 6.16(5)	$ 5.45
12/2/14	Options	63,635	$ 7.15	$ 7.15	$ 5.39
2/10/15	Options	466,276	$ 8.80	$ 8.80	$ 6.44
3/22/15	Options	106,632	$ 9.46	$ 9.46	$ 6.60

(1) The Exercise Price of Award per Share represents the fair value of our common stock on the date of grant, as determined by our board of directors, after taking into account our most recently available contemporaneous valuations of our common stock as well as additional factors that may have changed since the date of such contemporaneous valuation through the date of grant.

(2) The Per Share Estimated Fair Value of Award reflects the weighted average fair value of options as estimated at the date of grant using the Black-Scholes option-pricing model.

(3) For the purposes of recording stock-based compensation for grants of options to non-employees, we measure the fair value of the award on the service completion date (vesting date). At the end of each reporting period prior to completion of the services, we re-measure the value of any unvested portion of the award based on the then-current fair value of the award and adjust expense accordingly. Amounts in this column reflect only the grant date fair value of awards to non-employees.

(4) At the time of the option grants on July 30, 2014 and August 18, 2014, our board of directors determined that the fair value of our common stock of $1.87 per share calculated in the contemporaneous valuation as of January 6, 2014 reasonably reflected the per share fair value of our common stock as of the grant date. However, as described below, the fair value of common stock at the date of these grants was adjusted to $4.24 per share in connection with a retrospective fair value assessment for financial reporting purposes.

(5) At the time of the option grants on October 8, 2014, our board of directors determined that the fair value of our common stock of $1.87 per share calculated in the contemporaneous valuation as of January 6, 2014 reasonably reflected the per share fair value of our common stock as of the grant date. However, as described below, the fair value of common stock at the date of these grants was adjusted to $6.16 per share in connection with a retrospective fair value assessment for financial reporting purposes.

Determination of Fair Value of Common Stock on Grant Dates

We are a private company with no active public market for our common stock. Therefore, we have periodically determined the estimated per share fair value of our common stock at various dates using contemporaneous valuations performed in accordance with the guidance outlined in the American Institute of Certified Public Accountants Practice Aid, *Valuation of Privately-Held Company Equity Securities Issued as Compensation*, also known as the Practice Aid. Once a public

trading market for our common stock has been established in connection with the completion of this offering, it will no longer be necessary for us to estimate the fair value of our common stock in connection with our accounting for stock options and restricted stock, as the fair value of our common stock will be its trading price on The NASDAQ Global Select Market.

For financial reporting purposes, we performed common stock valuations, with the assistance of a third-party specialist, as of January 6, 2014, July 30, 2014, November 10, 2014, February 1, 2015 and March 1, 2015, which resulted in valuations of our common stock of $1.87, $4.24, $7.15, $8.80 and $9.46 per share, respectively, as of those dates. In conducting the valuations, we considered all objective and subjective factors that we believed to be relevant for each valuation conducted, including our best estimate of our business condition, prospects and operating performance at each valuation date. Within the valuations performed, a range of factors, assumptions and methodologies were used. The significant factors included:

- the lack of an active public market for our common and our convertible preferred stock;
- the prices of shares of our convertible preferred stock that we had sold to outside investors in arm's length transactions, and the rights, preferences and privileges of that convertible preferred stock relative to our common stock;
- our results of operations, financial position and the status of our research and pre-clinical development efforts;
- the material risks related to our business;
- our business strategy;
- the market performance of publicly traded companies in the life sciences and biotechnology sectors, and recently completed mergers and acquisitions of companies comparable to us;
- the likelihood of achieving a liquidity event for the holders of our common stock, such as an initial public offering or sale of the Company given prevailing market conditions; and
- any recent contemporaneous valuations of our common stock prepared in accordance with methodologies outlined in the Practice Aid.

The dates of our contemporaneous valuations have not always coincided with the dates of our stock option grants. In determining the exercise prices of the stock options set forth in the table above, we considered, among other things, the most recent contemporaneous valuations of our common stock and our assessment of additional objective and subjective factors we believed were relevant as of the grant date. The additional factors considered when determining any changes in fair value between the most recent contemporaneous valuation and the grant dates included our stage of research and pre-clinical development, our operating and financial performance and current business conditions.

There are significant judgments and estimates inherent in the determination of the fair value of our common stock. These judgments and estimates include assumptions regarding our future operating performance, the time to completing an initial public offering, or IPO, or other liquidity event, the related company valuations associated with such events, and the determinations of the appropriate valuation methods. If we had made different assumptions, our stock-based compensation expense, net loss and net loss per share applicable to common stockholders could have been significantly different.

Common Stock Valuation Methodologies. Our contemporaneous and retrospective valuations were prepared in accordance with the guidelines in the Practice Aid, which prescribes several valuation approaches for determining the value of an enterprise, such as the cost, market and income approaches, and various methodologies for allocating the value of an enterprise to its capital structure and specifically the common stock.

Our common stock valuation as of January 6, 2014 was prepared utilizing OPM. Our common stock as of July 30, 2014, November 10, 2014, February 1, 2015 and March 1, 2015 were prepared utilizing a hybrid of PWERM and the OPM, which we refer to as the hybrid method.

Methods Used to Allocate Our Enterprise Value to Classes of Securities. In accordance with the Practice Aid, we considered the various methods for allocating the enterprise value across our classes and series of capital stock to determine the fair value of our common stock at each valuation date. The methods we considered consisted of the following:

OPM. The OPM treats common stock and convertible preferred stock as call options on the total equity value of a company, with exercise prices based on the value thresholds at which the allocation among the various holders of a company's securities changes. Under this method, the common stock has value only if the funds available for distribution to stockholders exceeds the value of the liquidation preferences at the time of a liquidity event, such as a strategic sale or merger. The common stock is modeled as a call option on the underlying equity value at a predetermined exercise price. In the model, the exercise price is based on a comparison with the total equity value rather than, as in the case of a regular call option, a comparison with a per share stock price. Thus, common stock is considered to be a call option with a claim on the enterprise at an exercise price equal to the remaining value immediately after the convertible preferred stock liquidation preference is paid.

The OPM uses the Black-Scholes option-pricing model to price the call options. This model defines the securities' fair values as functions of the current fair value of a company and uses assumptions, such as the anticipated timing of a potential liquidity event and the estimated volatility of the equity securities.

The OPM backsolve approach was used to estimate enterprise value under the OPM. The OPM backsolve approach uses the OPM to derive the implied equity value for one type of equity security from a contemporaneous sale transaction involving another type of the company's equity securities. In the OPM, the assumed volatility factor was based on the historical trading volatility of our publicly traded peer companies. At each valuation date, a determination was made by us as to the appropriate volatility to be used, considering such factors as the expected time to a liquidity event and our stage of development.

To derive the fair value of the common stock using the OPM, the proceeds to the common stockholders were calculated based on the preferences and priorities of the convertible preferred stock and common stock. We then applied a discount for lack of marketability to the common stock to account for the lack of access to an active public market.

PWERM. Under the PWERM methodology, the fair value of common stock is estimated based upon an analysis of future values for the company, assuming various outcomes. The common stock value is based on the probability-weighted present value of expected future investment returns considering each of the possible outcomes available as well as the rights of each class of stock. The future value of the common stock under each outcome is discounted back to the valuation date at an appropriate risk-adjusted discount rate and probability weighted to arrive at an indication of value for the common stock.

Hybrid Method. The hybrid method is a PWERM where the equity value in one of the scenarios is calculated using an OPM. In the hybrid method used by us, two types of future-event scenarios were considered: an IPO and an unspecified liquidity event. The enterprise value for the IPO scenario was determined using a market approach. The enterprise value for the unspecified liquidity event scenario was determined using the OPM backsolve approach. The relative probability of each type of future-event scenario was determined based on an analysis of market conditions at

the time, including then-current IPO valuations of similarly situated companies, and expectations as to the timing and likely prospects of the future-event scenarios.

To determine the enterprise value for the IPO scenario, we used the guideline public company method, which includes comparisons to publicly traded companies in the biopharmaceutical industry that recently completed IPOs. That enterprise value was then discounted back to the valuation date at an appropriate risk-adjusted discount rate.

To derive the fair value of the common stock for each scenario under the hybrid method, the proceeds to the common stockholders were calculated based on the conversion rights and preferences of the convertible preferred stock. We then applied a discount for lack of marketability to the common stock to account for the lack of access to an active public market.

JOBS Act

In April 2012, the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, was enacted. Section 107 of the JOBS Act provides that an "emerging growth company," or EGC, can take advantage of the extended transition period provided in Section 7(a)(2)(B) of the Securities Act of 1933, as amended, or the Securities Act, for complying with new or revised accounting standards. Thus, an EGC can delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this extended transition period and, as a result, we will adopt new or revised accounting standards on the relevant dates on which adoption of such standards is required for other public companies.

We are in the process of evaluating the benefits of relying on other exemptions and reduced reporting requirements under the JOBS Act. Subject to certain conditions, as an EGC, we intend to rely on certain of these exemptions, including without limitation, (i) providing an auditor's attestation report on our system of internal controls over financial reporting pursuant to Section 404(b) of the Sarbanes-Oxley Act and (ii) complying with any requirement that may be adopted by the Public Company Accounting Oversight Board, or PCAOB, regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements, known as the auditor discussion and analysis. We will remain an EGC until the earlier of (i) the last day of the fiscal year in which we have total annual gross revenues of $1 billion or more; (ii) the last day of the fiscal year following the fifth anniversary of the date of the completion of this offering; (iii) the date on which we have issued more than $1 billion in nonconvertible debt during the previous three years; or (iv) the date on which we are deemed to be a large accelerated filer under the rules of the Securities and Exchange Commission.

Results of Operations

Comparison of Years Ended December 31, 2013 and 2014

The following table summarizes our results of operations for the years ended December 31, 2013 and 2014, together with the changes in those items in dollars and as a percentage:

(in thousands)	Years ended December 31, 2013	2014	Dollar Change	% Change
Operating expenses:				
Research and development	$ 15,928	$ 31,844	$ 15,916	100%
General and administrative	5,072	7,890	2,818	56
Total operating expenses	21,000	39,734	18,734	89
Other income (expense):				
Other income (expense), net	226	(98)	(324)	(143)
Interest and other expense	(138)	(453)	(315)	(228)
Total other income (expense)	88	(551)	(639)	(726)
Net loss	$ (20,912)	$ (40,285)	$ (19,373)	(93)%

Research and Development Expense

Research and development expense increased by $15.9 million from $15.9 million for the year ended December 31, 2013 to $31.8 million for the year ended December 31, 2014, an increase of 100%. The increase in research and development expense was primarily attributable to the following:

- approximately $7.6 million for external IND-enabling pre-clinical and toxicology studies as well as the commencement of manufacturing activities for our two lead programs;
- approximately $4.9 million primarily due to an increase of 46% in headcount as our programs advance towards clinical trials as well as higher stock-based compensation expense, including expense associated with stock-based awards issued to non-employees;
- approximately $1.9 million in chemistry expenses related to the continued build out of our proprietary compound library, increased chemical analysis for our lead programs, and the general progression of our drug candidate pipeline; and
- approximately $1.2 million for *in vivo* study costs leading up to and following the nomination of BLU-285 and BLU-554 as lead programs.

General and Administrative Expense

General and administrative expense increased by $2.8 million from $5.1 million for the year ended December 31, 2013 to $7.9 million for the year ended December 31, 2014, an increase of 56%. The increase in general and administrative expense was primarily attributable to the following:

- approximately $1.8 million in increased personnel costs primarily due to an increase in stock-based compensation expense (including expense associated with stock-based awards issued to non-employees) and a 23% increase in headcount as we build the infrastructure to support the growth of the research and development organization and advance our lead programs towards clinical trials; and

- approximately $0.6 million in increase in professional fees including external legal fees, corporate communications and public relations costs.

We expect that our general and administrative expense will increase in future periods as we expand our operations and incur additional costs in connection with being a public company. These increases will likely include legal, auditing and filing fees, additional insurance premiums and general compliance and consulting expenses.

Other Income (Expense), Net

Other income (expense) decreased by $0.3 million to $(0.1) million for the year ended December 31, 2014 from $0.2 million for the year ended December 31, 2013. The decrease in other income (expense) was primarily related to the recognition of $0.2 million of other income in the year ended December 31, 2013 related to an award received from the Massachusetts Life Sciences Investment Tax Credit (MLSC) program. Other income was not recognized related to this program in the year ended December 31, 2014. Also contributing to the decrease in other income (expense) was the impact of the re-measurement loss associated with the change in the fair value of the convertible preferred stock warrant liability.

Interest and Other Expense

Interest and other expense increased by $0.3 million to $0.4 million for the year ended December 31, 2014 from $0.1 million for the year ended December 31, 2013. The increase in interest expense was primarily related to a higher outstanding principal balance under the Loan and Security Agreement for the year ended December 31, 2014.

Liquidity and Capital Resources

Sources of Liquidity

We have financed our operations to date primarily through gross proceeds of $115.1 million from private placements of our convertible preferred stock and proceeds of $10.0 million from a debt financing. As of December 31, 2014, we had cash and cash equivalents of $47.2 million.

We entered into the Loan and Security Agreement in May 2013. Under the terms of the Loan and Security Agreement, we borrowed $5.0 million. Loan advances accrue interest at a fixed rate of 2.0% above the Prime Rate. In November 2014, we amended the Loan and Security Agreement and borrowed an additional $5.0 million. Each loan advance included an interest only payment period. During 2014 we paid principal payments of $0.7 million on the first $3.0 million of advances. Principal payments on the remaining $7.0 million of advances will begin in January and December of 2015. We are required to pay a fee of 4.0% of the total loan advances at the end of the term of the loan. There are no outstanding financial covenants associated with the Loan and Security Agreement. As of December 31, 2014, we had $9.3 million in outstanding principal under the Loan and Security Agreement.

The term loan is collateralized by a blanket lien on all corporate assets, excluding intellectual property, and by a negative pledge of our intellectual property. The term loan contains covenants, including restrictions on dividends and default provisions. We have determined that the risk of subjective acceleration under the material adverse events clause is remote and therefore has classified the outstanding principal in current and long-term liabilities based on scheduled principal payments.

Cash Flows

The following table provides information regarding our cash flows for the years ended December 31, 2013 and 2014:

	Year Ended December 31,	
(in thousands)	**2013**	**2014**
Net cash used in operating activities	$ (19,025)	$ (35,400)
Net cash used in investing activities	(257)	(700)
Net cash provided by financing activities	17,992	81,353
Net increase (decrease) in cash and cash equivalents	$ (1,290)	$ 45,253

Net Cash Used in Operating Activities

The use of cash in all periods resulted primarily from our net losses adjusted for non-cash charges and changes in components of working capital. Net cash used in operating activities was $35.4 million during the year ended December 31, 2014 compared to $19.0 million during the year ended December 31, 2013. The increase in cash used in operating activities was due to an increase in net loss of $19.4 million for the year ended December 31, 2014 as compared to the year ended December 31, 2013.

Net Cash Used in Investing Activities

Net cash used in investing activities was $0.7 million during the year ended December 31, 2014 compared to net cash used in investing activities of $0.3 million during the year ended December 31, 2013. Net cash used in investing activities for the year ended December 31, 2014 and 2013 consisted of purchases of property and equipment.

Net Cash Provided by Financing Activities

Net cash provided by financing activities was $81.4 million during the year ended December 31, 2014 compared to $18.0 million during the year ended December 31, 2013. The cash provided by financing activities for the year ended December 31, 2014 was primarily the result of $74.9 million of net proceeds received from private placements of our convertible preferred stock and $7.0 million principal that we drew under the Loan and Security Agreement. The cash provided by financing activities for the year ended December 31, 2013 was primarily the result of $15.0 million of proceeds received from private placements of our convertible preferred stock and $3.0 million principal that we drew under the Loan and Security Agreement.

Funding Requirements

We expect our expenses to increase in connection with our ongoing activities, particularly as we continue the research and development of, initiate clinical trials of, and seek marketing approval for, our drug candidates. In addition, if we obtain marketing approval for any of our drug candidates, we expect to incur significant commercialization expenses related to drug sales, marketing, manufacturing and distribution to the extent that such sales, marketing and distribution are not the responsibility of potential collaborators. Furthermore, upon the closing of this offering, we expect to incur additional costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. 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.

We expect that the net proceeds from this offering, together with our existing cash and cash equivalents, including the $15.0 million upfront payment received in March 2015 upon execution of the agreement with Alexion, will enable us to fund our operating expenses and capital expenditure requirements through at least early 2017. Our future capital requirements will depend on many factors, including:

- the scope, progress, results and costs of drug discovery, pre-clinical development, laboratory testing and clinical trials for our drug candidates;
- the scope, prioritization and number of our research and development programs;
- the costs, timing and outcome of regulatory review of our drug candidates;
- our ability to establish and maintain collaborations on favorable terms, if at all;
- the achievement of milestones or occurrence of other developments that trigger payments under any collaboration agreements we obtain;
- the extent to which we are obligated to reimburse, or entitled to reimbursement of, clinical trial costs under future collaboration agreements, if any;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;
- the extent to which we acquire or in-license other drug candidates and technologies;
- the costs of securing manufacturing arrangements for commercial production; and
- the costs of establishing or contracting for sales and marketing capabilities if we obtain regulatory approvals to market our drug candidates.

Identifying potential drug candidates and conducting pre-clinical testing and clinical trials is a time-consuming, expensive and uncertain process that takes many years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve drug sales. In addition, our drug candidates, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of drugs that we do not expect to be commercially available for many years, if at all. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms, or at all.

Until such time, if ever, as we can generate substantial drug revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances and licensing arrangements. We do not have any committed external source of funds outside of those to be earned in connection with our agreement with Alexion. 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.

If we raise funds through additional 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 drug 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 when needed, we may be required to delay, limit, reduce or terminate our drug development or future commercialization efforts or grant rights to develop and market drug candidates that we would otherwise prefer to develop and market ourselves.

Contractual Obligations

The following table summarizes our significant contractual obligations as of payment due date by period at December 31, 2014:

(Dollars in thousands)	Total	Less than 1 Year	1 to 3 Years	3 to 5 Years	More than 5 years
Operating lease commitments(1)	$ 18,784	1,453	4,717	5,004	7,610
Debt repayment(2)	$ 10,208	2,257	6,383	1,568	—

(1) Represents future minimum lease payments under our non-cancelable operating leases, which expire in October 2015 and October 2022, assuming occupancy in October 2015 on the lease entered into in February of 2015. The minimum lease payments above do not include any related common area maintenance charges or real estate taxes.

(2) Consists of payment obligations for principal and interest under the Loan and Security Agreement. As of December 31, 2014, we had $9.3 million in outstanding principal under the Loan and Security Agreement.

We enter into agreements in the normal course of business with contract research organizations for clinical trials and clinical supply manufacturing and with vendors for pre-clinical research studies, synthetic chemistry, and other services and products for operating purposes. We have not included these payments in the table of contractual obligations above since the contracts are cancelable at any time by us, generally upon 30 days prior written notice to the vendor. Milestone payments associated with our license agreements have not been included in the above table of contractual obligations as we cannot reasonably estimate if or when they will occur. As of the date of this prospectus, no milestone payments are likely to be due in 2015. Possible future payments under our license arrangements include up to $80,000 in payments to academic and research organizations upon the filing of an IND or FDA approval of a drug.

Off-Balance Sheet Arrangements

We did not have, during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined under applicable Securities and Exchange Commission rules.

Quantitative and Qualitative Disclosures About Market Risk

We are exposed to market risk related to changes in interest rates. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates, particularly because our investments, including cash and cash equivalents, are in a money market fund that invests in U.S. Treasury obligations.

We are also exposed to market risk related to changes in foreign currency exchange rates. We contract with vendors that are located Asia and Europe, which are denominated in foreign currencies. We are subject to fluctuations in foreign currency rates in connection with these agreements. We do not currently hedge our foreign currency exchange rate risk. As of December 30, 2013 and 2014, we had minimal or no liabilities denominated in foreign currencies.

Inflation generally affects us by increasing our cost of labor and clinical trial costs. We do not believe that inflation had a material effect on our business, financial condition or results of operations during the years ended December 31, 2013 and 2014.

BUSINESS

We are a biopharmaceutical company focused on improving the lives of patients with genomically defined diseases driven by abnormal kinase activation. Our approach is to systematically and reproducibly identify kinases that are drivers of genomically defined diseases and to craft drug candidates with therapeutic windows that provide significant and durable clinical responses to patients. This integrated biology and chemistry approach enables us to drug known kinases that have been difficult to inhibit selectively and also identify, characterize and drug novel kinase targets. By focusing on genomically defined diseases, we believe that we will have a more efficient development path with a greater likelihood of success. Over the past three years, we have developed a robust small molecule drug pipeline in cancer and a rare genetic disease. One of our lead drug candidates is BLU-285, which targets KIT Exon 17 and PDGFRa D842V, abnormally active receptor tyrosine kinase mutants that are drivers of cancer and proliferative disorders. BLU-285 will initially be developed in for patients with systemic mastocytosis, a myeloproliferative disorder of the mast cells, and defined subsets of patients with gastrointestinal stromal tumors, the most common sarcoma, or tumor of bone or connective tissue, of the gastrointestinal tract. Our other lead drug candidate is BLU-554, which targets FGFR4, a kinase that is aberrantly activated and is a driver of disease in a defined subset of patients with hepatocellular carcinoma, the most common type of liver cancer. Both drug candidates have demonstrated proof of concept in pre-clinical models and we expect to file Investigational New Drug applications, or INDs, in mid-2015 and initiate our Phase 1 clinical trials in mid-2015. We are also developing a drug candidate to target both RET, a receptor tyrosine kinase that can become abnormally activated when a portion of the gene that encodes RET is joined to part of another gene, and RET resistant mutants that we predict will arise from treatment with first generation therapies. We believe that our strategy will allow us to deliver transformative drugs to patients while building a fully-integrated biopharmaceutical company.

Approved kinase drugs, such as imatinib, have demonstrated significant benefit to patients and small molecule kinase drugs achieved over $14 billion in 2013 sales. Despite this success, there is room for further improvement in kinase drug discovery and development. Many of the approved drugs are multi-kinase inhibitors that are not selective for disease drivers. This results in off-target toxicities that limit dose levels and target inhibition, thereby reducing efficacy. Further, patients who initially respond to a targeted kinase treatment often relapse due to the development of resistance mutations. Finally, as of 2014, kinase drugs approved by the U.S. Food and Drug Administration, or FDA, only target less than five percent of the 518 kinases that constitute the kinome. For many of the known kinases, there is a strong link between genetic alterations in a kinase and disease, including specific forms of cancer and rare genetic diseases. However, the function of the majority of the kinome is unknown. Taken together, this represents a substantial opportunity for developing novel and transformative drugs for cancer, rare genetic diseases and other disease areas.

To capitalize on the kinase opportunity, we built a platform that integrates a novel target discovery engine and a proprietary compound library. Our novel target discovery engine, which was developed entirely in-house under the direction of our chief scientific officer, combines our expertise in genomics, bioinformatics, and cell and structural biology to provide new insights into the biology of kinases as drivers of disease. To develop kinase drugs, we start by interrogating our proprietary compound library. Our library is a unique collection of novel small molecules rationally designed and developed entirely in-house by Blueprint Medicines' scientists as kinase inhibitors and enriched for drug-like properties. We do not owe any royalties or other fees to any parties associated with our novel target discovery engine and our proprietary compound library. Using this platform, we have produced a drug pipeline of several promising drug candidates that target genomically-defined patient subsets.

Our two lead programs targeting KIT Exon 17 and FGFR4 provide strong evidence of the power of our proprietary compound library. These targets have been well characterized in scientific literature as disease drivers, but have been challenging to inhibit selectively with small molecules. Our RET program provides evidence of the strength of our novel target discovery engine and proprietary compound library. Leveraging our expertise in structural and cell biology, we predicted future resistance mutations resulting from treatment with drugs with RET inhibitory activity and have crafted drug candidates that will be effective against RET and the RET resistant mutants.

BLU-285 is an orally available, potent and selective inhibitor of several activating mutations of KIT that occur in Exon 17, which encodes a portion of the tyrosine kinase domain. BLU-285 also potently and selectively inhibits PDGFRa D842V. Due to the high degree of structural similarity of the kinase domains of KIT and PDGFRa, BLU-285 is able to inhibit both KIT Exon 17 mutants and the PDGFRa D842V mutant with minimal inhibition of other kinases. BLU-285 is a highly targeted therapeutic candidate for genomically-selected patients with diseases driven by these mutations, including systemic mastocytosis, or SM, and genomically-defined patient subsets within gastrointestinal stromal tumors, or GIST, which are KIT and PDGFRa mediated diseases.

Imatinib, which is an inhibitor of KIT, is approved in SM and GIST and validates this kinase as a therapeutic target in these diseases. Imatinib also inhibits PDGFRa, which is a driver in a subset of GIST. However, a meaningful percentage of patients harbor mutations in KIT and PDGFRa that are not targeted by imatinib and fail to respond to treatment with the drug. We plan to initially develop BLU-285 for targeted patient populations that harbor these mutations and currently lack adequate treatments. BLU-285 has shown significant tumor regression in pre-clinical models of SM and GIST, which we believe to be highly predictive of clinical response. IND enabling studies are nearly completed, and we expect to file our INDs in mid-2015 and initiate our Phase 1 clinical trials in mid-2015. Expansion cohorts in these trials will include genomically-selected patients.

BLU-554 is an orally available, potent, selective and irreversible inhibitor of the kinase FGFR4. FGFR4 has historically been a challenging target to drug selectively given the closely related paralogs, proteins encoded by closely related genes, namely FGFR1-3. Aberrantly active FGFR4 signaling is a driver of disease in a subset of patients with hepatocellular carcinoma, or HCC, a disease with high unmet need and no approved genomically-targeted therapies. We plan to initially develop BLU-554 for a genomically-defined patient population within HCC with aberrantly active FGFR4 signaling. BLU-554 has shown significant anti-tumor activity in several different pre-clinical models of HCC with aberrantly active FGFR4 signaling, including a model which we believe to be highly predictive of clinical response. IND-enabling studies are completed, and we anticipate filing our IND in mid-2015 and initiating our Phase 1 clinical trial in mid-2015. Expansion cohorts in this trial will include genomically-selected patients.

Our third program targets RET fusions and predicted RET resistant mutants. By using our proprietary compound library, we have crafted drug candidates to selectively inhibit not only RET but also the RET resistant mutants. We believe we can provide a treatment that results in a more meaningful and durable clinical response by prospectively inhibiting RET and RET resistant mutants early in the treatment of the disease. Our research suggests that RET is a driver of disease in a broad set of cancers including non-small cell lung cancer, and cancers of the thyroid, colon and breast.

To execute on this opportunity, we have assembled a team of employees, board of directors and scientific founders rich in experience and capabilities in biology, chemistry and the business of drug discovery, development and commercialization. Many of our employees have participated on teams that uncovered innovative scientific findings and delivered highly impactful drugs to the marketplace. Our management team has broad capabilities and successful track records in oncology and rare genetic diseases through previous experience at Algeta ASA, Genzyme

Corporation, Millennium Pharmaceuticals, Inc., Novartis AG and Sanofi S.A. We were founded by an internationally-recognized scientific team, including Brian Druker, Nicholas Lydon and Charles Sawyers, who led the discovery and development of imatinib. The approval of imatinib revolutionized the treatment of chronic myelogenous leukemia by converting it from an aggressive and deadly cancer to a chronic, manageable disease. Our vision is to emulate the success of imatinib in a reproducible way by leveraging our platform to transform the lives of patients while building a fully-integrated biopharmaceutical company. We believe this experienced and diverse team is a key differentiator of our company.

Our initial investors included funds managed by Fidelity Biosciences and Third Rock Ventures. Additional blue chip investors participated in our Series B and C financings, including funds managed by (listed alphabetically) Biotechnology Value Fund, Casdin Capital, Cowen Investments, Nextech Invest, Partner Fund Management, Perceptive Advisors, RA Capital Management, Redmile Group, Sabby Capital, and Tavistock Life Science.

Our Mission

Blueprint Medicines makes kinase drugs to treat patients with genomically defined diseases. Led by a team of industry innovators, Blueprint Medicines integrates a novel target discovery engine and proprietary compound library to understand the genetic blueprint of cancer and craft highly selective therapies. This empowers Blueprint Medicines to rapidly develop patient-defined drug candidates aimed at eradicating cancer and other genomically defined diseases.

Our Principles

We maintain a culture of high integrity that embraces the following guiding principles to provide long-term benefits to patients and our stakeholders:

- ***Patients First*** — Maintaining intense focus on improving patients' lives.
- ***Thoughtfulness*** — Exploring creative approaches by daring to make well-thought-out decisions and owning the outcomes.
- ***Trust*** — Through collaboration and cooperation, building and maintaining a cohesive team that has mutual respect of different viewpoints, opinions and talents.
- ***Optimism*** — Pursuing transformative therapies that we believe will make a difference.
- ***Urgency*** — Solving complex problems rapidly, with attention and care.

Our Strategy

Our strategy was created to enable us to achieve our mission. The key tenets of our strategy include the following:

- ***Rapidly advance our lead drug candidates, BLU-285 and BLU-554, through clinical development.*** We expect to file INDs for these drug candidates in mid-2015 and to initiate our Phase 1 clinical trials in mid-2015 and expect that expansion cohorts in genomically-selected patients will begin in 2016. We are working with physicians and patient advocacy groups to rapidly identify and enroll patients most likely to respond to our therapies. In order to select patients most likely to respond to our therapies and rapidly confirm mechanistic and clinical proof of concept, we are building corporate collaborations to create companion diagnostics and to develop assays to measure target engagement, which is confirmation that a drug binds to its intended protein target *in vivo*, and early response. We expect these approaches to enable early determination of efficacy, allowing for clear decision points. With early and encouraging clinical results, we plan to apply for

Breakthrough Therapy Designation which, if granted, is intended to accelerate clinical development and expedite regulatory review and approval.

- ***Build a pipeline of kinase drugs for genomically defined drivers of disease.*** We will continue to leverage our platform to systematically and reproducibly identify kinases that are drivers of genomically defined diseases and craft drug candidates that potently and selectively target these kinases. We aim to file one IND annually on average.

- ***Continuously invest in our proprietary platform to ensure future growth.*** We plan to enhance our target discovery engine to enable new insights into known kinase biology and to identify new kinase drug targets. We are focused on uncovering the potential role of the "kinases of unknown biology," or KUBs, which constitute the majority of the kinome. We plan to expand our proprietary compound library to cover close to 100% of the kinome and to increase the number of compound families that inhibit each kinase target.

- ***Maintain the Blueprint Medicines' culture as we grow our business.*** We are focused on building an entrepreneurial organization that is patient-focused and science-driven and fosters a culture of creativity and innovation, hard work, and urgency for producing quality results. As we grow, we intend to continue hiring the most qualified individuals in biology, chemistry, clinical development and business, who fit within our culture and incorporate our entrepreneurial spirit. We also intend to continue fostering an environment that encourages tight integration across disciplines to ensure a seamless flow of ideas and information exchange.

- ***Evaluate strategic collaborations to maximize value.*** We currently retain 100% of the commercial rights for our oncology-focused programs, and have a rare genetic disease program that is the subject of our collaboration with Alexion Pharma Holding, or Alexion. We will evaluate additional collaborations that could maximize the value for our programs and allow us to leverage the expertise of strategic collaborators. We are also focused on engaging in collaborations to capitalize on our platform outside of our primary strategic focus area of cancer.

Our Focus — Highly Selective Kinase Drugs for Genomically Defined Diseases

Kinases are enzymes that function in many signaling pathways to regulate critical cellular functions. Abnormal activation of kinases has been shown to drive several key activities of cancer cells, including growth, survival, metabolism, cell motility and angiogenesis. Kinases may become abnormally activated through a number of mechanisms, including when: (1) a gene mutates creating a change in the resulting protein sequence; (2) chromosomes become rearranged creating a translocation or a fusion gene; or (3) excessive amounts of protein are created due to gene duplication or dysregulation leading to overexpression. There is a strong link between genetic alterations in kinases and disease, including specific forms of cancer and rare genetic diseases. Several kinases have been validated as oncogenes, which are genes that when altered can initiate and maintain cancer growth. Examples of oncogenes are BCR-ABL, EGFR, B-RAF and ALK, amongst many others. Ongoing genomic analyses of tumor data sets continue to identify new roles for kinases as drivers of disease.

As of 2014, there were 28 FDA-approved small molecule drugs that target less than five percent of the 518 kinases, of which all but two are indicated for cancer. The targets of these therapies include the overactive kinases produced by the known oncogenes as well as kinases that promote angiogenesis such as VEGFRs. Kinase inhibition continues to be a fruitful approach for cancer drug development. From 2012 to 2014, eleven of 28 FDA-approved cancer drugs were kinase inhibitors.

Despite these successes, several opportunities remain in kinase drug discovery and development.

- ***Identifying novel kinase drivers of disease.*** Very few kinases are the focus of approved drugs. Further, the function of the majority of the kinome still remains unexplored. Thus, there is substantial opportunity for developing novel and transformative therapies that target well-characterized but currently undrugged kinases as well as KUBs.

- ***Crafting very selective kinase drugs.*** Due to the high degree of homology between kinases, specific targeting of a given kinase can be challenging. Many of the approved kinase drugs inhibit multiple kinases and are referred to as multi-kinase inhibitors. Due to inhibition of off-target kinases, these multi-kinase inhibitors often give rise to severe unwanted effects, which can negatively impact the ability to dose patients at sufficient levels to achieve optimal efficacy. We believe increasing selectivity will minimize off-target toxicities and will improve efficacy by enabling higher dose levels and greater target inhibition. Further, combination therapies require that the drugs have non-overlapping toxicities, which could be minimized with more selective agents.

- ***Generating novel chemical matter required to target difficult-to-drug kinases.*** Novel chemical matter is needed to address targets that are known but not yet drugged. Pharmaceutical companies generally rely on known chemical families as the basis of drug discovery programs. Consequently, the vast majority of pharmaceutical companies have similar compound libraries. New approaches are needed to develop novel chemistry and differentiated libraries that can inhibit difficult-to-drug kinases in alternate ways.

- ***Overcoming resistance mediated by the alteration of kinase targets.*** Most approved kinase inhibitors provide only temporary disease control. Patients may relapse due to the emergence of resistance mutations. Novel approaches are needed to predict and inhibit resistant mutants thus providing more durable clinical responses.

Our Approach and Platform

Our approach is to systematically and reproducibly identify kinases that are drivers of genomically defined diseases and to craft drug candidates with therapeutic windows that provide significant and durable clinical responses to patients. This approach enables us to drug known kinase targets that have been difficult to inhibit selectively and also identify, characterize and drug novel kinase targets. By focusing on genomically defined diseases, we believe that we can quickly identify the patients most likely to respond, resulting in a more efficient development path with a greater likelihood of success.

Our approach is enabled by our drug discovery platform consisting of two pillars:

- a proprietary, highly-annotated library of novel compounds; and

- a novel target discovery engine, which is a comprehensive process that interrogates kinase biology from many angles using genomics, structural biology and cell biology.

Our proprietary compound library is a unique collection of small molecules designed and developed entirely in-house by Blueprint Medicines' scientists as kinase inhibitors and enriched for drug-like properties. We do not owe royalties or other fees to any parties associated with our novel target discovery engine and our proprietary compound library. This provides high-quality compounds to start kinase drug discovery programs and to use in identifying new kinase targets. The compounds were designed as kinase inhibitors without specific targets in mind, a design strategy that yielded a diversity of novel chemical structures that provide access to unique chemical matter. Each compound has been extensively characterized for binding to over 450 kinases and disease-relevant kinase mutants; the majority of known kinases are targeted by at least one

compound family. Thus, this "annotated" compound library provides high-quality medicinal chemistry starting points that enable quick-starts to drug discovery programs, avoiding the expense and time spent running high throughput screens. Notably, our proprietary compound library has yielded high quality chemical starting points for previously difficult-to-drug kinases. We plan to expand our proprietary compound library to cover close to 100% of the kinome and to increase the number of compound families that inhibit each kinase target.

We have established a novel target discovery engine, which was developed entirely in-house under the direction of our chief scientific officer, to provide new insights into the biology of kinases as drivers of disease and to identify new kinase drug targets. There are two aspects to the novel target discovery engine:

(1) ***Genomics Approach to Identify Novel Kinase Targets.*** Our high-capacity computing infrastructure allows not only storage of very large genomic databases but also rapid analyses of these data using proprietary algorithms developed by our bioinformaticians. For example, using our proprietary kinase fusion detection algorithm to analyze human tumor sequences, we have identified both novel kinase fusions and new disease indications for several known kinase fusions. These results were published in *Nature Communications* in 2014.

(2) ***Cell-based Screens to Identify Novel Kinase Targets.*** In this approach, a subset of the compounds in our proprietary compound library that exhibit remarkable potency and/or selectivity for one or a few kinases — our "tool compounds" — are used as probes in disease-relevant cell-based screens. Many of these tool compounds inhibit KUBs and thus allow us to evaluate potential roles for these relatively unexplored kinases in human disease.

Another aspect of our novel discovery engine is predicting resistance mutations. Through our structural and cell biology expertise, we predict mutations in kinases that render the enzyme insensitive to inhibition by an approved drug or compound in development. While treatment of patients with genomically-defined cancers with a targeted therapy typically results in a significant anti-tumor response, frequently the response is not durable. In tumors driven by an activated kinase, kinase reactivation via mutation is a common mechanism of resistance. Using our structural biology and computational chemistry expertise, we predict what changes in the kinase might result in a resistant enzyme and then confirm this prediction in a relevant cell culture model. We have and may continue to form collaborations to track emerging patterns of resistance in the clinic to confirm our predictions. We have used this process of predicting resistance to inform the design of several of our next generation drugs.

Our platform has already yielded a robust pipeline. KIT Exon 17 mutants, while known drivers of disease, were not selectively drugged successfully. We developed BLU-285 as a selective inhibitor of KIT Exon 17 mutants, an effort facilitated by our proprietary compound library. Aberrant signaling through FGFR4 is a known genomic driver in a subset of HCC patients. This kinase has been difficult to drug selectively due to the close homology of the FGFR family members. We developed BLU-554 as a selective inhibitor of FGFR4 to address the unmet medical need in this genomically-defined HCC patient population. Additionally, we applied our resistance mutation prediction algorithm in our RET program to identify mutant forms of the kinase that are resistant to multi-kinase inhibitors with RET activity. We have designed potent and selective RET inhibitors with activity against both the wild-type and mutant enzymes, another effort that is facilitated by our proprietary compound library. Finally, we are currently using and will continue to use our tool compounds to explore the role of KUBs in human disease with the goal of identifying novel kinase targets.

Our Development Programs

We have leveraged our platform to develop a robust drug pipeline of orally available, potent and selective small molecule kinase inhibitors that target genomic drivers in several cancers and a rare genetic disease. We currently own worldwide commercial rights to all of our oncology-focused drug candidates, and have a rare genetic disease program that is the subject of our collaboration with Alexion Pharma Holding, or Alexion. Our most advanced drug candidates are summarized in the table below.

Drug Candidates	Genomic Drivers	Initial Diseases	Stage of Development	Commercial Rights
BLU-285 (KIT Exon 17 inhibitor)	KIT D816V	SM	IND-enabling activities	Blueprint Medicines
	PDGFRa D842V	GIST	IND-enabling activities	
	KIT Exon 17 mutants	GIST	IND-enabling activities	
BLU-554 (FGFR4 inhibitor)	Aberrant FGFR4 signaling	HCC	IND-enabling activities	Blueprint Medicines
RET fusions and predicted RET resistant mutants	RET fusions*	Non-small cell lung cancer Other solid tumors	Lead optimization	Blueprint Medicines
Rare genetic disease target	Undisclosed	Rare genetic disease	Undisclosed	Alexion

* A fusion protein is encoded by a fusion gene, which is a gene in which a portion of one gene is joined to part of another gene. In the case of RET, a portion of the RET gene that encodes the kinase domain is joined to part of another gene. RET fusion proteins are always active and are thought to be drivers in several cancers.

One of our lead drug candidates is BLU-285, which targets KIT Exon 17 and PDGFRa D842V, for patients with SM and defined subsets of patients with GIST. Our other lead drug candidate is BLU-554, which targets FGFR4, for a defined subset of patients with HCC. Both drug candidates have shown proof of concept in pre-clinical models and are expected to enter the clinic in mid-2015. We are also developing a drug candidate to target both RET fusions and RET resistant mutants that we predict will arise from treatment with first generation therapies.

All of these programs target genomically-defined patient subsets. As we advance our drug candidates through clinical development, we will enrich our Phase 1 trials by selecting patients most likely to respond to our drug candidates to confirm mechanistic and clinical proof of concept. We are working with a number of clinical advisors, including David Schenkein, M.D., a former member of our board of directors, due to his medical experience as an oncologist and extensive drug development background. We are collaborating with corporate partners to create companion diagnostics and to develop assays to measure target engagement and early response. The table below lists the frequencies of each of the driver mutations targeted across multiple known diseases

and the corresponding estimated number of patients in the United States, France, Germany, Italy, Spain, the United Kingdom and Japan, or the Major Markets, worldwide:

Drug Candidates	Diseases	Estimated Number of Prevalent Patients*		Genomic Drivers	Frequency of Mutations (% of Patients)
		United States	Total Major Markets		
BLU-285	SM	1,700 advanced SM 6,300 indolent SM	4,500 advanced SM 16,000 indolent SM	KIT D816V	Greater than or equal to 94%
		Total: 8,000	Total: 20,000	PDGFRa D842V	5 - 6% of primary GIST
	GIST**	1L: 3,000 2L: 2,700 3L: 2,300	1L: 8,000 2L: 7,000 3L: 5,000	KIT Exon 17	1L: <1% 2L: 23% 3L: 100%
BLU-554	HCC**	16,000 first line 5,000 second line	60,000 first line 20,000 second line	Aberrant FGFR4 signaling	Up to 30%

* The prevalence of HCC in China represents an additional opportunity for BLU-554 and is not included in these estimates.
** Prevalence represents metastatic and unresectable populations.

KIT Inhibitor Program

Overview

BLU-285 is an orally available, potent and selective inhibitor of several activating mutations of KIT that occur in Exon 17, which encodes a portion of the tyrosine kinase domain. BLU-285 also potently and selectively inhibits PDGFRa D842V. Due to the high degree of structural similarity of the kinase domains of KIT and PDGFRa, BLU-285 is able to inhibit both KIT Exon 17 mutants and the PDGFRa D842V mutant potently and selectively with minimal inhibition of other kinases.

Kinome tree locations of KIT and PDGFRa illustrating close structural similarity between these kinases. *Kinome illustration reproduced courtesy of Cell Signaling Technology, Inc., or CSTI, (www.cellsignal.com). Each branch of the dendogram represents an individual human kinase. The foregoing website is maintained by CSTI, and Blueprint Medicines is not responsible for its content.*

BLU-285 is a highly targeted therapeutic candidate for genomically-selected patients with diseases driven by these mutations, including SM and genomically-defined patient subsets within GIST. We plan to initially develop BLU-285 for these targeted patient populations, which currently lack adequate treatments. BLU-285 has demonstrated tumor regression in pre-clinical models of GIST and SM, including activity in aggressive and patient-derived xenograft models that we believe to be highly predictive of clinical response. This provides clear rationale to develop BLU-285 in genomically-defined patient populations with tumors that harbor mutations in KIT Exon 17 or in PDGFRa and are most likely to respond.

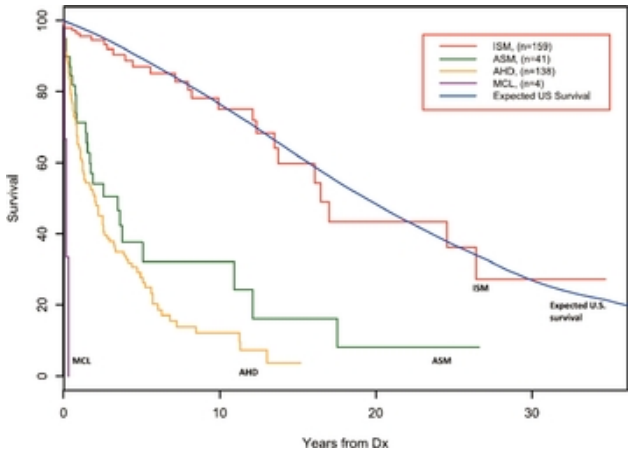
We plan to initially develop BLU-285 for SM and GIST secondary mutations in KIT Exon 17 and for GIST with the PDGFRa D842V mutation. IND-enabling studies are nearly completed, and we anticipate clinical trials will start in mid-2015. We may expand opportunistically into additional indications including a subset of acute myelogenous leukemia, or AML, patients who harbor the D816V mutation and other diseases driven by KIT Exon 17.

Systemic Mastocytosis (SM)

SM Disease Background

SM is a myeloproliferative disorder of the mast cells, the key effector cells of allergic inflammation, which have several physiologic roles including wound healing, regulation of vascular and epithelial permeability and immune cell recruitment. In myeloproliferative diseases, the bone marrow overproduces certain types of red blood cells, platelets, or white blood cells. The signature of SM is the accumulation of mast cell clusters in the bone marrow. In advanced forms of SM, abnormal mast cells may also accumulate in the liver, spleen, gastrointestinal tract and bones. Mast cell activation and histamine release can lead to severe allergic symptoms ranging from a skin rash to hives, fever and anaphylaxis, while mast cell accumulation in advanced cases of SM can eventually lead to organ dysfunction and failure.

Patients with SM are usually diagnosed in adulthood. The diagnosis involves a complex diagnostic algorithm that begins with confirmation of SM and subsequently categorizes patients into indolent or advanced subtypes of disease, a classification that has prognostic significance as shown below. Patients with indolent SM, or ISM, have a normal life expectancy; the primary burden of disease is the range of often unpredictable and debilitating allergic symptoms due to mast cell activation. Advanced SM includes three subsets with increasingly severe impact on life expectancy: aggressive SM, or ASM, SM with associated clonal hematological non-mast cell lineage diseases, or SM-AHNMD, and mast cell leukemia, or MCL. The advanced forms of SM have a median overall survival of three to five years and are characterized by prominent organopathy and dysfunction, as well as symptoms of mast cell activation. Smoldering SM, or SSM, previously listed as a subcategory of ISM, is increasingly considered as a variant of advanced SM. While SSM is not known to affect life expectancy, it has a greater degree of bone marrow infiltration, myeloproliferation, and/or presents with an enlarged liver and bears a greater risk of progression to ASM, SM-AHNMD or MCL.



Overall survival of SM patients. Republished with permission of the American Society of Hematology, from "How I treat patients with indolent and smoldering mastocytosis", A. Pardanani, *Blood*, 121(16):3085 - 3094 (2013); permission conveyed through Copyright Clearance Center, Inc.

Population studies, including a population-based epidemiology study sponsored by Blueprint Medicines, based on the Danish National Health Registry, estimate the incidence of all subtypes of SM from 0.5 to 1/100,000 new patients per year. This represents approximately 3,200 new patients diagnosed per year in the United States. Of all SM patients, ISM accounts for 50-80% and advanced SM accounts for the remaining 20-50% of patients.

The current treatment paradigm for SM varies by disease subtype. With the exception of imatinib, which does not address more than 94% of patients with the KIT D816V mutation, there are no approved therapies. For patients with advanced forms of SM, treatments include interferon-alpha or cytoreductive agents to reduce mast cell burden or treatments aimed at addressing the associated blood disorder. There are no disease-modifying agents and patients with advanced SM inevitably progress, with a three to five-year overall survival prognosis. We believe there are approximately 4,500 addressable patients with advanced forms of SM in the Major Markets.

For ISM, management is symptom-directed and includes avoidance of triggers of mast cell activation (such as insect stings). Treatments for ISM include histamine blockers, cromolyn, epinephrine, and, in cases of refractory patients, cytoreductive agents. Within ISM, key opinion leaders see the greatest degree of unmet need for the fraction of patients who have a heavy symptom burden that current therapies fail to address. We believe there are approximately 16,000 ISM patients in the Major Markets.

KIT Driver Mutations in SM

In all subtypes of SM, the mast cells of more than 94% of patients display a mutation at the D816V position in KIT that activates the kinase. KIT D816V status is routinely assessed as part of the workup in SM diagnosis.

KIT signaling is needed for normal blood cell production, including the differentiation and survival of mast cells. In patients with SM, abnormal mast cells bearing the KIT D816V mutation undergo constitutive kinase activation, leading to continuous survival and proliferative signals. Rare cases of SM have been found where alternative mutations in KIT occur that are responsive to imatinib; in these cases, treatment with imatinib can reduce mast cell burden in the bone marrow and other organs and improve symptoms, thereby clinically validating KIT as a therapeutic target for SM.

BLU-285 Pre-clinical Development in SM

We conducted comprehensive biochemical and cellular experiments to characterize the potency and selectivity of BLU-285. BLU-285 potently inhibits KIT D816V *in vitro* (IC_{50}, or the compound concentration at which 50% of the activity is inhibited relative to control lacking compound, = 0.27 nM). In contrast, imatinib inhibits KIT D816V at least 10,000-fold less potently (IC_{50} > 8,000 nM). In several cellular models driven by activated KIT mutant proteins, BLU-285 potently inhibits signaling of the oncogenic KIT mutant protein, as measured by inhibition of KIT autophosphorylation and inhibition of cellular proliferation. In HMC 1.2 cells, a human mast cell leukemia model driven by the KIT D816V mutation, BLU-285 potently inhibits signaling of the mutant KIT protein as measured by inhibition of KIT autophosphorylation (IC_{50} = 4 nM). In contrast, imatinib inhibits KIT autophosphorylation at least 2,000-fold less potently. In P815 cells, a mouse mastocytoma model driven by an Exon 17 mutation, BLU-285 potently inhibits signaling of the mutant KIT protein as measured by inhibition of KIT autophosphorylation (IC_{50} = 22 nM) as well as

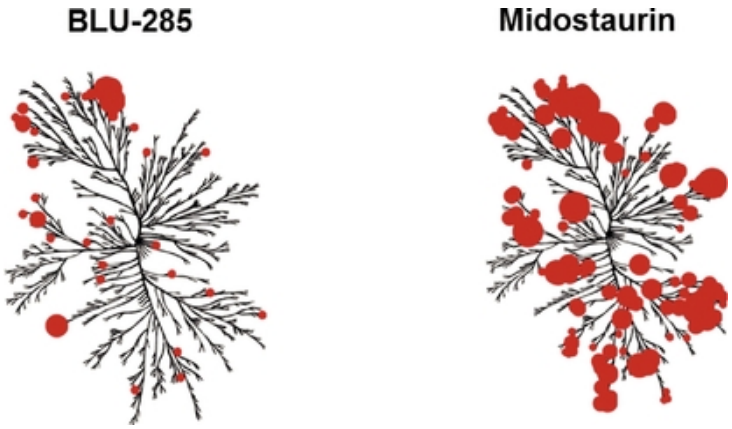
cellular proliferation (IC_{50} = 202 nM). By comparison, imatinib shows considerably lower cellular potency in the P815 model.

KIT D816V Inhibition

	Biochemical	Cellular		
IC_{50} (nM)	KIT D816V	HMC1.2 P-KIT	P815 P-KIT	P815 Prolif.
BLU-285	0.27	4	22	202
imatinib	8,150	9,229	1,235	2,811

Potency of BLU-285 against KIT D816 and other Exon 17 mutations compared to imatinib. The inhibitory potencies of BLU-285 and imatinib against the KIT D816V mutant protein were evaluated in an *in vitro* enzyme activity assay. The inhibitory potencies of BLU-285 and imatinib were also evaluated in two cell lines harboring KIT Exon 17 mutations, HMC 1.2 cells and P815 cells. Inhibition of KIT cellular signaling was measured by inhibition of KIT autophosphorylation (P-KIT). Inhibition of cellular proliferation was also measured in P815 cells.

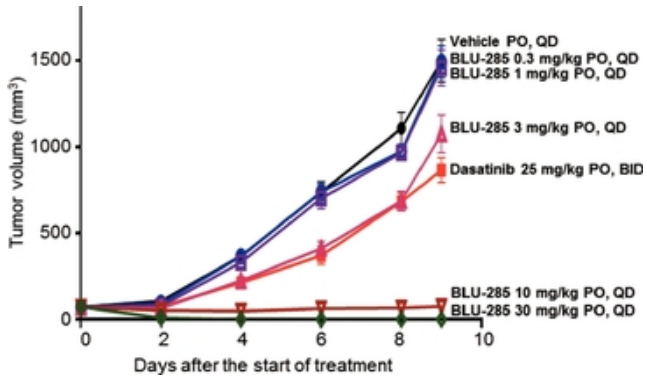
The selectivity of BLU-285 was further evaluated by profiling BLU-285 at a concentration of 3 µM across a panel of over 450 kinases and disease-relevant kinase mutants using KINOME*scan* methodology. BLU-285 demonstrated exquisite selectivity for KIT Exon 17 mutant proteins and PDGFRa D842V in this assay, binding significantly (greater than 90% inhibition relative to control) to only 12 other kinases. We also profiled midostaurin, a multi-kinase inhibitor with KIT D816V inhibitory activity (an inhibitory activity not present in imatinib), that is being studied in clinical trials of SM patients. Midostaurin demonstrated significant binding (greater than 90% inhibition relative to control at 3 µM) to 118 kinases, as indicated by the number of dots on the kinome tree shown below. We believe multi-kinase inhibitors that demonstrate *in vitro* activity against KIT D816V may not achieve full inhibition of KIT D816V in the clinic due to poor selectivity and the resulting dose limitations imposed by off-target toxicities.



Kinome selectivity of BLU-285 and a reference compound that has been studied in clinical trials of SM. Compounds were screened at 3 µM against a panel of over 450 kinases and disease-relevant mutants. Each branch of the dendogram represents an individual human kinase. Kinases bound by the compound are indicated by red circles on the kinome tree. The degree of binding corresponds to the size of the circle. *Kinome illustration reproduced courtesy of CSTI (www.cellsignal.com). The foregoing website is maintained by CSTI, and Blueprint Medicines is not responsible for its content.*

We demonstrated significant anti-tumor efficacy with BLU-285 in a P815 mouse mastocytoma xenograft model where tumor growth is driven by a KIT Exon 17 mutation. BLU-285 administered orally for nine days resulted in robust and dose-dependent growth inhibition of P815 tumors. At a

dose of 30 mg/kg once daily, a well-tolerated dose, BLU-285 caused tumor regression. We observed a correlation between the concentration of BLU-285 in mouse plasma and the level of phosphorylated KIT in the tumor, which is a measure of KIT signaling activity. At a dose of 30 mg/kg, the level of phosphorylated KIT was inhibited by greater than or equal to 90% over the 24 hour dosing period. This is an expected consequence of inhibiting KIT signaling. This correlation between BLU-285 plasma concentration, the level of phosphorylated KIT protein and anti-tumor efficacy supports the observation that anti-tumor response is due to inhibition of KIT signaling. The anti-tumor efficacy of dasatinib, a multi-kinase inhibitor with KIT D816V activity, which has been studied in clinical trials of SM patients, was also evaluated in this study. Dasatinib dosed twice daily at 25 mg/kg, a dose that resulted in significant body weight loss in mice, had only a modest effect on tumor growth.



BLU-285 elicits dose-dependent tumor regression in a mouse mastocytoma xenograft model of SM.

To emulate the systemic nature of the disease, we developed an aggressive systemic mouse model of SM. In this model, whereas vehicle-treated animals were terminated on day seven due to high disease burden, treatment with BLU-285 enabled significant disease control such that animals treated with BLU-285 at 30 mg/kg were terminated on day 22.

We have completed the 28-day GLP toxicology studies and have identified what we believe to be the dose limiting toxicity and anticipated first-in-human dose for BLU-285.

BLU-285 Clinical Development Plan in SM

We plan to initiate development of BLU-285 in SM in mid-2015. Based on our ongoing pre-IND discussions relating to our BLU-285 program, we may be required to submit pre-IND data from our ongoing 13-week toxicology studies to further support our recommended safe starting dose and define the dose limiting toxicity. In the event that we provide such data, the start of our clinical trials for BLU-285 may be delayed. We plan to file an IND for BLU-285 in SM in mid-2015, initiate our Phase 1 clinical trial in mid-2015 and we expect that expansion cohorts in genomically-selected patients will begin in 2016. We expect data to be available approximately 12 months after the start of the Phase 1 clinical trial. Our Phase 1 clinical trial will test the safety and tolerability in multiple ascending doses in patients with advanced SM, including ASM, SM-AHNMD and MCL, with the goal of establishing a maximum tolerated dose, or MTD, or a recommended dose if the MTD is not achieved. All patients will be tested retrospectively for KIT D816V mutational status. We will then open SM subtype-specific expansion cohorts for ASM patients, SM-AHNMD patients, and MCL patients. The key primary endpoints of the trial are to determine safety, tolerability and the MTD of BLU-285 in SM. Secondary endpoints include assessment of the pharmacokinetic profile of BLU-285, assessment of response rate by the International Working Group-Myeloproliferative Neoplasms Research and Treatment, or IWG-MRT, criteria and changes in quality of life.

Early signs of biological activity will be assessed as measured by changes in serum tryptase and KIT D816V allele burden. Serum tryptase is a recognized marker of mast cell burden and reduction of serum tryptase is one component of the IWG-MRT response criteria. In the expansion cohorts, clinical efficacy will be assessed by measuring overall response rate using IWG-MRT response criteria for SM, or a modified version thereof. In addition, change in total symptom score will be assessed to determine the effect of BLU-285 on symptom burden. As there is currently no validated patient reported outcomes tool for SM, we are collaborating with a health research outcomes group to develop a disease-specific tool to measure changes in total symptom score. We anticipate conducting additional trials to support development in SSM and ISM patients with high symptom burden who are refractory to current therapies.

We are working with patient advocacy groups relevant to SM in order to:

- raise awareness of our upcoming clinical trial;
- build a patient registry to identify patients for rapid enrollment; and
- incorporate the SM patient perspective into our ongoing activities.

Gastrointestinal Stromal Tumor (GIST)

GIST Disease Background

GIST is the most common sarcoma of the gastrointestional tract, or GI tract. Tumors arise within cells in the wall of the GI tract and occur most often in the stomach or small intestine. Most patients are diagnosed between the ages of 50-80 with diagnosis triggered by GI bleeding, incidental findings during surgery or imaging, or in rare cases acute presentation due to tumor rupture or GI obstruction. The standard workup at primary presentation includes pathologic confirmation and imaging to assess extent of disease.

The GIST treatment paradigm has advanced dramatically over the past 13 years. Patients diagnosed with localized disease undergo potentially curative tumor resection, while imatinib is given to high risk resected patients to prolong the time to recurrence. The advent of imatinib has improved the prognosis of patients with unresectable or metastatic disease to a 5-year median overall survival. Unresectable or metastatic patients typically receive imatinib, followed by sunitinib and regorafenib as the disease progresses.

Patients with PDGFRa D842V-driven GIST have great unmet medical need, as no approved medical therapies are effective. Progression can occur within as little as three months, and the median overall survival is 15 months for patients with advanced disease. The PDGFRa D842V mutation is found in 5-6% of frontline unresectable or metastatic GIST patients. We believe there are up to 500 addressable patients with PDGFRa D842V-driven, unresectable or metastatic GIST in the Major Markets.

For patients with KIT-driven GIST, current medical therapies slow the course of disease but progression is inevitable. Up to 50% of patients treated with frontline imatinib relapse within approximately 18 months. Of the secondary resistance mutations that lead to relapse, mutations in KIT Exon 17 (including D816 and other mutations) are not addressed by current therapies. KIT Exon 17 mutations are rare in treatment-naïve patients (<1%); however selective pressure due to treatment with imatinib and sunitinib causes KIT Exon 17 mutations to emerge with increasing frequency (approximately 23% of second line imatinib-resistant patients and 100% of third line imatinib/sunitinib resistant patients). These mutations confer resistance to current treatments. A therapy that effectively suppresses these mutants and that is potentially amenable to combinations with existing agents is needed. We believe there are approximately 6,600 addressable patients in the Major Markets with KIT Exon 17 secondary mutations that have led to disease progression during treatment with imatinib or sunitinib. Finally, we believe frontline combinations with imatinib will have the potential to dramatically increase the duration of therapy. We estimate there are

approximately 20,000 addressable patients in the Major Markets with unresectable or metastatic frontline GIST.

KIT Primary, KIT Exon 17 and PDGFRa Driver Mutations in GIST

GIST is a tumor type that depends on continued signaling of a single, aberrantly active kinase. Most GISTs result from primary mutations in KIT or PDGFRa. Up to 80% of patients have KIT-driven GIST. Imatinib effectively inhibits most of KIT primary mutations; however over time, secondary mutations occur elsewhere in the KIT gene that lead to kinase activation despite the presence of imatinib, thereby leading to disease progression. There is currently no therapeutic option for patients with PDGFRa-driven GIST. The most common mutation is PDGFRa D842V, found in approximately 5-6% of frontline unresectable or metastatic GIST patients. PDGFRa has a very similar active site structure to KIT and the PDGFRa D842V mutation is homologous to KIT D816V. As in the case of KIT D816V mutant receptors, PDGFRa D842V mutations confer ligand-independent constitutive signaling of the mutant PDGFRa kinase.

BLU-285 Pre-clinical Development in GIST

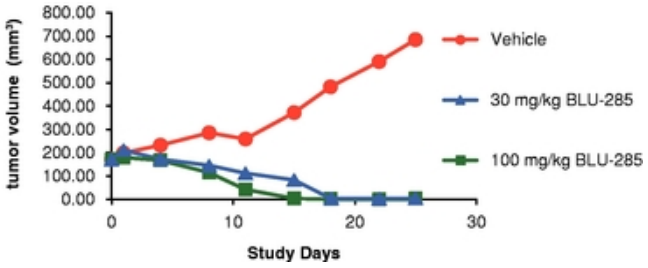
We have conducted comprehensive pre-clinical experiments to characterize the potency and selectivity of BLU-285. BLU-285 potently inhibits PDGFRa D842V *in vitro* (IC_{50} = 0.24 nM). In contrast, imatinib inhibits PDGFRa D842V at least 3,000-fold less potently (IC_{50} = 759 nM). In a cellular model driven by an activated PDGFRa D842V mutant protein, BLU-285 potently inhibits signaling of the oncogenic PDGFRa mutant protein as measured by inhibition of PDGFRa autophosphorylation (IC_{50} = 30 nM). By comparison, imatinib shows at least 100-fold lower potency in the cellular model (IC_{50} = 3,145 nM). The selectivity of BLU-285 has been discussed with the KINOME*scan* data shown in the section on SM.

PDGFRa D842V Inhibition

	Biochemical	Cellular
IC_{50} (nM)	PDGFRα D842V	P-PDGFRα D842V
BLU-285	0.24	30
imatinib	759	3,145

Inhibitory potency of BLU-285 compared to imatinib. The inhibitory potency of BLU-285 and imatinib against PDGFRa D842V was evaluated in an *in vitro* enzyme activity assay and in a cellular model driven by an activated PDGFRa D842V mutant protein.

We have demonstrated significant anti-tumor efficacy with BLU-285 in an imatinib resistant patient-derived xenograft model with a KIT Exon 17 resistance mutation, similar to what is found in relapsed/refractory KIT-driven GIST as shown below. BLU-285 administered orally for 25 days resulted in tumor regression at both tested doses.



BLU-285 elicits dose-dependent tumor regression in a patient-derived GIST xenograft model with a KIT Exon 11 mutation and a KIT Exon 17 resistance mutation.

In addition, we have developed an understanding of the biology that will inform the development of combinations to address these resistance mutations. We performed a comprehensive analysis of these secondary KIT Exon 17 mutations, analyzing the literature and unpublished data from opinion leaders to understand which mutations occur and to quantify their frequency in the clinical setting. We also conducted a series of *in vitro* biochemistry experiments using compounds from our proprietary compound library and currently available therapies (imatinib, sunitinib and regorafenib) to interrogate their activity against the range of KIT Exon 17 mutations. The result is a deep understanding of the spectrum of activity of BLU-285, additional compounds from our proprietary compound library and available therapies across the range of possible mutations. This will enable combination therapy development to address KIT Exon 17 secondary mutations.

BLU-285 Clinical Development Plan for GIST

We plan to initiate development of BLU-285 in GIST in mid-2015. Based on our ongoing pre-IND discussions with the FDA relating to our BLU-285 program, we may be required to submit data from our ongoing 13-week toxicology studies to further support our recommended safe starting dose and define the dose limiting toxicity. In the event that we provide such data, the start of our clinical trials for BLU-285 may be delayed. We plan to file an IND for BLU-285 in GIST in mid-2015, initiate our Phase 1 clinical trial in mid-2015 and we expect that expansion cohorts in genomically-selected patients will begin in 2016. We expect data to be available approximately 12 months after the start of the Phase 1 clinical trial. The Phase 1 clinical trial will test the safety and tolerability of BLU-285 in multiple ascending doses in patients with GIST, with the goal of establishing an MTD, or a recommended dose if the MTD is not achieved. All patients will be tested retrospectively for KIT Exon 17 and PDGFRa D842V mutational status. Once the MTD is achieved, or a recommended dose is established, we will open expansion cohorts for patients with relapsed GIST carrying the PDGFRa D842V mutation and KIT Exon 17 mutations. The key primary endpoints of the trial are to determine safety, tolerability and the MTD of BLU-285 in GIST. Secondary endpoints include assessing response rate by Response Evaluation Criteria In Solid Tumors, or RECIST, criteria commonly used to measure clinical responses in solid tumors, and allelic burden using circulating tumor DNA.

In the expansion cohorts, clinical efficacy will be assessed using MRI/CT imaging to assess overall response rate by RECIST criteria. Once the tolerability and biological activity of BLU-285 monotherapy is understood, we anticipate conducting additional studies with BLU-285 in combination with other therapies selected to address the broadest possible spectrum of mutations in GIST, including a potential front line study of BLU-285 with imatinib.

We are working with patient advocacy groups relevant to GIST in order to:

- raise awareness of our upcoming clinical trial;
- identify and use existing patient registries to identify patients for rapid enrollment; and
- incorporate the GIST patient perspective into our ongoing activities.

FGFR4 Inhibitor Program

Overview

BLU-554 is an orally available, potent, selective and irreversible inhibitor of the kinase FGFR4. FGFR4 functions as a receptor whose aberrant activation is a driver of HCC. FGFR4 belongs to a family of highly homologous receptors, which include FGFR1-4. BLU-554 targets FGFR4, while sparing the other three FGFR paralogs, and demonstrates exquisite kinome selectivity. Pre-clinical *in vitro* and *in vivo* efficacy data provides a strong rationale for the development of BLU-554 for the subset of HCC patients whose tumors are driven by aberrant FGFR4 signaling. Based on a

meta-analysis of publicly available HCC genomic datasets, we estimate that up to 30% of patients with HCC have tumors with aberrantly activated FGFR4 signaling.

HCC Disease Background

Liver cancer is the second leading cause of cancer-related deaths worldwide, with HCC accounting for most liver cancers. The highest incidence of HCC occurs in regions with endemic hepatitis B virus, or HBV, including Southeast Asia and sub-Saharan Africa. In the United States, HCC is the fastest rising cause of cancer-related death; over the past two decades, the incidence of HCC has tripled while the five-year survival rate has remained below 12%.

Cirrhosis is a key risk factor for HCC; the disease etiology varies by geography with the common theme of chronic conditions that lead to cirrhosis. In North America, the main risk factors for cirrhosis are infection with hepatitis C virus, or HCV, followed by HBV infection, alcohol consumption and nonalcoholic steatohepatitis. In Europe, the main risk factors for cirrhosis are HCV, HBV and alcohol consumption. In Southeast Asia and sub-Saharan Africa, the major risk factor is chronic HBV infection.

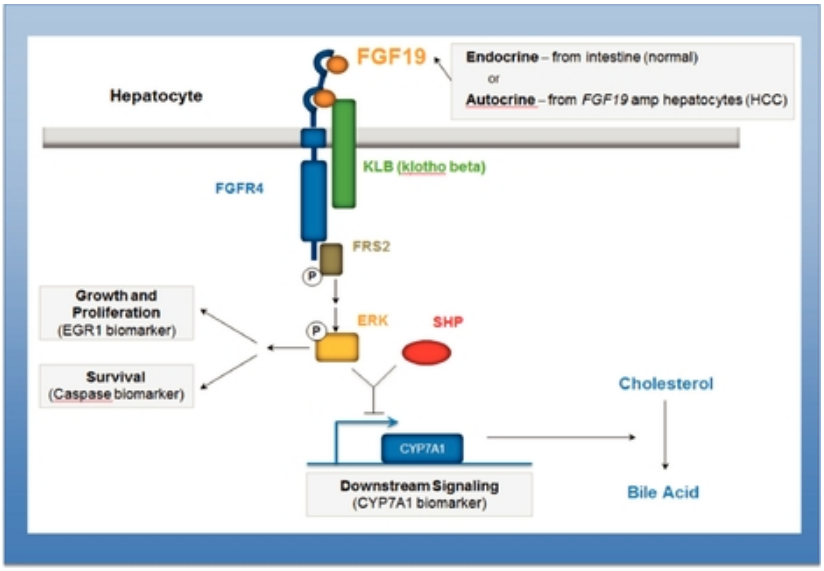
The diagnosis is typically made in adults, peaking around age 70. Disease management is complicated by concurrent liver disease, which often compromises liver function in these patients. Patients are staged depending on extent of liver disease, performance status and liver function status; these factors guide treatment selection. The stage distribution at diagnosis varies by region. For example, countries such as Taiwan and Japan with active national screening programs tend to diagnose many more patients in the early stages of disease. There are currently no treatments for genomically-defined patient subgroups in HCC.

The HCC treatment paradigm has advanced incrementally over the past decade. Patients diagnosed at an early stage receive potentially curative transplant, resection or ablative therapies. Intermediate to advanced stage patients receive high-dose chemotherapy delivered directly to the liver (transarterial chemoembolization) and ultimately sorafenib, the only approved systemic therapy for HCC, which became broadly available in the late 2000s. Sorafenib is a multi-kinase inhibitor that targets VEGFR and many other kinases and exhibits anti-angiogenic effects. In a pivotal trial conducted primarily in European Union and U.S. sites, sorafenib improved median overall survival by nearly three months and 2% of patients responded. In clinical practice, patients often require dose modifications or discontinue therapy due to tolerability issues. There is a clear need for medical therapies with a favorable risk-benefit profile.

FGFR4 as a Driver in HCC

The link between aberrant FGFR4 signaling and HCC was first established when an amplicon, a region of replicated DNA, that includes FGF19, the ligand that activates FGFR4, was identified in 6-12% of HCC patients. The physiologic role of the receptor, FGFR4, and its ligand, FGF19, is to regulate bile acid metabolism in hepatocytes. FGF19 is normally produced in the small intestine and signals to hepatocytes through an endocrine mechanism. FGF19 forms an active signaling complex together with FGFR4 and its co-receptor Klotho-b. Signaling of the active complex leads to decreased CYP7A1 transcription with a resultant decrease in bile acid synthesis, as well as increased growth, proliferation and survival signals.

FGFR4 Signaling in the Liver



Subsequent data suggest that FGFR4 signaling is a driver in a subset of HCC patients in whom the pathway is aberrantly activated. In these patients, FGF19 is overexpressed in hepatocytes (which do not normally express FGF19), leading to autocrine signaling and tumor growth. Pre-clinical experiments in a genetically engineered mouse model demonstrate that exogenous FGF19 expression is sufficient to induce liver tumor growth and that tumorigenesis is dependent on FGFR4. The three elements that constitute an active FGFR4 signaling complex, FGF19, FGFR4 and Klotho-b, are expressed together uniquely in HCC, although it is possible that they may also occur in rare cases of other solid tumors.

We have used our platform to identify a broader target responder population in addition to the FGF19-amplified patient population. In collaboration with a key opinion leader, we have potentially identified an additional approximately one quarter of HCC tumors that overexpress FGF19 without amplification. We have demonstrated a significant anti-tumor response with an FGFR4 inhibitor in an HCC patient-derived xenograft model that overexpresses FGF19 in the absence of amplification. Some of these results were published this year in *Cancer Discovery*. Together, these data suggest that aberrant activation of the FGFR4 signaling pathway is the driver in up to 30% of all cases of HCC.

The FGFR4 signaling pathway is a promising new driver for the development of molecularly targeted therapy in HCC. We estimate that in the Major Markets, there are approximately 18,000 first line and 6,000 second line addressable HCC patients with aberrantly active FGFR4 signaling as indicated by FGF19 overexpression.

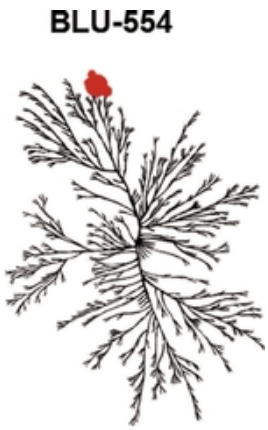
BLU-554 Pre-clinical Development in HCC

Efforts to discover selective, reversible inhibitors of FGFR4 have been challenging given the high sequence similarity among the four FGFR paralogs. A cysteine located near the ATP binding site in FGFR4 is unique among the paralogs. We therefore focused on developing a covalent inhibitor with paralog specificity and kinome selectivity. Our team of experienced medicinal chemists applied structure-based design principles to develop a potent and selective FGFR4 inhibitor starting from known FGFR inhibitor templates. This effort yielded our development candidate, BLU-554. We have conducted comprehensive *in vitro* experiments to characterize the potency and selectivity of BLU-554. BLU-554 potently inhibits FGFR4 enzyme activity (IC_{50} = 5 nM) and inhibits the activity of

FGFR1-3 at least 100-fold less potently (IC_{50} ³ 600 nM). In contrast, pan-FGFR inhibitors such as BGJ-398 fail to exhibit paralog specificity. The selectivity of BLU-554 was further evaluated by profiling BLU-554 at a concentration of 3 µM across a panel of over 450 kinases and disease relevant kinase mutants using KINOME*scan* methodology. BLU-554 displayed significant binding (greater than 90% inhibition relative to control) only to FGFR4 in this assay. In contrast, BGJ-398 significantly bound to 14 kinases (greater than 90% inhibition relative to control).

Paralog Selectivity		
FGFR4 Paralog	**BLU-554**	**BGJ-398**
FGFR4 IC_{50} (nM)	5	26
FGFR1 IC_{50} (nM)	624	<1
FGFR2 IC_{50} (nM)	1,202	<1
FGFR3 IC_{50} (nM)	2,203	<1

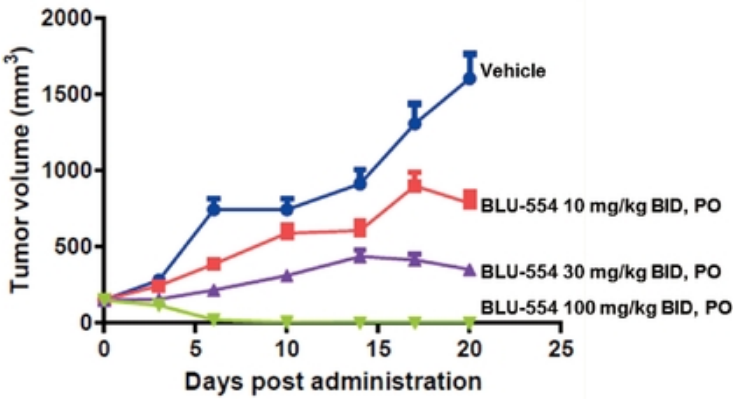
Paralog selectivity of BLU-554 compared to the pan-FGFR inhibitor BGJ-398. The inhibitory potency of BLU-554 and BGJ-398 against each of the FGFR paralogs was evaluated in an *in vitro* enzyme activity assay.



Kinome selectivity of BLU-554 as determined using the KINOME scan assay. BLU-554 was screened at 3 µM against a panel of over 450 kinases and disease-relevant mutants. Each branch of the dendogram represents an individual human kinase. Kinases bound by the compound are indicated by red circles on the kinome tree. The degree of binding corresponds to the size of the circle. *Kinome illustration reproduced courtesy of CSTI (www.cellsignal.com). The foregoing website is maintained by CSTI, and Blueprint Medicines is not responsible for its content.*

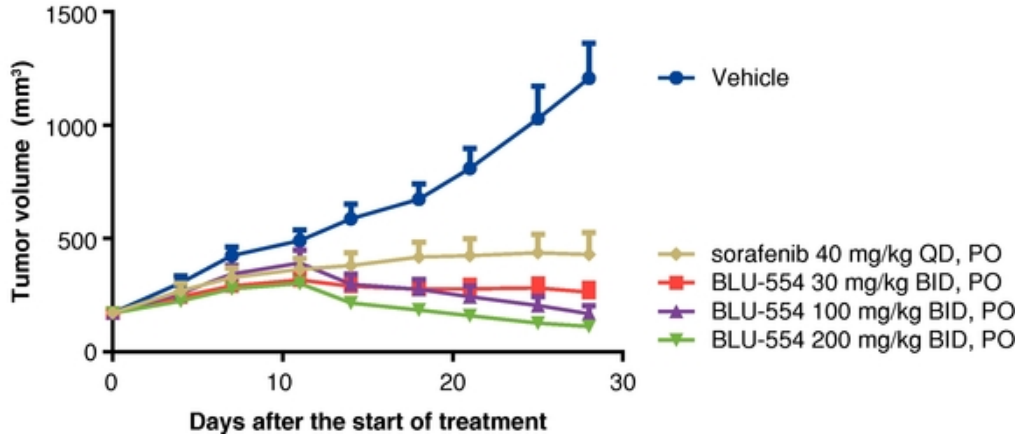
We demonstrated significant anti-tumor efficacy with BLU-554 in two *in vivo* HCC xenograft models where tumor growth is driven by FGFR4 signaling. BLU-554 administered orally for 21 days resulted in robust and dose-dependent growth inhibition of Hep3B tumors, an FGF19-amplified model. At a dose of 100 mg/kg twice daily, a well-tolerated dose, BLU-554 induced complete remission in a subset of mice for at least 30 days after cessation of treatment. We observed a correlation between the concentration of BLU-554 in mouse plasma and the level of expression of CYP7A1, a downstream biomarker, in the tumor. At the 100 mg/kg twice daily dose, significant induction of CYP7A1 expression was seen, which is an expected consequence of inhibiting FGFR4 signaling. This correlation between BLU-554 plasma concentration, the level of induction of CYP7A1

expression and anti-tumor efficacy supports that the observed anti-tumor response is due to inhibition of FGFR4 signaling.



BLU-554 elicits dose-dependent tumor inhibition in the Hep3B tumor xenograft mouse model, a model of FGF19 amplification. In the figure above, BID means twice a day and PO means orally.

Aberrant FGFR4 signaling can also be driven by FGF19 overexpression in the absence of amplification. Hence, we have also evaluated the anti-tumor efficacy of BLU-554 in a patient-derived xenograft model driven by FGF19 overexpression in the absence of amplification. Treatment with BLU-554 led to dose-dependent tumor growth inhibition. The anti-tumor efficacy of sorafenib, the only approved systemic treatment for HCC, was also evaluated in this study. Sorafenib dosed once daily at 40 mg/kg, a dose that led to body weight loss in the mice, had only a modest effect on tumor growth.



BLU-554 elicits dose-dependent tumor inhibition in a patient-derived tumor xenograft mouse model in which tumor growth is driven by FGF19 overexpression in the absence of FGF19 amplification. In the figure above, BID means twice a day; QD means once a day; and PO means orally.

Taken together, the data presented above indicate that potent and selective FGFR4 inhibition leads to robust anti-tumor effects in *in vivo* models where tumor growth is driven by FGF19 amplification or FGF19 overexpression in the absence of amplification. These findings, together with analysis of genomic data from HCC patients (indicating that up to 30% of HCC patients have FGF19 overexpression, with or without amplification), provide critical information to identify a potential responder population and will inform patient selection criteria in our planned clinical trial.

We have completed 28-day GLP toxicology studies and have identified what we believe to be the dose limiting toxicity and anticipated first-in-human dose for BLU-554.

BLU-554 Clinical Development Plan

We plan to submit an IND for BLU-554 in mid-2015, initiate our Phase 1 clinical trial in mid-2015 and and expect that expansion cohorts in genomically-selected patients will begin in 2016. Our Phase 1 clinical trial will test the safety and tolerability of BLU-554 in multiple ascending doses in patients with HCC and other advanced solid tumors with the goal of establishing an MTD, or a recommended dose if the MTD is not achieved. In the dose escalation phase, FGF19 expression and amplification status will be assessed in patients with available archival tumor tissue. We will then open expansion cohorts for HCC patients selected based on FGF19 expression and stratified according to FGF19 amplification status. The key primary endpoints of the trial are to determine safety, tolerability and the MTD of BLU-554 in HCC. Secondary endpoints include assessing pharmacokinetics, pharmacodynamics and efficacy. We expect data to be available approximately 12 months after the start of Phase 1 clinical trial to determine activity of our BLU-554 in the target population.

Early signs of biological activity will be assessed using disease-specific circulating biomarkers including serum alpha-fetoprotein and, when on-treatment biopsies are available, pharmacodynamic markers such as CYP7A1 expression. Clinical efficacy will be assessed in the expansion phase using MRI/CT imaging to assess overall response rate by RECIST criteria. We anticipate conducting additional trials to support development in front-line advanced HCC. Additional development beyond HCC will be considered pending further evidence of FGFR4 pathway relevance in cholangiocarcinoma and other solid tumors.

RET Fusion Program

Our third program targets RET fusions and predicted RET resistant mutants. RET is a receptor tyrosine kinase that activates multiple downstream pathways involved in cell proliferation and survival. Sometimes a portion of the RET gene that encodes the kinase domain is joined to part of another gene creating a fusion gene that encodes an aberrantly activated RET fusion protein. RET fusions are implicated in several cancers including papillary thyroid carcinoma (approximately 35% of patients) and non-small cell lung cancer (1-2% of patients). Our recently published genomics analyses on the landscape of kinase fusions identified RET fusions in breast and colon cancer patient samples (both <1% of patients), providing a therapeutic rationale for the use of RET inhibitors in multiple patient subpopulations.

The identification of RET fusions as drivers in some cancers prompted the use of approved multi-kinase inhibitors with RET inhibitory activity to treat patients whose tumors express a RET fusion protein. However, we believe these drugs cannot be dosed at levels required to sufficiently inhibit RET due to toxicities that result from inhibition of the primary targets. Further, one of the greatest challenges in treating cancer is the ability of tumor cells to become resistant to therapy. Kinase reactivation via mutation is a common mechanism of resistance. We have predicted future resistance mutations of drugs with RET inhibitory activity and are collaborating with opinion leaders to understand patterns of emerging clinical resistance. Thus, there is a clear need for a selective RET inhibitor that targets both wild-type RET fusions and their predicted RET resistant mutants.

We leveraged our proprietary compound library to identify compounds that fit this challenging drug profile. We have identified library compounds that inhibit both wild-type and mutant RET but not key off-target kinases and are using these as the basis for designing potent and selective RET inhibitors suitable for clinical development.

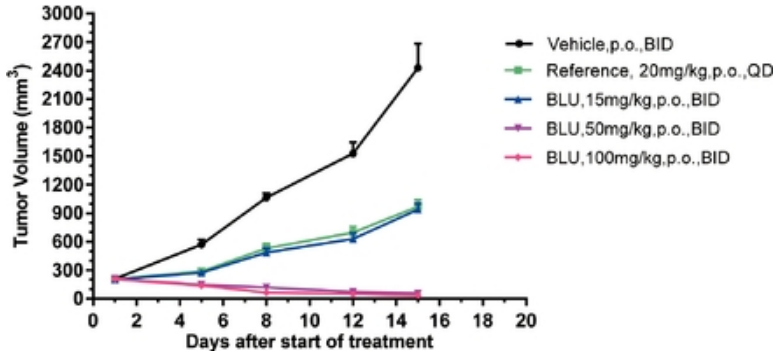
We have conducted pre-clinical experiments to characterize the potency of one of our RET inhibitors in biochemical and cellular assays. This compound potently inhibits the kinase activity of both wild-type RET and a RET resistance mutant *in vitro* (IC_{50} of 1.5 nM and 0.9 nM, respectively). We have also assessed a panel of seven clinically-approved multi-kinase inhibitors with RET inhibitory activity in these assays. These compounds inhibit the kinase activity of the RET resistance

mutant between 1 to >1000-fold less potently than wild-type RET. In cellular models driven by either a wild-type RET fusion or a resistant RET fusion, our compound exhibited similar potent growth inhibitory activity in both cell lines (IC_{50} of 105 nM and 160 nM, respectively). In contrast, the multi-kinase inhibitors exhibited between 1 to >100-fold less growth inhibitory activity against the cell line driven by the mutant RET fusion as compared to the wild-type RET fusion.

IC_{50} (nM)	Biochemical		Cellular	
	RET wt	RET Resistance Mutant	RET wt	RET Resistance Mutant
BLU	1.5	0.9	105	160
Vandetanib	1.8	3597	589	9190
Cabozantinib	54	265	344	2513
Regorafenib	9.8	47	186	2884
Sorafenib	5.6	91	260	2816
Ponatinib	0.6	6	10	267
Lenvatinib	1.5	430	115	13572
Sunitinib	2.7	1.6	734	892

Potency of a Blueprint RET inhibitor against wild-type RET and a RET resistance mutant compared to a panel of clinically-approved multi-kinase inhibitors with RET inhibitory activity. The inhibitory potencies of BLU and the multi-kinase inhibitors against RET wild type and RET resistance mutant protein were evaluated in *in vitro* enzyme activity assays. The inhibitory potencies of these compounds were also evaluated in cell lines driven by either a wild-type RET fusion or a mutant RET fusion.

We have demonstrated significant anti-tumor efficacy with our RET inhibitor in a wild-type RET fusion xenograft model. Administration of our compound orally twice daily for 15 days resulted in robust and dose-dependent tumor growth inhibition. At a dose of 50 mg/kg twice daily, a well-tolerated dose, the compound induced tumor regression. The anti-tumor efficacy of a multi-kinase inhibitor with RET inhibitory activity that is being evaluated in the clinic for treatment of patients with RET fusion positive lung cancer (reference compound) was also evaluated in this study. This reference compound dosed orally once daily at 20 mg/kg, a well-tolerated dose, had a modest effect on tumor growth.



A Blueprint RET inhibitor elicits dose-dependent tumor growth inhibition in a wild-type RET fusion xenograft model. In the figure above, BID means twice a day, QD means once a day and PO means orally.

Collaborations

In March 2015, we entered into a research, development and commercialization agreement with Alexion to research, develop and commercialize drug candidates for an undisclosed activated kinase target, which is the cause of a rare genetic disease. Under the terms of this agreement, which we refer to as the Alexion agreement, we granted Alexion an exclusive, sublicenseable license under certain of our patents and technology. Under the Alexion agreement, we will be

responsible for research and pre-clinical development activities related to drug candidates and Alexion will be responsible for all clinical development, manufacturing and commercialization activities related to drug candidates.

Alexion is responsible for funding 100% of our research and development costs incurred under the research plan, including pass-through costs and our employees' time devoted to the research plan at a negotiated yearly rate per full-time equivalent for our employees' time and associated overhead expenses. We received a $15.0 million non-refundable upfront payment in March 2015 upon execution of the Alexion agreement and are eligible to receive over $250 million in payments upon the successful achievement of pre-specified pre-clinical, clinical, regulatory and commercial milestones as follows: (i) up to $6.0 million in pre-clinical milestone payments for the first licensed product, (ii) up to $83.0 million and $61.5 million in development milestone payments for the first and second licensed products, respectively, and (iii) up to $51.0 million in commercial milestone payments for each of the first and second licensed products. Alexion will pay us tiered royalties, ranging from the mid-single to low-double digit percentages, on a country-by-country and licensed product-by-licensed product basis, on worldwide net product sales of licensed products. The royalty term for each licensed product in each country is the period commencing with first commercial sale of such licensed product in such country and ending on the later of (i) the expiration of the last-to-expire valid claim of specified patents covering such licensed product, (ii) the expiration of the applicable regulatory exclusivity period, and (iii) 10 or 15 years from specified commercial sales, whichever comes earlier.

The term of the Alexion agreement will expire on a country-by-country basis and a licensed-product-by-licensed-product basis at the end of each applicable royalty term, unless terminated earlier by either party. Alexion has the right to terminate the Alexion agreement if we undergo a change of control or become an affiliate of a biotechnology or pharmaceutical company, and may terminate at-will upon 90 days, prior written notice. We and Alexion have the right to terminate the Alexion agreement in the event of the other party's uncured breach or insolvency, and in certain other circumstances agreed to by the parties.

Intellectual Property

Our commercial success depends in part on our ability to obtain and maintain proprietary or intellectual property protection for our drug candidates, including BLU-285 and BLU-554, and our core technologies, including our novel target discovery engine and our proprietary compound library, and other know-how; to operate without infringing on the proprietary rights of others; and to prevent others from infringing our proprietary or intellectual property rights. Our policy is to seek to protect our proprietary and intellectual property position by, among other methods, filing U.S., international and foreign patent applications related to our proprietary technology, inventions and improvements that are important to the development and implementation of our business. We also rely on trade secrets, know-how and continuing technological innovation to develop and maintain our proprietary and intellectual property position.

We file patent applications directed to our drug candidates in an effort to establish intellectual property positions regarding these new chemical entities as well as uses of these new chemical entities in the treatment of diseases. We also file patent applications directed to novel fusions that we have discovered through our target discovery engine and the use of these fusions in diagnosing and treating disease. As of March 31, 2015, we owned one issued U.S. patent, 16 pending U.S. patent applications, 41 foreign patent applications pending in a number of jurisdictions, including Australia, Brazil, Canada, China, Europe, Israel, India, Japan, South Korea, Mexico New Zealand, Russia, South Africa, and seven pending Patent Cooperation Treaty, or PCT, patent applications. A significant portion of our pending patent applications pertain to our key discovery programs, specifically novel recurrent fusions. Our issued U.S. patent is projected to expire in 2033, and any

patents that may issue from our pending U.S. applications would be projected to expire between 2034 and 2036.

The intellectual property portfolios for our most advanced drug candidates as of March 31, 2015 are summarized below. Each of these portfolios is in its very early stages and, with respect to most of the pending patent applications covering our drug candidates, prosecution has yet to commence. Prosecution is a lengthy process, during which the scope of the claims initially submitted for examination by the USPTO often significantly narrowed by the time they issue, if they issue at all. We expect this to be the case with respect to our pending patent applications referred to below.

KIT Exon 17

The intellectual property portfolio for our KIT Exon 17 program contains patent applications directed to compositions of matter for BLU-285 and analogs, compositions of matter for KIT Exon 17 inhibitors with different compound families, as well as methods of use for these novel compounds. As of March 31, 2015, we owned four pending U.S. patent applications, nine pending foreign patent applications in a number of jurisdictions, including Argentina, Bolivia, Pakistan, Taiwan and Venezuela, and three pending PCT patent applications directed to this program. Any U.S. or ex-U.S. patents issuing from the pending applications covering BLU-285 will have a statutory expiration date of October 2034. Patent term adjustments or patent term extensions could result in later expiration dates.

FGFR4

The intellectual property portfolio for our FGFR4 program contains patent applications directed to compositions of matter for BLU-554 and analogs, as well as compositions of matter for FGFR4 inhibitors with multiple compound families. The portfolio also includes patent applications directed to methods of use for the novel compounds as well as patent applications directed broadly to FGFR4 selective inhibitors. As of March 31, 2015, we owned one issued U.S. patent, three pending U.S. patent applications, 32 foreign patent applications in a number of jurisdictions, including Australia, Brazil, Canada, China, Europe, Israel, India, Japan, South Korea, Mexico New Zealand, Russia, South Africa, and two pending PCT patent applications directed to this program. Any U.S. or ex-U.S. patent issuing from the pending applications covering BLU-554 will have a statutory expiration date of July 2033, December 2033, or October 2034. Patent term adjustments or patent term extensions could result in later expiration dates.

RET

The intellectual property portfolio for our RET program contains a patent application directed to compositions of matter for inhibitors of the predicted RET resistant mutants, as well as methods of use for these novel compounds. As of March 31, 2015, we owned one pending U.S. patent application directed to this program, which, if issued, will have a statutory expiration date of 2036.

Platform

The intellectual property portfolio directed to our platform includes patent applications directed to novel gene fusions and the uses of these fusions for detecting and treating conditions implicated with these fusions. As of March 31, 2015, we owned eight pending U.S. patent applications and two pending PCT patent applications directed to this technology, which, if issued, will have a statutory expiration date of 2036.

The term of individual patents depends upon the legal term for 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 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. See "— Government Regulation — U.S. Patent Term Restoration and Marketing Exclusivity" below for additional information on such exclusivity. In the future, if and when our drug candidates receive approval by the FDA or foreign regulatory authorities, we expect to apply for patent term extensions on issued patents covering those drugs, 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 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 drug candidates and technologies will depend on our success in obtaining effective patent claims and enforcing those claims if granted. However, our pending patent applications, and any patent applications that we may in the future 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, we cannot be certain of the priority of inventions covered by pending third-party patent applications. If third parties prepare and file patent applications in the United States that also claim technology or therapeutics to which we have rights, 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, which is highly unpredictable. In addition, because of the extensive time required for clinical development and regulatory review of a drug candidate we may develop, it is possible that, before any of our drug candidates can be commercialized, any related patent may expire or remain in force for only a short period following commercialization, thereby limiting protection such patent would afford the respective product and any competitive advantage such patent may provide.

In addition to patents, we rely upon unpatented trade secrets and know-how and continuing technological innovation to develop and maintain our competitive position. We seek to protect our proprietary information, in part, by executing confidentiality agreements with our collaborators and scientific advisors, and non-competition, non-solicitation, confidentiality, and invention assignment agreements with our employees and consultants. We have also executed agreements requiring assignment of inventions with selected scientific advisors and collaborators. The confidentiality agreements we enter into are designed to protect our proprietary information and the agreements or clauses requiring assignment of inventions to us are designed to grant us ownership of technologies that are developed through our relationship with the respective counterparty. We cannot guarantee, however, that these agreements will afford us adequate protection of our intellectual property and proprietary information rights.

With respect to the building of our proprietary compound library, we consider trade secrets and know-how to be our primary intellectual property. Trade secrets and know-how can be difficult to protect. In particular, we anticipate that with respect to this technology platform, these trade secrets and know-how will over time be disseminated within the industry through independent development and public presentations describing the methodology.

Competition

The pharmaceutical and biotechnology industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary drugs. 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 drug candidates that we successfully develop and commercialize will compete with existing drugs and new drugs that may become available in the future.

We compete in the segments of the pharmaceutical, biotechnology and other related markets that address inhibition of kinases in cancer and other rare genetic diseases. There are other companies working to develop therapies in the field of kinase inhibition for cancer and other diseases. These companies include divisions of large pharmaceutical companies and biotechnology companies of various sizes.

Many of the companies against which we are competing or against which we may compete in the future have significantly greater financial resources and expertise in research and development, manufacturing, pre-clinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved drugs 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. Smaller or early stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. 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.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize drugs that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any drugs that we or our collaborators may develop. Our competitors also may obtain FDA or other regulatory approval for their drugs more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we or our collaborators are able to enter the market. The key competitive factors affecting the success of all of our drug candidates, if approved, are likely to be their efficacy, safety, convenience, price, the effectiveness of companion diagnostics in guiding the use of related therapeutics, the level of generic competition and the availability of reimbursement from government and other third-party payors.

If the drug candidates for our priority programs are approved for the indications for which are currently planning clinical trials, they will compete with the drugs discussed below and will likely compete with other drugs that are currently in development.

BLU-285

We are initially developing BLU-285, which is designed to target KIT Exon 17, for advanced SM and GIST patients, as well as for patients with GIST with the PDGFRa D842V mutation.

For advanced SM, the only approved medical therapy is imatinib for patients without the KIT D816V mutation or mutational status unknown. Several treatments are used off-label for cytoreduction including interferon-a and cytoreductive agents for advanced forms of SM. If BLU-285 receives marketing approval, it may face competition from other drug candidates in development for advanced SM, including drug candidates in development from AB Science S.A., Plexxikon Inc., a wholly-owned subsidiary of Daiichi Sankyo Company, Limited, Deciphera Pharmaceuticals, LLC and Novartis AG.

For GIST, the current approved standards of care for unresectable or metastatic patients are first-line imatinib, followed by second-line sunitinib upon imatinib progression, followed by third-line regorafenib upon sunitinib progression. While these agents do not address patients with the

PDGFRa D842V mutation, they may be competitor therapies if the recommended mutational status testing is not performed. If BLU-285 receives marketing approval for this indication, it may also face competition from drug candidates in development by AROG Pharmaceuticals, Inc., Plexxikon Inc. and ARIAD Pharmaceuticals, Inc.

BLU-554

The development of BLU-554 will focus on a subset of patients with HCC with FGF19 overexpression. The only approved systemic medical therapy for HCC is sorafenib. In addition, there are potentially competitive drug candidates in development by AstraZeneca plc, Bayer AG, Johnson & Johnson, Novartis AG, Taiho Pharmaceutical Co., Ltd. and Xoma Ltd.

Commercialization Plans

Our vision is to become a fully-integrated biopharmaceutical company. This will enable us to realize our goal of delivering transformative drugs to patients. Given our stage of development, we have not yet established our own commercial organization or distribution capabilities. Our initial focus is on genomically-defined patient populations in oncology allowing us to efficiently commercialize our drug candidates in the United States on our own initially and worldwide longer-term. We believe we can successfully launch and commercialize our initial drug candidates on our own, using a small and highly specialized sales force similar to those of other rare disease companies. However, we may establish collaborations with pharmaceutical companies to leverage their capabilities to maximize the potential of our drug candidates.

Manufacturing and Supply

We do not own or operate, and currently have no plans to establish, any manufacturing facilities. We currently rely, and expect to continue to rely, on third parties for the manufacture of our drug candidates for pre-clinical and clinical testing, as well as for commercial manufacture of any drugs that we may commercialize. To date, we have obtained active pharmaceutical ingredients, or API, and drug substance for BLU-285 and BLU-554 for our pre-clinical and planned Phase 1 testing from one third-party manufacturer and drug product from another third party manufacturer. We obtain our supplies from these manufacturers on a purchase order basis and do not have a long-term supply arrangement in place. We do not currently have arrangements in place for redundant supply for API, drug product or drug substance. For all of our drug candidates, we intend to identify and qualify additional manufacturers to provide the API, drug product and drug substance prior to submission of a new drug application to the FDA and/or a marketing authorization application to the European Medicines Agency.

BLU-285 and BLU-554 are compounds of low molecular weight, generally called small molecules. They can be manufactured in reliable and reproducible synthetic processes from readily available starting materials. The chemistry is amenable to scale-up and does not require unusual equipment in the manufacturing process. We expect to continue to develop drug candidates that can be produced cost-effectively at contract manufacturing facilities.

We generally expect to rely on third parties for the manufacture of any companion diagnostics we develop.

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 and clinical development, testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, post-approval monitoring and reporting, marketing, pricing and export and import of drug products, such as those we are developing. Generally, before a new drug can be

marketed, considerable data demonstrating its quality, safety and efficacy must be obtained, organized into a format specific to each regulatory authority, submitted for review and approved by the regulatory authority.

Drugs are also subject to other federal, state and local statutes and regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources. Failure to comply with the applicable regulatory requirements at any time during the product development process, approval process or after approval, may subject an applicant to administrative or judicial sanctions. These sanctions could include, among other actions, the regulatory authority's refusal to approve pending applications, withdrawal of an approval, clinical holds, untitled or warning letters, voluntary product recalls or withdrawals from the market, product seizures, total or partial suspension of production or distribution injunctions, disbarment, fines, refusals of government contracts, restitution, disgorgement, or civil or criminal penalties. Any agency or judicial enforcement action could have a material adverse effect on us.

U.S. Drug Development

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and its implementing regulations. Drugs are also subject to other federal, state and local statutes and regulations. Our drug candidates must be approved by the FDA through the NDA process before they may be legally marketed in the United States. The process required by the FDA before a drug may be marketed in the United States generally involves the following:

- Completion of extensive pre-clinical, sometimes referred to as pre-clinical laboratory tests, pre-clinical animal studies and formulation studies all performed in accordance with applicable regulations, including the FDA's GLP regulations;
- Submission to the FDA of an IND, which must become effective before human clinical trials may begin and must be updated annually;
- Performance of adequate and well-controlled human clinical trials in accordance with applicable IND and other clinical trial-related regulations, sometimes referred to as good clinical practices, or GCPs, to establish the safety and efficacy of the proposed drug for its proposed indication;
- Submission to the FDA of an NDA, for a new drug;
- A determination by the FDA within 60 days of its receipt of an NDA to file the NDA for review;
- Satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities at which the API and finished drug product are produced to assess compliance with the FDA's current good manufacturing practice requirements, or cGMP;
- Potential FDA audit of the pre-clinical and/or clinical trial sites that generated the data in support of the NDA; and
- FDA review and approval of the NDA prior to any commercial marketing or sale of the drug in the United States.

The data required to support an NDA is generated in two distinct development stages: pre-clinical and clinical. For new chemical entities, the pre-clinical development stage generally involves synthesizing the active component, developing the formulation and determining the manufacturing process, as well as carrying out non-human toxicology, pharmacology and drug metabolism studies in the laboratory, which support subsequent clinical testing. The conduct of the pre-clinical tests must comply with federal regulations, including GLPs. The sponsor must submit

the results of the pre-clinical tests, together with manufacturing information, analytical data, any available clinical data or literature and a proposed clinical protocol, to the FDA as part of the IND. An IND is a request for authorization from the FDA to administer an investigational drug product to humans. The central focus of an IND submission is on the general investigational plan and the protocol(s) for human trials. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA raises concerns or questions regarding the proposed clinical trials and places the IND on clinical hold within that 30-day time period. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns or questions before the clinical trial can begin. The FDA may also impose clinical holds on a drug candidate at any time before or during clinical trials due to safety concerns or non-compliance. Accordingly, we cannot be sure that submission of an IND will result in the FDA allowing clinical trials to begin, or that, once begun, issues will not arise that could cause the trial to be suspended or terminated.

The clinical stage of development involves the administration of the drug candidate to healthy volunteers or patients under the supervision of qualified investigators, generally physicians not employed by or under the trial sponsor's control, in accordance with GCPs, which include the requirement that all research subjects provide their informed consent for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria, and the parameters to be used to monitor subject safety and assess efficacy. Each protocol, and any subsequent amendments to the protocol, must be submitted to the FDA as part of the IND. Further, each clinical trial must be reviewed and approved by an independent institutional review board, or IRB, at or servicing each institution at which the clinical trial will be conducted. An IRB is charged with protecting the welfare and rights of trial participants and considers such items as whether the risks to individuals participating in the clinical trials are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the informed consent form that must be provided to each clinical trial subject or his or her legal representative and must monitor the clinical trial until completed. There are also requirements governing the reporting of ongoing clinical trials and completed clinical trial results to public registries.

Clinical trials are generally conducted in three sequential phases that may overlap or be combined, known as Phase 1, Phase 2 and Phase 3 clinical trials. Phase 1 clinical trials generally involve a small number of healthy volunteers who are initially exposed to a single dose and then multiple doses of the drug candidate. The primary purpose of these clinical trials is to assess the metabolism, pharmacologic action, side effect tolerability and safety of the drug. Phase 2 clinical trials typically involve studies in disease-affected patients to determine the dose required to produce the desired benefits. At the same time, safety and further pharmacokinetic and pharmacodynamic information is collected, as well as identification of possible adverse effects and safety risks and preliminary evaluation of efficacy. Phase 3 clinical trials generally involve large numbers of patients at multiple sites, in multiple countries (from several hundred to several thousand subjects) and are designed to provide the data necessary to demonstrate the efficacy of the drug for its intended use, its safety in use, and to establish the overall benefit/risk relationship of the drug and provide an adequate basis for drug approval. Phase 3 clinical trials may include comparisons with placebo and/or other comparator treatments. The duration of treatment is often extended to mimic the actual use of a drug during marketing. Generally, two adequate and well-controlled Phase 3 clinical trials are required by the FDA for approval of an NDA.

A pivotal study is a clinical study that adequately meets regulatory agency requirements for the evaluation of a drug candidate's efficacy and safety such that it can be used to justify the approval of the drug. Generally, pivotal studies are also Phase 3 studies but may be Phase 2 studies if the trial design provides a well-controlled and reliable assessment of clinical benefit, particularly in situations where there is an unmet medical need. Post-approval trials, sometimes referred to as Phase 4 clinical trials, may be conducted after initial marketing approval. These trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication. In certain instances, FDA may mandate the performance of Phase 4 clinical trials.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and written IND safety reports must be submitted to the FDA and the investigators for serious and unexpected adverse reactions, any finding from other clinical studies, tests in laboratory animals, or in vitro testing that suggests a significant risk for human subjects, or any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, if at all. The FDA, the IRB, or the clinical trial sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients. Additionally, some clinical trials are overseen by an independent group of qualified experts organized by the clinical trial sponsor, known as a data safety monitoring board or committee. This group provides authorization for whether or not a trial may move forward at designated check points based on access to certain data from the trial. We may also suspend or terminate a clinical trial based on evolving business objectives and/or competitive climate. Concurrent with clinical trials, companies usually complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the drug as well as finalize a process for manufacturing the drug in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the drug candidate and, among other things, cGMPs impose extensive procedural, substantive and recordkeeping requirements to ensure and preserve the long term stability and quality of the final drug product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the drug candidate does not undergo unacceptable deterioration over its shelf life.

NDA and FDA Review Process

Following trial completion, trial data are analyzed to assess safety and efficacy. The results of pre-clinical studies and clinical trials are then submitted to the FDA as part of an NDA, along with proposed labeling for the drug and information about the manufacturing process and facilities that will be used to ensure drug quality, results of analytical testing conducted on the chemistry of the drug, and other relevant information. The NDA is a request for approval to market the drug and must contain adequate evidence of safety and efficacy, which is demonstrated by extensive pre-clinical and clinical testing. The application includes both negative or ambiguous results of pre-clinical studies and clinical trials as well as positive findings. Data may come from company- sponsored clinical trials intended to test the safety and efficacy of a use of a drug, or from a number of alternative sources, including studies initiated by investigators. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety and efficacy of the investigational drug product to the satisfaction of the FDA. The submission of an NDA is subject to the payment of substantial user fees; a waiver of such fees may be obtained under certain limited circumstances. FDA approval of an NDA must be obtained before a drug may be offered for sale in the United States.

In addition, under the Pediatric Research Equity Act, or PREA, an NDA or supplement to an NDA must contain data to assess the safety and efficacy of the drug for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the drug is safe and effective. The FDA may grant deferrals for submission of data or full or partial waivers.

Under the Prescription Drug User Fee Act, or PDUFA, as amended, each NDA must be accompanied by a user fee. The FDA adjusts the PDUFA user fees on an annual basis. According

to the FDA's fee schedule, effective through September 30, 2015, the user fee for an application requiring clinical data, such as an NDA, is $2,335,200. PDUFA also imposes an annual product fee for human drugs ($110,370) and an annual establishment fee ($569,200) on facilities used to manufacture prescription drugs. Fee waivers or reductions are available in certain circumstances, including a waiver of the application fee for the first application filed by a small business. Additionally, no user fees are assessed on NDAs for products designated as orphan drugs, unless the product also includes a non-orphan indication.

The FDA reviews all NDAs submitted before it accepts them for filing and may request additional information rather than accepting an NDA for filing. The FDA must make a decision on accepting an NDA for filing within 60 days of receipt. Once the submission is accepted for filing, the FDA begins an in-depth review of the NDA. Under the goals and policies agreed to by the FDA under PDUFA, the FDA has ten months from the filing date in which to complete its initial review of a standard NDA and respond to the applicant, and six months from the filing date for a priority NDA. The FDA does not always meet its PDUFA goal dates for standard and priority NDAs, and the review process is often significantly extended by FDA requests for additional information or clarification.

After the NDA submission is accepted for filing, the FDA reviews the NDA to determine, among other things, whether the proposed drug is safe and effective for its intended use, and whether the drug is being manufactured in accordance with cGMP to assure and preserve the drug's identity, strength, quality and purity. The FDA may refer applications for novel drugs or drug candidates 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 and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions. The FDA will likely re-analyze the clinical trial data, which could result in extensive discussions between the FDA and us during the review process. The review and evaluation of an NDA by the FDA is extensive and time consuming and may take longer than originally planned to complete, and we may not receive a timely approval, if at all.

Before approving an NDA, the FDA will conduct a pre-approval inspection of the manufacturing facilities for the new drug to determine whether they comply with cGMPs. The FDA will not approve the drug unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the drug within required specifications. In addition, before approving an NDA, the FDA may also audit data from clinical trials to ensure compliance with GCP requirements. After the FDA evaluates the application, manufacturing process and manufacturing facilities where the drug product and/or its API will be produced, it 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 indicates that the review cycle of the application is complete and the application is not ready for approval. A Complete Response Letter usually describes all of the specific deficiencies in the NDA identified by the FDA. The Complete Response Letter may require additional clinical data and/or an additional pivotal clinical trial(s), and/or other significant, expensive and time-consuming requirements related to clinical trials, pre-clinical studies or manufacturing. If a Complete Response Letter is issued, the applicant may either resubmit the NDA, addressing all of the deficiencies identified in the letter, or withdraw the application. Even if such data and information is submitted, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval. Data obtained from clinical trials are not always conclusive and the FDA may interpret data differently than we interpret the same data.

There is no assurance that the FDA will ultimately approve a drug product for marketing in the United States and we may encounter significant difficulties or costs during the review process. If a

drug receives marketing approval, the approval may be significantly limited to specific diseases and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the drug. Further, the FDA may require that certain contraindications, warnings or precautions be included in the drug labeling or may condition the approval of the NDA on other changes to the proposed labeling, development of adequate controls and specifications, or a commitment to conduct post-market testing or clinical trials and surveillance to monitor the effects of approved drugs. For example, the FDA may require Phase 4 testing which involves clinical trials designed to further assess a drug's safety and effectiveness and may require testing and surveillance programs to monitor the safety of approved drugs that have been commercialized. The FDA may also place other conditions on approvals including the requirement for a Risk Evaluation and Mitigation Strategy, or REMS to assure the safe use of the drug. If the FDA concludes a REMS is needed, the sponsor of the NDA must submit a proposed REMS. The FDA will not approve the NDA without an approved REMS, if required. A REMS could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. Any of these limitations on approval or marketing could restrict the commercial promotion, distribution, prescription or dispensing of drugs. Drug approvals may be withdrawn for non-compliance with regulatory standards or if problems occur following initial marketing.

Special FDA Expedited Review and Approval Programs

The FDA has various programs, including Fast Track Designation, accelerated approval, priority review and Breakthrough Therapy Designation, that are intended to expedite or simplify the process for the development and FDA review of drugs that are intended for the treatment of serious or life threatening diseases or conditions and demonstrate the potential to address unmet medical needs. The purpose of these programs is to provide important new drugs to patients earlier than under standard FDA review procedures. To be eligible for a Fast Track Designation, the FDA must determine, based on the request of a sponsor, that a drug is intended to treat a serious or life threatening disease or condition and demonstrates the potential to address an unmet medical need. The FDA will determine that a product will fill an unmet medical need if it will provide a therapy where none exists or provide a therapy that may be potentially superior to existing therapy based on efficacy or safety factors.

The FDA may give a priority review designation to drugs that offer major advances in treatment, or provide a treatment where no adequate therapy exists. A priority review means that the goal for the FDA to review an application is six months, rather than the standard review of ten months under current PDUFA guidelines. These six and ten month review periods are measured from the "filing" date rather than the receipt date for NDAs for new molecular entities, which typically adds approximately two months to the timeline for review and decision from the date of submission. Most products that are eligible for Fast Track Designation are also likely to be considered appropriate to receive a priority review.

In addition, drugs studied for their safety and effectiveness in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit over existing treatments may receive accelerated approval and may be approved on the basis of adequate and well-controlled clinical trials establishing that the drug has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity or prevalence of the condition and the availability or lack of alternative treatments. As a condition of approval, the FDA may require a sponsor of a drug receiving accelerated approval to perform post-marketing

studies to verify and describe the predicted effect on irreversible morbidity or mortality or other clinical endpoint, and the drug may be subject to accelerated withdrawal procedures.

Moreover, under the provisions of the new 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 drug 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 qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened. Furthermore, Fast Track Designation, priority review, accelerated approval and Breakthrough Therapy Designation, do not change the standards for approval and may not ultimately expedite the development or approval process.

Pediatric Trials

Pursuant to FDASIA, which was signed into law on July 9, 2012, a sponsor who is planning to submit a marketing application for a drug that includes a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration must submit an initial Pediatric Study Plan, or PSP, within sixty days of an end-of-Phase 2 meeting or as may be agreed between the sponsor and FDA. The initial PSP must include an outline of the pediatric study or studies that the sponsor plans to conduct, including study objectives and design, age groups, relevant endpoints and statistical approach, or a justification for not including such detailed information, and any request for a deferral of pediatric assessments or a full or partial waiver of the requirement to provide data from pediatric studies along with supporting information. FDA and the sponsor must reach agreement on the PSP. A sponsor can submit amendments to an agreed-upon initial PSP at any time if changes to the pediatric plan need to be considered based on data collected from pre-clinical studies, early phase clinical trials, and/or other clinical development programs.

Post-Marketing Requirements

Following approval of a new drug, a pharmaceutical company and the approved drug are subject to continuing regulation by the FDA, including, among other things, monitoring and recordkeeping activities, reporting to the applicable regulatory authorities of adverse experiences with the drug, providing the regulatory authorities with updated safety and efficacy information, drug sampling and distribution requirements, and complying with promotion and advertising requirements, which include, among others, standards for direct-to-consumer advertising, restrictions on promoting drugs for uses or in patient populations that are not described in the drug's approved labeling (known as "off-label use"), limitations on industry-sponsored scientific and educational activities, and requirements for promotional activities involving the internet. Although physicians may prescribe legally available drugs for off-label uses, manufacturers may not market or promote such off-label uses. Modifications or enhancements to the drug or its labeling or changes of the site of manufacture are often subject to the approval of the FDA and other regulators, which may or may not be received or may result in a lengthy review process.

Prescription drug advertising is subject to federal, state and foreign regulations. In the United States, the FDA regulates prescription drug promotion, including direct-to-consumer advertising.

Prescription drug promotional materials must be submitted to the FDA in conjunction with their first use. Any distribution of prescription drugs and pharmaceutical samples must comply with the U.S. Prescription Drug Marketing Act, or the PDMA, a part of the FDCA.

In the United States, once a drug is approved, its manufacture is subject to comprehensive and continuing regulation by the FDA. The FDA regulations require that drugs be manufactured in specific approved facilities and in accordance with cGMP. We rely, and expect to continue to rely, on third parties for the production of clinical and commercial quantities of our drugs in accordance with cGMP regulations. cGMP regulations require among other things, quality control and quality assurance as well as the corresponding maintenance of records and documentation and the obligation to investigate and correct any deviations from cGMP. Drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP and other laws. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance. These regulations also impose certain organizational, procedural and documentation requirements with respect to manufacturing and quality assurance activities. NDA holders using contract manufacturers, laboratories or packagers are responsible for the selection and monitoring of qualified firms, and, in certain circumstances, qualified suppliers to these firms. These firms and, where applicable, their suppliers are subject to inspections by the FDA at any time, and the discovery of violative conditions, including failure to conform to cGMP, could result in enforcement actions that interrupt the operation of any such facilities or the ability to distribute drugs manufactured, processed or tested by them. Discovery of problems with a drug after approval may result in restrictions on a drug, manufacturer, or holder of an approved NDA, including, among other things, recall or withdrawal of the drug from the market, and may require substantial resources to correct.

The FDA also may require post-approval testing, sometimes referred to as Phase 4 testing, risk minimization action plans and post-marketing surveillance to monitor the effects of an approved drug or place conditions on an approval that could restrict the distribution or use of the drug. Discovery of previously unknown problems with a drug or the failure to comply with applicable FDA requirements can have negative consequences, including adverse publicity, judicial or administrative enforcement, untitled or warning letters from the FDA, mandated corrective advertising or communications with doctors, and civil or criminal penalties, among others. Newly discovered or developed safety or effectiveness data may require changes to a drug's approved labeling, including the addition of new warnings and contraindications, and also may require the implementation of other risk management measures. Also, new government requirements, including those resulting from new legislation, may be established, or the FDA's policies may change, which could delay or prevent regulatory approval of our drugs under development.

Other Regulatory Matters

Manufacturing, sales, promotion and other activities following drug approval are also subject to regulation by numerous regulatory authorities in addition to the FDA, including, in the United States, the Centers for Medicare & Medicaid Services, other divisions of the Department of Health and Human Services, the Drug Enforcement Administration for controlled substances, the Consumer Product Safety Commission, the Federal Trade Commission, the Occupational Safety & Health Administration, the Environmental Protection Agency and state and local governments. In the United States, sales, marketing and scientific/educational programs must also comply with state and federal fraud and abuse laws. Pricing and rebate programs must comply with the Medicaid rebate requirements of the U.S. Omnibus Budget Reconciliation Act of 1990 and more recent requirements in the Patient Protection and Affordable Care Act as amended by the Health Care and

Education Reconciliation Act, or ACA. If drugs are made available to authorized users of the Federal Supply Schedule of the General Services Administration, additional laws and requirements apply. The handling of any controlled substances must comply with the U.S. Controlled Substances Act and Controlled Substances Import and Export Act. Drugs must meet applicable child-resistant packaging requirements under the U.S. Poison Prevention Packaging Act. Manufacturing, sales, promotion and other activities are also potentially subject to federal and state consumer protection and unfair competition laws.

The distribution of pharmaceutical drugs is subject to additional requirements and regulations, including extensive record-keeping, licensing, storage and security requirements intended to prevent the unauthorized sale of pharmaceutical drugs.

The failure to comply with regulatory requirements subjects firms to possible legal or regulatory action. Depending on the circumstances, failure to meet applicable regulatory requirements can result in criminal prosecution, fines or other penalties, injunctions, recall or seizure of drugs, total or partial suspension of production, denial or withdrawal of product approvals, or refusal to allow a firm to enter into supply contracts, including government contracts. In addition, even if a firm complies with FDA and other requirements, new information regarding the safety or efficacy of a product could lead the FDA to modify or withdraw product approval. Prohibitions or restrictions on sales or withdrawal of future products marketed by us could materially affect our business in an adverse way.

Changes in regulations, statutes or the interpretation of existing regulations could impact our business in the future by requiring, for example: (i) changes to our manufacturing arrangements; (ii) additions or modifications to product labeling; (iii) the recall or discontinuation of our products; or (iv) additional record-keeping requirements. If any such changes were to be imposed, they could adversely affect the operation of our business.

U.S. Patent Term Restoration and Marketing Exclusivity

Depending upon the timing, duration and specifics of the FDA approval of our drug candidates, some of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, commonly referred to as the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date. The patent term restoration period is generally one-half the time between the effective date of an IND and the submission date of an NDA plus the time between the submission date of an NDA and the approval of that application. Only one patent applicable to an approved drug is eligible for the extension and the application for the extension must be submitted prior to the expiration of the patent. The USPTO, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. In the future, we intend to apply for restoration of patent term for one of our currently owned or licensed patents to add patent life beyond its current expiration date, depending on the expected length of the clinical trials and other factors involved in the filing of the relevant NDA.

Marketing exclusivity provisions under the FDCA can also delay the submission or the approval of certain marketing applications. The FDCA provides a five-year period of non-patent marketing exclusivity within the United States to the first applicant to obtain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not accept for review an abbreviated new drug application, or ANDA, or a 505(b)(2) NDA submitted by another company for

another drug based on the same active moiety, regardless of whether the drug is intended for the same indication as the original innovator drug or for another indication, where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement to one of the patents listed with the FDA by the innovator NDA holder. The FDCA also provides three years of marketing exclusivity for an NDA, or supplement to an existing NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example new indications, dosages or strengths of an existing drug. This three-year exclusivity covers only the modification for which the drug received approval on the basis of the new clinical investigations and does not prohibit the FDA from approving ANDAs for drugs containing the active agent for the original indication or condition of use. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the pre-clinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness. Orphan drug exclusivity, as described below, may offer a seven-year period of marketing exclusivity, except in certain circumstances. Pediatric exclusivity is another type of regulatory market exclusivity in the United States. Pediatric exclusivity, if granted, adds six months to existing exclusivity periods and patent terms. This six-month exclusivity, which runs from the end of other exclusivity protection or patent term, may be granted based on the voluntary completion of a pediatric trial in accordance with an FDA-issued "Written Request" for such a trial.

Orphan Drug Designation

The FDA may grant Orphan Drug Designation to drugs intended to treat a rare disease or condition that affects fewer than 200,000 individuals in the United States, or if it affects more than 200,000 individuals in the United States, there is no reasonable expectation that the cost of developing and marketing the drug for this type of disease or condition will be recovered from sales in the United States. In the European Union, the European Commission, after receiving the opinion of the EMA's Committee for Orphan Medicinal Products, or COMP, grants Orphan Drug Designation to promote the development of products that are intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating conditions affecting not more than five in 10,000 persons in the European Union Community. Additionally, designation is granted for products intended for the diagnosis, prevention or treatment of a life-threatening, seriously debilitating or serious and chronic condition and when, without incentives, it is unlikely that sales of the drug in the European Union would be sufficient to justify the necessary investment in developing the drug or biological product.

In the United States, Orphan Drug Designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers. In addition, if a product receives the first FDA approval for the indication for which it has orphan designation, the product is entitled to orphan drug exclusivity, which means the FDA may not approve any other application to market the same drug for the same indication for a period of seven years, except in limited circumstances, such as a showing of clinical superiority over the product with orphan exclusivity.

In the European Union, Orphan Drug Designation also entitles a party to financial incentives such as reduction of fees or fee waivers and ten years of market exclusivity is granted following drug or biological product approval. This period may be reduced to six years if the Orphan Drug Designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity.

Orphan drug designation must be requested before submitting an application for marketing approval. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

Regulation of Diagnostic Tests

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

PMA applications must be supported by valid scientific evidence, which typically requires extensive data, including technical, preclinical, clinical and manufacturing data, to demonstrate to the FDA's satisfaction the safety and effectiveness of the device. For diagnostic tests, a PMA application typically includes data regarding analytical and clinical validation studies. As part of its review of the PMA, the FDA will conduct a pre-approval inspection of the manufacturing facility or facilities to ensure compliance with the Quality System Regulation, or QSR, which requires manufacturers to follow design, testing, control, documentation and other quality assurance procedures. FDA review of an initial PMA may require several years to complete. If the FDA evaluations of both the PMA application and the manufacturing facilities are favorable, the FDA will either issue an approval letter or an approvable letter, which usually contains a number of conditions that must be met in order to secure the final approval of the PMA. If the FDA's evaluation of the PMA or manufacturing facilities is not favorable, the FDA will deny approval of the PMA or issue a not approvable letter. A not approvable letter will outline the deficiencies in the application and, where practical, will identify what is necessary to make the PMA approvable. The FDA may also determine that additional clinical trials are necessary, in which case the PMA approval may be delayed for several months or years while the trials are conducted and then the data submitted in an amendment to the PMA. Once granted, PMA approval may be withdrawn by the FDA if compliance with post approval requirements, conditions of approval or other regulatory standards is not maintained or problems are identified following initial marketing.

On August 6, 2014, the FDA issued a final guidance document addressing the development and approval process for "In Vitro Companion Diagnostic Devices." According to the guidance, for novel drugs such as our drug candidates, a companion diagnostic device and its corresponding drug should be approved or cleared contemporaneously by FDA for the use indicated in the therapeutic product labeling. The guidance also explains that a companion diagnostic device used to make treatment decisions in clinical trials of a drug generally will be considered an investigational device, unless it is employed for an intended use for which the device is already approved or cleared. If used to make critical treatment decisions, such as patient selection, the diagnostic device generally will be considered a significant risk device under the FDA's Investigational Device Exemption, or IDE, regulations. Thus, the sponsor of the diagnostic device will be required to comply with the IDE regulations. According to the guidance, if a diagnostic device and a drug are to be studied together to support their respective approvals, both products

can be studied in the same investigational study, if the study meets both the requirements of the IDE regulations and the IND regulations. The guidance provides that depending on the details of the study plan and subjects, a sponsor may seek to submit an IND alone, or both an IND and an IDE.

In the EEA, in vitro medical devices are required to conform with the essential requirements of the E.U. Directive on in vitro diagnostic medical devices (Directive No 98/79/EC, as amended). To demonstrate compliance with the essential requirements, the manufacturer must undergo a conformity assessment procedure. The conformity assessment varies according to the type of medical device and its classification. For low-risk devices, the conformity assessment can be carried out internally, but for higher risk devices it requires the intervention of an accredited EEA Notified Body. If successful, the conformity assessment concludes with the drawing up by the manufacturer of an EC Declaration of Conformity entitling the manufacturer to affix the CE mark to its products and to sell them throughout the EEA.

European Drug Development

In Europe, our future drugs may also be subject to extensive regulatory requirements. As in the United States, medicinal products can only be marketed if a marketing authorization from the competent regulatory agencies has been obtained.

Similar to the United States, the various phases of pre-clinical and clinical research in Europe are subject to significant regulatory controls. Although the EU Clinical Trials Directive 2001/20/EC has sought to harmonize the European Union clinical trials regulatory framework, setting out common rules for the control and authorization of clinical trials in the European Union, the European Union Member States have transposed and applied the provisions of the Directive differently. This has led to significant variations in the member state regimes. Under the current regime, before a clinical trial can be initiated it must be approved in each of the European Union countries where the trial is to be conducted by two distinct bodies: the National Competent Authority, or NCA, and one or more Ethics Committees, or ECs. Under the current regime all suspected unexpected serious adverse reactions to the investigated drug that occur during the clinical trial have to be reported to the NCA and ECs of the Member State where they occurred.

The European Union clinical trials legislation is currently undergoing a revision process mainly aimed at uniforming and streamlining the clinical trials authorization process, simplifying adverse event reporting procedures, improving the supervision of clinical trials, and increasing their transparency.

European Drug Review and Approval

In the European Economic Area, or EEA, (which is comprised of the 27 Member States of the European Union (excluding Croatia) plus Norway, Iceland and Liechtenstein), medicinal products can only be commercialized after obtaining a Marketing Authorization, or MA. There are two types of marketing authorizations:

The Community MA, which is issued by the European Commission through the Centralized Procedure, based on the opinion of the Committee for Medicinal Products for Human Use, or CHMP, of the EMA and which is valid throughout the entire territory of the EEA. The Centralized Procedure is mandatory for certain types of drugs, such as biotechnology medicinal drugs, orphan medicinal drugs, and medicinal drugs containing a new active substance indicated for the treatment of AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune and viral diseases. The Centralized Procedure is optional for drugs containing a new active substance not yet authorized in the EEA, or for drugs that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the European Union.

National MAs, which are issued by the competent authorities of the Member States of the EEA and only cover their respective territory, are available for drugs not falling within the mandatory scope of the Centralized Procedure. Where a drug has already been authorized for marketing in a Member State of the EEA, this National MA can be recognized in another Member States through the Mutual Recognition Procedure. If the drug has not received a National MA in any Member State at the time of application, it can be approved simultaneously in various Member States through the Decentralized Procedure. Under the Decentralized Procedure an identical dossier is submitted to the competent authorities of each of the Member States in which the MA is sought, one of which is selected by the applicant as the Reference Member State, or RMS. The competent authority of the RMS prepares a draft assessment report, a draft summary of the drug characteristics, or SPC, and a draft of the labeling and package leaflet, which are sent to the other Member States (referred to as the Member States Concerned) for their approval. If the Member States Concerned raise no objections, based on a potential serious risk to public health, to the assessment, SPC, labeling, or packaging proposed by the RMS, the drug is subsequently granted a national MA in all the Member States (i.e. in the RMS and the Member States Concerned).

Under the above described procedures, before granting the MA, the EMA or the competent authorities of the Member States of the EEA make an assessment of the risk-benefit balance of the drug on the basis of scientific criteria concerning its quality, safety and efficacy.

European Chemical Entity Exclusivity

In Europe, new chemical entities, sometimes referred to as new active substances, qualify for eight years of data exclusivity upon marketing authorization and an additional two years of market exclusivity. This data exclusivity, if granted, prevents regulatory authorities in the European Union from referencing the innovator's data to assess a generic application for eight years, after which generic marketing authorization can be submitted, and the innovator's data may be referenced, but not approved for two years. The overall ten-year period will be extended to a maximum of 11 years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies.

Rest of the World Regulation

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

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

Coverage and Reimbursement

Sales of our drugs will depend, in part, on the extent to which our drugs will be covered by third-party payors, such as government health programs, commercial insurance and managed healthcare organizations. These third-party payors are increasingly reducing reimbursements for medical drugs and services. Additionally, the containment of healthcare costs has become a priority of federal and state governments, and the prices of drugs have been a focus in this effort. The U.S. government, state legislatures and foreign governments have shown significant interest in

implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic drugs. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit our net revenue and results. Decreases in third-party reimbursement for our drug candidates, if approved, or a decision by a third-party payor to not cover our drug candidates could reduce physician usage of such drugs and have a material adverse effect on our sales, results of operations and financial condition.

The Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or the MMA, established the Medicare Part D program to provide a voluntary prescription drug benefit to Medicare beneficiaries. Under Part D, Medicare beneficiaries may enroll in prescription drug plans offered by private entities that provide coverage of outpatient prescription drugs. Unlike Medicare Part A and B, Part D coverage is not standardized. Part D prescription drug plan sponsors are not required to pay for all covered Part D drugs, and each drug plan can develop its own drug formulary that identifies which drugs it will cover and at what tier or level. However, Part D prescription drug formularies must include drugs within each therapeutic category and class of covered Part D drugs, though not necessarily all the drugs in each category or class. Any formulary used by a Part D prescription drug plan must be developed and reviewed by a pharmacy and therapeutic committee. Government payment for some of the costs of prescription drugs may increase demand for drugs for which we receive marketing approval. However, any negotiated prices for our drugs covered by a Part D prescription drug plan will likely be lower than the prices we might otherwise obtain. Moreover, while the MMA applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own payment rates. Any reduction in payment that results from the MMA may result in a similar reduction in payments from non-governmental payors.

The American Recovery and Reinvestment Act of 2009 provides funding for the federal government to compare the effectiveness of different treatments for the same illness. The plan for the research was published in 2012 by the Department of Health and Human Services, the Agency for Healthcare Research and Quality and the National Institutes for Health, and periodic reports on the status of the research and related expenditures will be made to Congress. Although the results of the comparative effectiveness studies are not intended to mandate coverage policies for public or private payors, it is not clear what effect, if any, the research will have on the sales of our drug candidates, if any such drug or the condition that they are intended to treat are the subject of a trial. It is also possible that comparative effectiveness research demonstrating benefits in a competitor's drug could adversely affect the sales of our drug candidate. If third-party payors do not consider our drugs to be cost-effective compared to other available therapies, they may not cover our drugs after approval as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow us to sell our drugs on a profitable basis.

The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively the ACA, enacted in March 2010, has had a significant impact on the health care industry. The ACA expanded coverage for the uninsured while at the same time containing overall healthcare costs. With regard to pharmaceutical products, the ACA, among other things, addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected, increased the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extended the rebate program to individuals enrolled in Medicaid managed care organizations, established annual fees and taxes on manufacturers of certain branded prescription drugs, and a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts off negotiated prices of

applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D.

In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted. On August 2, 2011, the Budget Control Act of 2011 among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, started in April 2013, and, due to subsequent legislative amendments, will stay in effect through 2024 unless additional Congressional action is taken. On January 2, 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, or the ATRA, which among other things, also reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. We expect that additional federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare drugs and services, and in turn could significantly reduce the projected value of certain development projects and reduce our profitability.

In addition, in some foreign countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. For example, the European Union provides options for its member states to restrict the range of medicinal drugs for which their national health insurance systems provide reimbursement and to control the prices of medicinal drugs for human use. A member state may approve a specific price for the medicinal drug or it may instead adopt a system of direct or indirect controls on the profitability of the Company placing the medicinal drug on the market. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical drugs will allow favorable reimbursement and pricing arrangements for any of our drugs. Historically, drugs launched in the European Union do not follow price structures of the United States and generally tend to be significantly lower.

Other Healthcare Laws

We may also be subject to healthcare regulation and enforcement by the federal government and the states and foreign governments where we may market our product candidates, if approved. These laws include, without limitation, state and federal anti-kickback, fraud and abuse, false claims, privacy and security and physician sunshine laws and regulations.

The federal Anti-Kickback Statute prohibits, among other things, any person from knowingly and willfully offering, soliciting, receiving or providing remuneration, directly or indirectly, to induce either the referral of an individual, for an item or service or the purchasing or ordering of a good or service, for which payment may be made under federal healthcare programs such as the Medicare and Medicaid programs. The Anti-Kickback Statute is subject to evolving interpretations. In the past, the government has enforced the Anti-Kickback Statute to reach large settlements with healthcare companies based on sham consulting and other financial arrangements with physicians. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal False Claims Act. The majority of states also have anti-kickback laws, which establish similar prohibitions and in some cases may apply to items or services reimbursed by any third-party payor, including commercial insurers.

Additionally, the civil False Claims Act prohibits knowingly presenting or causing the presentation of a false, fictitious or fraudulent claim for payment to the U.S. government. Actions under the False Claims Act may be brought by the Attorney General or as a qui tam action by a private individual in the name of the government. Violations of the False Claims Act can result in very significant monetary penalties and treble damages. The federal government is using the False Claims Act, and the accompanying threat of significant liability, in its investigation and prosecution of pharmaceutical and biotechnology companies throughout the U.S., for example, in connection with the promotion of products for unapproved uses and other sales and marketing practices. The government has obtained multi-million and multi-billion dollar settlements under the False Claims Act in addition to individual criminal convictions under applicable criminal statutes. Given the significant size of actual and potential settlements, it is expected that the government will continue to devote substantial resources to investigating healthcare providers' and manufacturers' compliance with applicable fraud and abuse laws.

The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, also created new federal criminal statutes that prohibit among other actions, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private third-party payors, knowingly and willfully embezzling or stealing from a healthcare benefit program, willfully obstructing a criminal investigation of a healthcare offense, and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.

There has also been a recent trend of increased federal and state regulation of payments made to physicians and other healthcare providers. The ACA, among other things, imposes new reporting requirements on drug manufacturers for payments made by them to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Failure to submit required information may result in civil monetary penalties of up to an aggregate of $150,000 per year (or up to an aggregate of $1 million per year for "knowing failures"), for all payments, transfers of value or ownership or investment interests that are not timely, accurately and completely reported in an annual submission. Drug manufacturers were required to begin collecting data on August 1, 2013 and submit reports to the government by March 31, 2014 and June 30, 2014, and the 90th day of each subsequent calendar year. Certain states also mandate implementation of compliance programs, impose restrictions on drug manufacturer marketing practices and/or require the tracking and reporting of gifts, compensation and other remuneration to physicians.

We may also be subject to data privacy and security regulation by both the federal government and the states in which we conduct our business. HIPAA, as amended by the Health Information Technology and Clinical Health Act, or HITECH, and their respective implementing regulations, including the final omnibus rule published on January 25, 2013, imposes specified requirements relating to the privacy, security and transmission of individually identifiable health information. Among other things, HITECH makes HIPAA's privacy and security standards directly applicable to "business associates," defined as independent contractors or agents of covered entities that create, receive, maintain or transmit protected health information in connection with providing a service for or on behalf of a covered entity. HITECH also increased the civil and criminal penalties that may be imposed against covered entities, business associates and possibly other persons, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorney's fees and costs associated with pursuing federal civil actions. In addition, state laws govern the privacy and security

of health information in certain circumstances, many of which differ from each other in significant ways, thus complicating compliance efforts.

Employees

As of March 31, 2015, we had 60 full-time employees, including 30 employees with M.D. or Ph.D. degrees. Of these full-time employees, 48 employees are engaged in research and development activities and 12 are engaged in general and administrative activities. None of our employees is represented by a labor union or covered by a collective bargaining agreement. We consider our relationship with our employees to be good.

Facilities

We occupy approximately 20,000 rentable square feet of office and laboratory space in Cambridge, Massachusetts under a lease that expires on October 31, 2015.

On February 12, 2015, we entered into a lease for approximately 38,500 rentable square feet of office and laboratory space in Cambridge, Massachusetts, with a lease term commencing June 15, 2015 and ending on October 31, 2022, assuming occupancy in October 2015. We have an option to extend the lease term for five additional years. We believe that this new office and laboratory space is sufficient to meet our needs for the foreseeable future and that suitable additional space will be available as and when needed.

Legal Proceedings

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

MANAGEMENT

Executive Officers and Directors

The following table sets forth information regarding our executive officers and directors as of the date hereof:

Name	Age	Position(s)
Executive Officers:		
Jeffrey W. Albers	43	President, Chief Executive Officer and Director
Anthony L. Boral, M.D., Ph.D.	52	Senior Vice President, Clinical Development
Kyle D. Kuvalanka	46	Chief Business Officer
Christoph Lengauer, Ph.D.	50	Chief Scientific Officer
Directors:		
Daniel S. Lynch(1)(2)	56	Chairman
Alexis Borisy(3)(4)	43	Director
George D. Demetri, M.D.(1)(2)(3)(4)	58	Director
Stephen C. Knight, M.D.(5)	55	Director
Nicholas Lydon, Ph.D.(4)	58	Director
Charles A. Rowland, Jr., MBA(1)(2)(3)	56	Director
Thilo Schroeder, Ph.D.(5)	33	Director

(1) Member of the audit committee.
(2) Member of the compensation committee.
(3) Member of the nominating and corporate governance committee.
(4) Member of the research and development committee.
(5) Each of Drs. Knight and Schroeder resigned from our board of directors immediately prior to the declaration of effectiveness of the registration statement of which this prospectus forms a part.

Executive Officers

Jeffrey W. Albers has served as our Chief Executive Officer and President and a member of our board of directors since July 2014. Mr. Albers has nearly a decade of experience in leadership roles in the biopharmaceutical industry. Prior to joining us, from January 2012 to April 2014, he was president of the U.S. subsidiary of Algeta ASA, or Algeta U.S., a Norwegian biopharmaceutical company, where he oversaw the commercial and business functions. At Algeta U.S., Mr. Albers was responsible for the U.S. launch of Radium-223 in metastatic castrate resistant prostate cancer. Prior to Algeta U.S., from July 2005 to November 2011, Mr. Albers was at Genzyme Corporation, or Genzyme, a biotechnology company which is now a wholly-owned subsidiary of Sanofi S.A., most recently as vice president of the U.S. hematology and oncology business unit. Mr. Albers received his B.S. from Indiana University and an M.B.A. and a J.D. from Georgetown University. We believe that Mr. Albers' leadership in the life sciences industry qualifies him to serve on our board of directors.

Anthony L. Boral, M.D., Ph.D. has served as our Senior Vice President, Clinical Development since February 2015. Prior to joining us, from November 2010 to February 2015 Dr. Boral worked at the Novartis Institutes for BioMedical Research, or Novartis, as Executive Director, Oncology Clinical Research, serving as Deputy Site Head for the Cambridge, Massachusetts site since 2013. At Novartis Dr. Boral was responsible for the clinical aspects of various first-in-human compounds, including most recently ceritinib, an anaplastic lymphoma kinase inhibitor, and Novartis' immune checkpoint inhibitor programs. Prior to Novartis, from 2002 to 2010 he worked at Millennium

Pharmaceuticals, Inc., or Millennium, a biotechnology company in Cambridge, Massachusetts, which is now a wholly-owned subsidiary of Takeda Pharmaceutical Company Limited, or Takeda, including as Vice President of Oncology Clinical Research from October 2007 to October 2010. At Millennium, Dr. Boral was responsible for various aspects of the development of VELCADE®, a first-in-class cancer therapy now approved to treat multiple myeloma and non-Hodgkins lymphoma. Dr. Boral received his B.A. from Wesleyan University, and an M.D. and a Ph.D. from the Albert Einstein College of Medicine, in New York.

Kyle D. Kuvalanka has served as our Chief Business Officer since September 2013. Mr. Kuvalanka has more than 15 years of business and strategy experience in the biopharmaceutical industry. Prior to joining us, from March 2002 to September 2013, Mr. Kuvalanka worked at Takeda and Millennium, prior to its takeover by Takeda, including as Vice President, Corporate Strategy and Development from 2009 to 2012 and as Vice President, Business Development, Corporate Strategy and Alliance Management from 2012 to 2013. Earlier in his career at Millennium, Mr. Kuvalanka held leadership positions in finance and led the investor relations effort until the company's acquisition by Takeda. Mr. Kuvalanka holds a B.A. from Wesleyan University and an M.B.A. from The Wharton Business School at the University of Pennsylvania.

Christoph Lengauer, Ph.D. has served as our Chief Scientific Officer since January 2012. Prior to joining us, Dr. Lengauer was Vice President and Global Head of Oncology Drug Discovery and Pre-Clinical Development at Sanofi S.A., a multinational pharmaceutical company, from May 2008 to January 2012. Dr. Lengauer has served as an adjunct associate professor of oncology at the Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins University since 2005. Dr. Lengauer received an M.Sc. from the University of Salzburg, Austria, a Ph.D. in biology from the University of Heidelberg, Germany, and an M.B.A. in medical services management from The Johns Hopkins University.

Non-Management Directors

Daniel S. Lynch has served as Chairman of our board of directors since September 2012. Mr. Lynch has served as a venture partner at Third Rock Ventures, or Third Rock, a life sciences venture capital firm focused on the formation, development and strategy of new companies, since May 2013 and as an entrepreneur-in-residence from May 2011 to May 2013. Since 2005, Mr. Lynch has served on the boards of directors of several life sciences companies, including on the board of directors of BIND Therapeutics, Inc. since 2012, on the board of directors of bluebird bio, Inc. since 2011, and on the board of directors of U.S. Oncology, Inc. from 2005 to 2010. Prior to that, Mr. Lynch served as the Chief Financial Officer and then the Chief Executive Officer of ImClone Systems Inc. Mr. Lynch received a B.A. in mathematics from Wesleyan University and an M.B.A. from the Darden Graduate School of Business Administration at the University of Virginia. We believe that Mr. Lynch's experience as a senior executive and service on the boards of directors of other life sciences companies qualifies him to serve as a member of our board of directors.

Alexis Borisy has served as a member of our board of directors since April 2011. Mr. Borisy co-founded Blueprint Medicines and served as our interim Chief Executive Officer from May 2013 through July 2014. Since 2010, Mr. Borisy has been a partner at Third Rock. In addition, since 2011, Mr. Borisy has served as executive chairman of Warp Drive Bio, LLC, a life sciences company focusing on genomics where he served as chief executive officer from 2011 to July 2013. From 2007 to 2012, Mr. Borisy served as chairman of FORMA Therapeutics, Inc., a biopharmaceutical company focused on discovering and developing medicines in cancer and other genetically-driven diseases. Mr. Borisy co-founded Foundation Medicine, Inc. and served as its interim Chief Executive Officer from 2009 to 2011. Mr. Borisy holds an A.B. in chemistry from the University of Chicago, and an A.M. from Harvard University. We believe Mr. Borisy's detailed knowledge of our company and long tenure with us, having served as one of our founders, along with his experience working with

and serving on the boards of directors of life sciences companies and his experience working in the venture capital industry qualifies him to serve on our board of directors.

George D. Demetri, M.D. has served as a member of our board of directors since December 2014. Since 1988, he has served as a Professor of Medicine at Harvard Medical School and as an academic medical oncologist at the Dana-Farber Cancer Institute, or Dana-Farber, and Harvard Medical School. Dr. Demetri's research and clinical interests have centered on mechanism-based drug development for solid tumors, with a particular emphasis on molecularly-defined subsets of sarcomas such as gastrointestinal stromal tumours. Dr. Demetri has contributed to the development of several new drugs for sarcomas and other malignancies, including imatinib, sunitinib, dasatinib, trabectedin, vemurafenib, everolimus, pazopanib and regorafenib. Dr. Demetri serves as chair of the medical advisory board for the Sarcoma Foundation of America as well as several scientific and editorial advisory boards. With an interest in internet-based patient support, he also serves on the Medical Advisory Board of ASCO's CancerNet as well as CancerCommons.org. He received an A.B. in biochemistry from Harvard College and his M.D. from Stanford University School of Medicine. We believe that Dr. Demetri's more than 25 years of experience as an oncologist and his significant leadership experience on various scientific and editorial advisory boards qualifies him to serve as a member of our board of directors.

Stephen C. Knight, M.D. has served as a member of our board of directors since March 2012. Dr. Knight is currently the president and managing partner of Fidelity Biosciences Corp., or Fidelity, a healthcare venture firm owned by Fidelity Investments, which he joined in 2003. Prior to joining Fidelity in 2003, Dr. Knight was president and chief operating officer for EPIX Pharmaceuticals, Inc. in Cambridge, Massachusetts. Dr. Knight currently serves as chairman of the board of directors for FORUM Pharmaceuticals, Inc., a biopharmaceutical company based in Watertown, Massachusetts. Dr. Knight previously served on the boards of several public healthcare companies including FoldRx Pharmaceuticals, Inc., now a wholly-owned subsidiary of Pfizer Inc., Ironwood Pharmaceuticals, Inc. and Respivert, Ltd., which was acquired by Centocor Ortho Biotech Inc., a division of Johnson & Johnson. Dr. Knight holds an M.D. from the Yale University School of Medicine, an M.B.A. from the Yale School of Organization and Management, and a B.S. in biology from Columbia University. We believe that Dr. Knight's detailed knowledge of the life sciences industry and substantial experience as member of the board of directors of numerous other life sciences companies qualifies him to serve on our board of directors. Dr. Knight resigned from our board of directors immediately prior to the declaration of effectiveness of the registration statement of which this prospectus forms a part.

Nicholas Lydon, Ph.D. has served as a member of our board of directors since April 2011. He is a scientific founder of Blueprint Medicines. Since 2006, Dr. Lydon has served as a scientific advisor and member of the board of directors of AnaptysBio Inc., a company he co-founded. From 2003 to 2011, Dr. Lydon served as a scientific advisor and member of the board of directors of Ambit Biosciences Corp., a biopharmaceutical company. From 2000 to 2002, Dr. Lydon served as vice president, small molecule drug discovery at Amgen, Inc., or Amgen. Prior to joining Amgen, in 1997 Dr. Lydon founded Kinetix Pharmaceuticals, Inc., or Kinetix, a biotechnology company focused on the discovery and development of selective protein kinase inhibitors, which was acquired by Amgen in 2000, and served as its chief executive officer and on its board of directors. Dr. Lydon earned a B.S. in biochemistry and zoology from the University of Leeds, England, and received his Ph.D. in biochemistry from the Medical Sciences Institute, University of Dundee, Scotland. We believe Dr. Lydon's detailed knowledge of our company and long tenure with us, having served as one of our scientific founders, along with his experience working with and serving on the boards of directors of life sciences companies and his experience as a senior executive with several life sciences companies qualifies him to serve on our board of directors.

Charles A. Rowland, Jr., MBA has served as a member of our board of directors since March 2015. Mr. Rowland was the Vice President and Chief Financial Officer of ViroPharma Incorporated, or ViroPharma, an international biopharmaceutical company, from October 2008 until it was acquired by Shire plc in January 2014. Prior to joining ViroPharma, Mr. Rowland was the Executive Vice President and Chief Financial Officer, as well as the interim Co-Chief Executive Officer, for Endo Pharmaceuticals Inc., a specialty pharmaceutical company with a primary focus in pain management, where he served from 2006 to 2008. Mr. Rowland previously held positions of increasing responsibility at Biovail Corporation, Breakaway Technologies, Inc., Pharmacia Corporation, Novartis AG and Bristol-Myers Squibb Co., each a biopharmaceutical company. Mr. Rowland joined the board of directors of Idenix Pharmaceuticals, Inc., a biopharmaceutical company, in June 2013 and served as a member of its audit committee until Idenix was acquired by Merck & Co., Inc. in August 2014. He is a member of the board of directors and chairs the audit committee of Bind Therapeutics, Inc. as of May 2014, Aurinia Pharmaceuticals Inc. as of July 2014 and Vitae Pharmaceuticals, Inc. as of September 2014, each a biotechnology company. Since January 2015, he has served as a member of the supervisory board and chair of the audit committee of Nabriva Therapeutics, AG, a biotechnology company based in Vienna Austria. He is also a member of the board of the Philadelphia chapter of Financial Executives International. Mr. Rowland holds an M.B.A. with a finance concentration from Rutgers University and a B.S. in Accounting from Saint Joseph's University. We believe that Mr. Rowland's extensive professional experience as a chief financial executive in the biotechnology and pharmaceutical industries and his experience serving as a director of various publicly traded biotechnology companies qualifies him to serve as a member of our board of directors.

Thilo Schroeder, Ph.D. has served as a member of our board of directors since January 2014. Since 2013, he has served as a partner at Nextech Invest Ltd., or Nextech, a global venture fund, focused on investing in oncology companies. Prior to joining Nextech, from 2007 to 2013, Dr. Schroeder was president of SiROP Global, a web based technology company that connects universities in Europe and world-wide. Dr. Schroeder served as an observer of the board of Tracon Pharmaceuticals, a biopharmaceutical company from December 2012 to January 2014. He received a B.Sc. in biology from the Technical University of Darmstadt in Germany, an M.Sc. in biotechnology from the Ecole Supérieure de Biotechnologie de Strasbourg in France, and a Ph.D. in biochemistry from the University of Zurich in Switzerland. We believe that Dr. Schroeder's extensive experience working with various life sciences companies as an executive and a member of the board of directors qualifies him to serve as a member of our board of directors. Dr. Schroeder resigned from our board of directors immediately prior to the effectiveness of the registration statement of which this prospectus forms a part.

Board Composition

As of the date hereof, our board of directors consisted of eight members, and we anticipate that it will consist of six members upon the effectiveness of the registration statement of which this prospectus forms a part. Currently, each of our directors are members pursuant to the board composition provisions of our existing certificate of incorporation and Second Amended and Restated Stockholders Agreement, dated November 7, 2014, which agreement is described under "Certain Relationships and Related Party Transactions" in this prospectus. These board composition provisions will terminate upon the completion of this offering. Upon the termination of these provisions, there will be no further contractual obligations regarding the election of our directors. Our nominating and corporate governance committee and our board of directors may therefore consider a broad range of factors relating to the qualifications and background of nominees, which may include diversity, which is not only limited to race, gender or national origin. We have no formal policy regarding board diversity. Our nominating and corporate governance committee's and our board of directors' priority in selecting board members is identification of

persons who will further the interests of our stockholders through his or her established record of professional accomplishment, the ability to contribute positively to the collaborative culture among board members, knowledge of our business, understanding of the competitive landscape and professional and personal experiences and expertise relevant to our growth strategy. Our directors hold office until their successors have been elected and qualified or until the earlier of their death, resignation or removal. Our amended and restated certificate of incorporation and amended and restated bylaws that will become effective upon the completion of this offering also provide that our directors may be removed only for cause by the affirmative vote of the holders of at least 75% of the votes that all our stockholders would be entitled to cast in an annual election of directors, and that any vacancy on our board of directors, including a vacancy resulting from an enlargement of our board of directors, may be filled only by vote of a majority of our directors then in office.

Director Independence. Our board of directors currently consists of six members. Our board of directors has determined that two of our six directors, Dr. Demetri and Mr. Rowland, are independent directors, including for purposes of the rules of The NASDAQ Stock Market and relevant federal securities laws and regulations. Pursuant to The NASDAQ Stock Market rules, within a year of the effectiveness of the registration statement of which this prospectus is a part, our board must consist of a majority of independent directors. We intend to be in compliance with these rules within a year of the effectiveness of the registration statement of which this prospectus is a part. The NASDAQ Stock Market independence definition includes a series of objective tests, including that a director is not, and has not been for at least three years, one of our employees and that neither a director nor any of his family members has engaged in various types of business dealings with us. In addition, as required by The NASDAQ Stock Market rules, our board of directors has made a subjective determination as to each independent director that no relationships exist, which, in the opinion of our board of directors, would interfere with the exercise of independent judgment in carrying out the responsibilities of a director. In making these determinations, our board of directors reviewed and discussed information provided by the directors and us with regard to each director's business and personal activities and relationships as they may relate to us and our management. There are no family relationships among any of our directors or executive officers.

Staggered Board. In accordance with the terms of our amended and restated certificate of incorporation and amended and restated bylaws that will become effective upon the completion of this offering, our board of directors will be divided into three staggered classes of directors of the same or nearly the same number and each will be assigned to one of the three classes. Each of Drs. Knight and Schroeder will resign from our board of directors upon the declaration of effectiveness of the registration statement of which this prospectus forms a part. At each annual meeting of the stockholders, a class of directors will be elected for a three-year term to succeed the directors of the same class whose terms are then expiring. The terms of the directors will expire upon the election and qualification of successor directors at the annual meeting of stockholders to be held during the years 2016 for Class I directors, 2017 for Class II directors and 2018 for Class III directors:

- Our Class I directors will be Jeffrey W. Albers and Nicholas Lydon;
- Our Class II directors will be Alexis Borisy and Charles A. Rowland, Jr.; and
- Our Class III directors will be Daniel S. Lynch and George D. Demetri.

Our amended and restated certificate of incorporation and amended and restated by-laws provide that the number of our directors shall be fixed from time to time by a resolution of the majority of our board of directors. 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 shall consist of one third of the board of directors.

The division of our board of directors into three classes with staggered three-year terms may delay or prevent stockholder efforts to effect a change of our management or a change in control.

Board Committees

Our board of directors plans on establishing four standing committees: an audit committee, a compensation committee, a nominating and corporate governance committee and a research and development committee, each of which will operate pursuant to a charter to be adopted by our board of directors and will be effective upon completion of the offering. Upon the completion of this offering, the composition and functioning of all of our committees will comply with all applicable requirements of the Sarbanes-Oxley Act of 2002, The NASDAQ Stock Market and SEC rules and regulations.

Audit Committee

Effective upon completion of this offering, our audit committee will be comprised of Charles A. Rowland, Jr., George D. Demetri and Daniel S. Lynch, with Charles A. Rowland, Jr. serving as chairman of the committee. Our board of directors has determined that Charles A. Rowland, Jr. and George D. Demetri meet the independence requirements of Rule 10A-3 under the Exchange Act and the applicable NASDAQ Stock Market rules, and have sufficient knowledge in financial and auditing matters to serve on the audit committee. The composition of our audit committee meets the requirements for independence under the listing standards of The NASDAQ Stock Market and the applicable rules of the SEC, including the applicable transition rules. Our board of directors intends to cause our audit committee to be comprised of only directors that are independent under the rules of both The NASDAQ Stock Market and the SEC within one year of the date of this prospectus. Our board of directors has determined that Charles A. Rowland, Jr. is an "audit committee financial expert" within the meaning of the SEC regulations and the applicable rules of The NASDAQ Stock Market. The audit committee's responsibilities upon completion of this offering will include:

- appointing, approving the compensation of, and assessing the independence of our independent registered public accounting firm;
- pre-approving auditing and permissible non-audit services, and the terms of such services, to be provided by our independent registered public accounting firm;
- reviewing the overall audit plan with our independent registered public accounting firm and members of management responsible for preparing our financial statements;
- reviewing and discussing with management and the independent registered public accounting firm our annual and quarterly financial statements and related disclosures as well as critical accounting policies and practices used by us;
- coordinating the oversight and reviewing the adequacy of our internal control over financial reporting;
- establishing policies and procedures for the receipt and retention of accounting-related complaints and concerns;
- recommending, based upon the audit committee's review and discussions with management and the independent registered public accounting firm, whether our audited financial statements shall be included in our Annual Report on Form 10-K;
- approving all Quarterly Reports on Form 10-Q;

- monitoring the integrity of our financial statements and our compliance with legal and regulatory requirements as they relate to our financial statements and accounting matters;
- preparing the audit committee report required by SEC rules to be included in our annual proxy statement;
- reviewing all related party transactions for potential conflict of interest situations and approving all such transactions; and
- reviewing quarterly earnings releases and scripts as well as any other press releases containing financial information.

Compensation Committee

Effective upon completion of this offering, our compensation committee will be composed of Charles A. Rowland, Jr., George D. Demetri and Daniel S. Lynch, with Charles A. Rowland, Jr. serving as chairman of the committee. Our board of directors has determined that each of Charles A. Rowland, Jr. and George D. Demetri is "independent" as defined in the rules of The NASDAQ Stock Market. The composition of our compensation committee meets the requirements for independence under the listing standards of The NASDAQ Stock Market, including the applicable transition rules. Our board of directors intends to cause our compensation committee to be comprised of only directors that are independent under the rules of The NASDAQ Stock Market within one year of the date of this prospectus. The compensation committee's responsibilities upon completion of this offering will include:

- annually reviewing and approving corporate goals and objectives relevant to the compensation of our chief executive officer;
- evaluating the performance of our chief executive officer in light of such corporate goals and objectives and determining the compensation of our chief executive officer;
- reviewing and approving the compensation of our other executive officers;
- reviewing and establishing our overall management compensation, philosophy and policy;
- overseeing and administering our compensation and similar plans;
- reviewing and approving our policies and procedures for the grant of equity-based awards;
- reviewing and making recommendations to the board of directors with respect to director compensation;
- reviewing and discussing with management the compensation discussion and analysis to be included in our annual proxy statement or Annual Report on Form 10-K; and
- reviewing and discussing with the board of directors corporate succession plans for the chief executive officer and other key officers.

Nominating and Corporate Governance Committee

Effective upon completion of this offering, our nominating and corporate governance committee will be composed of George D. Demetri, Alexis Borisy and Charles A. Rowland, Jr., with George D. Demetri serving as chairman of the committee. Our board of directors has determined that each of Charles A. Rowland, Jr. and George D. Demetri is "independent" as defined in the applicable rules of The NASDAQ Stock Market. The composition of our nominating and corporate governance committee meets the requirements for independence under the listing standards of The NASDAQ Stock Market, including the applicable transition rules. Our board of directors intends to cause our nominating and corporate governance committee to be comprised of only directors that

are independent under the rules of The NASDAQ Stock Market within one year of the date of this prospectus. The nominating and corporate governance committee's responsibilities upon completion of this offering will include:

- developing and recommending to the board of directors criteria for board and committee membership;
- establishing procedures for identifying and evaluating board of director candidates, including nominees recommended by shareholders;
- identifying individuals qualified to become members of the board of directors;
- recommending to the board of directors the persons to be nominated for election as directors and to each of the board's committees;
- developing and recommending to the board of directors a set of corporate governance guidelines; and
- overseeing the evaluation of the board of directors and management.

Our board of directors may establish other committees from time to time.

Research and Development Committee

Effective upon completion of this offering, our research and development committee will be composed of Nicholas Lydon, Alexis Borisy and George D. Demetri, with Nicholas Lydon serving as chairman of the committee. The research and development committee's responsibilities upon completion of this offering will include:

- providing a general oversight function regarding pre-clinical and clinical decision-making through a series of semi-annual pipeline reviews and in-depth assessments of select project strategies and plans;
- providing recommendations regarding key molecules in our discovery and development pipelines through reports and select in-depth project reviews;
- providing recommendations regarding our pipeline/portfolio balance from a scientific and clinical perspective, including new molecular entity versus new indication balance, mechanism balance, target balance and general risk balance;
- providing recommendations regarding key discovery and development strategies to align with our business needs; and
- providing feedback to the board of directors and to our research and development group.

Leadership Structure and Risk Oversight

Our board of directors is currently chaired by Mr. Lynch. As a general policy, our board of directors believes that separation of the positions of chairman and chief executive officer reinforces the independence of the board of directors from management, creates an environment that encourages objective oversight of management's performance and enhances the effectiveness of the board of directors as a whole. As such, Mr. Albers serves as our president and chief executive officer while Mr. Lynch serves as our chairman of the board of directors but is not an officer.

Our board of directors oversees the management of risks inherent in the operation of our business and the implementation of our business strategies. Our board of directors performs this oversight role by using several different levels of review. In connection with its reviews of the operations and corporate functions of our company, our board of directors addresses the primary

risks associated with those operations and corporate functions. In addition, our board of directors reviews the risks associated with our company's business strategies periodically throughout the year as part of its consideration of undertaking any such business strategies.

Each of our board committees also oversees the management of our company's risk that falls within the committee's areas of responsibility. In performing this function, each committee has full access to management, as well as the ability to engage advisors. Our chief executive officer reports to the audit committee and is responsible for identifying, evaluating and implementing risk management controls and methodologies to address any identified risks. In connection with its risk management role, our audit committee meets privately with representatives from our independent registered public accounting firm and our chief executive officer. The audit committee oversees the operation of our risk management program, including the identification of the primary risks associated with our business and periodic updates to such risks, and reports to our board of directors regarding these activities.

Compensation Committee Interlocks and Insider Participation

None of the members of our compensation committee has at any time during the prior three years been one of our officers or employees. None of our executive officers currently serves, or in the past fiscal year has served, as a member of the board of directors or compensation committee of any entity that has one or more executive officers serving on our board of directors or compensation committee. For a description of transactions between us and members of our compensation committee and affiliates of such members, please see "Certain Relationships and Related Party Transactions."

Code of Business Conduct and Ethics

We plan to adopt a code of business conduct and ethics that applies to all of our employees, officers and directors, including those officers responsible for financial reporting, which will be effective upon completion of this offering. Upon the completion of this offering, our code of business conduct and ethics will be available on our website at www.blueprintmedicines.com. We intend to disclose any amendments to the code, or any waivers of its requirements, on our website or in a Current Report on Form 8-K.

EXECUTIVE AND DIRECTOR COMPENSATION

Summary Compensation Table

The following table sets forth the compensation paid or accrued during the fiscal year ended December 31, 2014 to our chief executive officer, our interim chief executive officer and our next two highest-paid executive officers as of December 31, 2014. We refer to these officers as our named executive officers.

Name and Principal Position	Year	Salary ($)	Bonus ($)(1)	Option Awards(2) ($)	Non-equity Incentive Plan Compensation ($)	All Other Compensation ($)	Total ($)
Jeffrey W. Albers(3) *Chief Executive Officer and President*	2014	169,231	141,986	2,060,939	—	—	2,372,156
Alexis Borisy(4) *Interim Chief Executive Officer*	2014	—	—	—	—	—	—
Kyle D. Kuvalanka *Chief Business Officer*	2014	330,000	82,500	52,405	—	—	464,905
Christoph Lengauer, Ph.D. *Chief Scientific Officer*	2014	400,000	120,000	104,809	—	—	624,809

(1) Amounts represent cash bonuses earned for the 12-month period from January 1, 2014 to December 31, 2014 and exclude payments made in 2014 for 2013 bonuses. For Mr. Albers, this amount also includes a $75,000 sign-on bonus paid to him when he commenced employment with us.

(2) Amounts represent the aggregate grant-date fair value of option awards granted to our named executive officers in 2014 computed in accordance with FASB ASC Topic 718. The assumptions used in the valuation of these awards are consistent with the valuation methodologies specified in the notes to our financial statements and discussions in "Management's Discussion and Analysis of Financial Condition and Results of Operations" included elsewhere in this prospectus. The amounts above reflect our aggregate accounting expense for these awards and do not necessarily correspond to the actual value that will be recognized by the named executive officers.

(3) Mr. Albers became our Chief Executive Officer and President in July 2014. Amounts shown represent compensation earned by Mr. Albers since July 2014.

(4) Mr. Borisy served as Interim Chief Executive Officer from May 2013 to July 2014. Pursuant to our arrangement with Third Rock Ventures, LLC, we incurred consulting fees to Third Rock Ventures, LLC for Mr. Borisy's services as interim Chief Executive Officer. None of these consulting fees were paid directly to Mr. Borisy.

Narrative Disclosure to Summary Compensation Table

Employment Arrangements with our Named Executive Officers

We have entered into an offer letter agreement with each of the named executive officers in connection with their employment with us. Except as noted below, these offer letters provide for "at will" employment and were each subject to execution of our standard confidential information and invention assignment agreement.

Jeffrey W. Albers. We entered into a letter agreement with Mr. Albers on May 29, 2014, and he assumed the role of Chief Executive Officer in July 2014. The agreement entitles Mr. Albers to an initial base salary of $375,000 and eligibility to participate in our bonus pool with a target bonus of 40% of his base salary, with the actual bonus earned based upon the achievement of corporate and individual goals, all as determined by the Board in its discretion. Under the agreement, we agreed to pay Mr. Albers a one-time sign-on bonus of $75,000, reflecting his 12 month commitment to the Company, which was paid in 2014 and which must be repaid if he is terminated by the Company for "cause" within one year of commencing employment. We agreed to make an equity award to Mr. Albers in the form of options to purchase 573,945 shares of our common stock with an exercise price equal to the fair market value of our common stock on the day of the option grant, with such

options vesting on the terms set forth in the applicable option agreements with Mr. Albers. This amount represented approximately 4% of our shares on a fully-diluted basis. Pursuant to his letter agreement, Mr. Albers is entitled to 12 months of base salary as severance in the event we terminate his employment without Cause or Mr. Albers terminates his employment for Good Reason (each as defined in the letter agreement), subject to his executing a release of claims in our favor. In addition, in the event Mr. Albers' employment is terminated by us without Cause or by Mr. Albers for Good Reason within 12 months following a change in control, all stock options and other stock based awards held by Mr. Albers will vest and become exercisable and nonforfeitable.

Kyle Kuvalanka. We entered into a letter agreement with Mr. Kuvalanka on August 1, 2013, and he assumed the role of Chief Business Officer in September 2013. The agreement entitles Mr. Kuvalanka to an initial base salary of $330,000 and eligibility to participate in our bonus pool with a target bonus of 25% of his base salary, with the actual bonus earned based upon the achievement of corporate and individual goals agreed to between Mr. Kuvalanka and the Company's Chief Executive Officer. Under the agreement, we agreed to pay Mr. Kuvalanka a one-time sign-on bonus of $50,000, reflecting his 12-month commitment to the Company, which was paid in 2013. We agreed to make an equity award to Mr. Kuvalanka in the form of options to purchase 136,363 shares of our common stock with an exercise price equal to the fair market value of our common stock on the day of the option grant, with such options vesting on the terms set forth in the applicable option agreements with Mr. Kuvalanka. Pursuant to his letter agreement, Mr. Kuvalanka is entitled to 12 months of base salary as severance in the event we terminate his employment without Cause (as defined in the letter agreement).

Christoph Lengauer. We entered into a letter agreement with Dr. Lengauer on November 22, 2011, which was later amended on November 1, 2013. He assumed the role of Chief Scientific Officer in January 2012. The amended agreement entitles Dr. Lengauer to an initial base salary of $400,000 and eligibility to participate in our bonus pool with a target bonus of 30% of his base salary, with the actual bonus earned based upon the achievement of corporate and individual goals agreed to between Dr. Lengauer and the Company's Chief Executive Officer. Under the agreement, we agreed to pay Dr. Lengauer a one-time sign-on bonus of $50,000, reflecting his 12 month commitment to the Company, which was paid in 2013. We agreed to make an equity award to Dr. Lengauer in the form of options to purchase 136,363 shares of our common stock with an exercise price equal to the fair market value of our common stock on the day of the option grant, with such options vesting on the terms set forth in the applicable option agreements with Dr. Lengauer. Pursuant to his letter agreement, as amended, Mr. Lengauer is entitled to 12 months of base salary as severance in the event we terminate his employment without Cause (as defined in the letter agreement), subject to his executing a release of claims in our favor. In addition, upon a change in control, Mr. Lengauer's currently outstanding awards of restricted stock will vest and become nonforfeitable upon such change in control.

Employee Confidentiality, Non-competition, Non-solicitation and Assignment Agreements

Each of our named executive officers has entered into a standard form agreement with respect to confidential information and assignment of inventions. Among other things, this agreement obligates each named executive officer to refrain from disclosing any of our proprietary information received during the course of employment and to assign to us any inventions conceived or developed during the course of employment. Such agreement also provides that during the period of the named executive officer's employment and for 12 months thereafter, the named executive officer will not compete with us and will not solicit our employees, consultants, customers or suppliers.

Equity Compensation

Outstanding Equity Awards at December 31, 2014

The following table sets forth information concerning the outstanding equity awards held by each of the named executive officers as of December 31, 2014.

	Option Awards					Stock Awards	
Name	Number of securities underlying unexercised options exercisable (#)	Number of securities underlying unexercised options unexercisable (#)	Number of securities underlying unexercised unearned options (#)	Option exercise price ($/share)	Option expiration date	Number of shares or Units of Stock that have not vested (#)	Market value of shares that have not vested ($)(1)
Jeffrey W. Albers	—	—	—	—	—	143,486(2)	2,582,755
	—	213,903(3)	—	$ 1.87	7/30/2024	—	—
	—	163,080(4)	—	$ 1.87	7/30/2024	—	—
	53,475(5)	—	—	$ 1.87	7/30/2024	—	—
Kyle D. Kuvalanka	—	—	—	—	—	23,148(6)	416,667
	32,091	70,602(7)	—	$ 1.48	9/17/2023	—	—
	1,212	13,333(8)	—	$ 1.87	8/14/2024	—	—
Christoph Lengauer	—	—	—	—	—	51,136(9)	920,455
	14,772	39,772(10)	—	$ 1.48	11/1/2023	—	—
	2,424	26,666(11)	—	$ 1.87	8/14/2024	—	—

(1) There was no public market for our common stock at December 31, 2014. We have estimated the market value of the unvested stock awards based on the initial public offering price of $18.00 per share.

(2) On July 30, 2014, Mr. Albers was granted an option for 143,486 shares of our common stock, 100% of such option to vest on July 21, 2015. Pursuant to the terms of his option agreement, Mr. Albers early exercised his option on August 8, 2014 in exchange for shares of restricted stock. Pursuant to the terms of Mr. Albers' corresponding restricted stock agreement, the unvested shares will be fully vested on July 21, 2015. Vesting of the restricted shares subject to the agreement accelerates in connection with a change in control.

(3) Represents options to purchase shares of our common stock granted on July 30, 2014. The shares underlying these options vest in four equal tranches and installments as follows: (i) 53,476 vests in five installments at a rate of 11,957 on each of August 21, 2015, September 21, 2015, October 21, 2015 and November 21, 2015, and the remaining 5,648 vests on December 21, 2015, (ii) 53,476 vests in five installments at a rate of 11,957 on each of January 21, 2016, February 21, 2016, March 21, 2016 and April 21, 2016, and the remaining 5,648 vests on May 21, 2016, (iii) 53,476 vests in five installments at a rate of 11,957 on each of January 21, 2017, February 21, 2017, March 21, 2017 and April 21, 2017, and the remaining 5,648 vests on May 21, 2017, and (iv) 53,475 vests in five installments at a rate of 11,957 on each of January 21, 2018, February 21, 2018, March 21, 2018 and April 21, 2018, and the remaining 5,647 vests on May 21, 2018. Vesting of the options subject to the agreement accelerates in connection with a change in control.

(4) Represents options to purchase shares of our common stock granted on July 30, 2014. The shares underlying these options vest in three tranches and installments as follows: (i) 42,845 vests in four installments at a rate of 6,974 on September 21, 2016, and 11,957 on each of October 21, 2016 and November 21, 2016, and 11,957 on December 21, 2016, (ii) 90,010 vests in eight installments at a rate of 6,311 on May 21, 2017 and 11,957 on each of June 21, 2017, July 21, 2017, August 21, 2017, September 21, 2017, October 21, 2017, November 21, 2017 and December 21, 2017, and (iii) 30,225 vests in three installments at a rate of 6,311 on May 21, 2018, 11,957 on June 21, 2018 and 11,957 on July 21, 2018. Vesting of the options subject to the agreement accelerates in connection with a change in control.

(5) Represents options to purchase shares of our common stock granted on July 30, 2014, none of which are vested but are eligible for early exercise. The shares underlying these options vest as follows: (i) 6,310 vests on each of December 21, 2015 and May 21, 2016, (ii) 11,957 vests on each of June 21, 2016, July 21, 2016 and August 21, 2016, and (iii) 4,984 vests on September 21, 2016. Vesting of the options subject to the agreement accelerates in connection with a change in control.

(6) On September 17, 2013, Mr. Kuvalanka was granted an option for 33,670 shares of our common stock, 25% of such option to vest on September 16, 2014, and the remaining unvested shares to vest in equal monthly installments through September 16, 2017. Pursuant to the terms of his option agreement, Mr. Kuvalanka early exercised his option on October 2, 2013 in exchange for shares of restricted stock. Under the terms of Mr. Kuvalanka's corresponding restricted stock agreement, 25% of the shares vested on September 16, 2014 and the remaining unvested shares will vest in equal monthly installments through September 16, 2017.

(7) Represents options to purchase shares of our common stock granted on September 17, 2013. The shares underlying these options vest as follows: 25% vest on September 16, 2014, with the remainder of the shares vesting in equal monthly installments over the following three years through September 16, 2017.

(8) Represents options to purchase shares of our common stock granted on August 14, 2014. The shares underlying these options vest in equal monthly installments over four years through August 18, 2018.

(9) Under the terms of Dr. Lengauer's December 15, 2011 and January 31, 2013 restricted stock agreements, the remaining unvested shares will vest in equal monthly installments through January 1, 2016 and January 1, 2017, respectively. Vesting of the restricted shares accelerates in connection with a change in control.

(10) Represents options to purchase shares of our common stock granted on November 3, 2013. The shares underlying these options vest in equal monthly installments over four years through November 1, 2017. Vesting of the options subject to the agreement accelerates in connection with a change in control.

(11) Represents options to purchase shares of our common stock granted on August 14, 2014. The shares underlying these options vest in equal monthly installments over four years through August 18, 2018.

Director Compensation

The following table sets forth a summary of the compensation we paid to our non-employee directors during 2014. Other than as set forth in the table and described more fully below, we did not pay any compensation, reimburse any expense of, make any equity awards or non-equity awards to, or pay any other compensation to any of the other non-employee members of our board of directors in 2014. Jeffrey W. Albers, our President and Chief Executive Officer, receives no compensation for his service as a director, and, consequently, is not included in this table. The compensation received by Mr. Albers as an employee during 2014 is presented in the "Summary Compensation Table" above.

Name	Fees Earned or Paid in Cash ($)	Option Awards ($)	All Other Compensation ($)	Total ($)
Daniel S. Lynch(1)	—	—	130,000	130,000
Nicholas Lydon, Ph.D.(2)	—	—	65,000	65,000
David Schenkein, M.D.(3)	35,000	—	—	35,000
George D. Demetri, M.D.(4)	—	—	100,000	100,000

(1) Mr. Lynch received payment for service as a director and consultant pursuant to a consulting agreement. Amount includes cash bonus of $30,000 earned for the 12-month period from January 1, 2014 to December 31, 2014. As of December 31, 2014, Mr. Lynch held 272,727 shares of restricted common stock.

(2) Mr. Lydon received payment for service as a consultant pursuant to a consulting agreement. As of December 31, 2014, Mr. Lydon held 272,727 shares of restricted common stock.

(3) Dr. Schenkein, our former director who resigned on February 26, 2015, received payment for service as a director during the 2014 fiscal year pursuant to a board service agreement. As of December 31, 2014, trusts for the benefit of Dr. Schenkein and certain of his family members held 33,636 shares of restricted common stock.

(4) Dr. Demetri received payment for service as an advisor pursuant to an advisory agreement. As of December 31, 2014, Dr. Demetri held an option to purchase 9,090 shares of common stock and 18,181 shares of restricted common stock.

Compensation Risk Assessment

We believe that our executive compensation program does not encourage excessive or unnecessary risk taking. This is primarily due to the fact that our compensation programs are designed to encourage our executive officers and other employees to remain focused on both short-term and long-term strategic goals, in particular in connection with our pay-for-performance compensation philosophy. As a result, we do not believe that our compensation programs are reasonably likely to have a material adverse effect on us.

Equity Compensation Plans and Other Benefit Plans

2011 Stock Option Plan

The 2011 Stock Option Plan, was approved by our board of directors and our stockholders on April 4, 2011 and was most recently amended on February 10, 2015. Under the 2011 Stock Option Plan, 3,590,927 shares of common stock have been reserved for issuance in the form of incentive stock options, non-qualified stock options, restricted stock, unrestricted stock, restricted stock units, or any combination of the foregoing. The shares issuable pursuant to awards granted under the 2011 Stock Option Plan are authorized but unissued shares.

The 2011 Stock Option Plan is administered by our board or at the discretion of the board, a committee of the board comprised of not less than two (2) directors, which has full power to select the employees, directors and service providers to whom awards will be granted and to determine the specific terms and conditions of each award, subject to the provisions of the 2011 Stock Option Plan.

The option exercise price of each option granted under the 2011 Stock Option Plan is determined by our board and may not be less than the fair market value of a share of common stock on the date of grant. The term of each option is fixed by the board and may not exceed ten years from the date of grant. The board determines at what time or times each option may be exercised when granting the option.

The board of directors may grant awards under the 2011 Stock Option Plan entitling the participants to acquire shares of common stock subject to the right of repurchase (or forfeiture if issued at no cost) in the event the conditions specified by the board in connection with the awards are not met. The board may also grant awards of restricted stock units under the 2011 Stock Option Plan entitling the participants to receive shares of common stock or cash at the time the awards vest.

The board of directors may also grant other stock-based awards under the 2011 Stock Option Plan such as stock appreciation rights and other types of awards which entitle the participants to receive shares of common stock or cash in the future.

The 2011 Stock Option Plan provides that, upon a sale transaction of the Company, unless provision is made in connection with the sale transaction in the sole discretion of the parties thereto for the assumption or continuation of the awards by the successor entity or substitution of the awards with new awards of the successor entity, with appropriate adjustment, all options not exercised will terminate upon the closing of the sale transaction, and all restricted stock and restricted stock unit awards will be forfeited immediately prior to the closing of the sale transaction.

Our board may amend the 2011 Stock Option Plan but no such action may adversely affect the rights of an award holder without such holder's consent. Approval by our stockholders of amendments to the 2011 Stock Option Plan must be obtained if required by law.

As of March 31, 2015, options to purchase 1,887,098 shares of common stock were outstanding, and 1,502,906 shares of restricted stock were outstanding under the 2011 Stock Option Plan. Our board has determined not to make any further awards under the 2011 Stock Option Plan following the completion of this offering.

2015 Stock Option Plan

Our 2015 Stock Option Plan, or the 2015 Stock Option Plan, was adopted by our board of directors and approved by our stockholders on April 8, 2015 and will become effective immediately prior to the closing of this offering. The 2015 Stock Option Plan will replace the 2011 Stock Option Plan. The 2015 Stock Option Plan provides us flexibility to use various equity-based incentive and

other awards as compensation tools to motivate our workforce. These tools include stock options, stock appreciation rights, restricted stock, restricted stock units, unrestricted stock, performance share awards and cash-based awards.

We have initially reserved 1,460,084 shares of our common stock for the issuance of awards under the 2015 Stock Option Plan, which will be cumulatively increased on January 1 of each calendar year by 4% of the number of shares of common stock issued and outstanding on the immediately preceding December 31. This number is subject to adjustment in the event of a stock split, stock dividend or other change in our capitalization.

The shares issuable pursuant to awards granted under the 2015 Stock Option Plan will be authorized but unissued shares or shares that we reacquire. The shares of common stock underlying any awards from the 2015 Stock Option Plan and the 2011 Stock Option Plan that are forfeited, cancelled, held back upon exercise or settlement of an award to satisfy the exercise price or tax withholding, reacquired by us prior to vesting, satisfied without any issuance of common stock, expire or are otherwise terminated (other than by exercise) under the 2015 Stock Option Plan or the 2011 Stock Option Plan, as applicable, will be added back to the shares available for issuance under the 2015 Stock Option Plan.

Under the 2015 Stock Option Plan, stock options or stock appreciation rights with respect to no more than 1,460,084 shares may be granted to any one individual in any one calendar year and the maximum aggregate number of shares that may be issued in the form of incentive stock options shall not exceed the initial number of shares reserved and available for issuance under the 2015 Stock Option Plan, cumulatively increased on January 1 of each calendar year.

The 2015 Stock Option Plan will be administered by the compensation committee of the board of directors. The compensation committee has full power to select, from among the individuals eligible for awards, the individuals to whom awards will be granted, to make any combination of awards to participants, and to determine the specific terms and conditions of each award, subject to the provisions of the 2015 Stock Option Plan. Employees, nonemployee directors and other key persons (including consultants) are eligible to receive awards under the 2015 Stock Option Plan.

The 2015 Stock Option Plan permits the granting of both options to purchase common stock intended to qualify as incentive stock options under Section 422 of the Code and options that do not so qualify. The exercise price of each stock option will be determined by our compensation committee but may not be less than 100% of the fair market value of our common stock on the date of grant or, in the case of an incentive stock option granted to a 10% owner, less than 110% of the fair market value of our common stock on the date of grant. The term of each stock option will be fixed by the compensation committee and may not exceed ten years from the date of grant (or five years in the case of an incentive stock option granted to a 10% owner). The compensation committee will also determine the vesting schedule for granted stock options.

The compensation committee may award stock appreciation rights subject to such conditions and restrictions as it may determine. Stock appreciation rights entitle the recipient to shares of common stock, or cash, equal to the value of the appreciation in our stock price over the exercise price. The exercise price of each stock appreciation right may not be less than 100% of the fair market value of the common stock on the date of grant.

The compensation committee may award restricted stock or restricted stock units to participants subject to such conditions and restrictions as it may determine. These conditions and restrictions may include the achievement of certain performance goals and/or continued employment or service with us through a specified vesting period. The compensation committee may also grant cash-based awards to participants subject to such conditions and restrictions as it may determine. Our compensation committee may also grant shares of common stock that are free

from any restrictions under the 2015 Stock Option Plan. Unrestricted stock may be granted to participants in recognition of past services or for other valid consideration and may be issued in lieu of cash compensation due to such participant.

The compensation committee may grant performance share awards to participants that entitle the recipient to receive share awards of common stock upon the achievement of certain performance goals and such other conditions as our compensation committee shall determine.

The compensation committee may grant cash bonuses under the 2015 Stock Option Plan to participants, subject to the achievement of certain performance goals.

The compensation committee may grant performance-based awards to participants in the form of restricted stock, restricted stock units, performance shares or cash-based awards upon the achievement of certain performance goals and such other conditions as the compensation committee shall determine. The compensation committee may grant such performance-based awards under the 2015 Stock Option Plan that are intended to qualify as "performance-based compensation" under Section 162(m) of the Code. Those awards would only vest or become payable upon the attainment of performance goals that are established by our compensation committee and related to one or more performance criteria. The performance criteria that could be used with respect to any such awards include: total shareholder return, earnings before interest, taxes, depreciation and amortization, net income (loss) (either before or after interest, taxes, depreciation and/or amortization), changes in the market price of our common stock, economic value-added, sales or revenue, development, clinical or regulatory milestones, acquisitions or strategic transactions, operating income (loss), cash flow (including, but not limited to, operating cash flow and free cash flow), return on capital, assets, equity, or investment, return on sales, gross or net profit levels, productivity, expense, margins, operating efficiency, customer satisfaction, working capital, earnings (loss) per share of stock, sales or market shares and number of customers, any of which may be measured either in absolute terms or as compared to any incremental increase or as compared to results of a peer group. From and after the time that we become subject to Section 162(m) of the Code, the maximum award that is intended to qualify as "performance-based compensation" under Section 162(m) of the Code that may be made to any one employee during any one calendar year period is 1,460,084 shares with respect to a stock-based award and $2,000,000 with respect to a cash-based award.

The 2015 Stock Option Plan provides that upon the effectiveness of a "sale event," as defined in the 2015 Stock Option Plan, all options and stock appreciation rights that are not exercisable immediately prior to the effective time of the sale event shall become fully exercisable as of the effective time of the sale event, all other awards with time-based vesting, conditions or restrictions, shall become fully vested and nonforfeitable as of the effective time of the sale event and all awards with conditions and restrictions relating to the attainment of performance goals may become vested and nonforfeitable in the discretion of the compensation committee and all awards granted under the 2015 Stock Option Plan shall terminate. In addition, in connection with the termination of the 2015 Stock Option Plan upon a sale event, we may make or provide for a cash payment to participants holding options and stock appreciation rights equal to the difference between the per share cash consideration payable to stockholders in the sale event and the exercise price of the options or stock appreciation rights.

Our board of directors may amend or discontinue the 2015 Stock Option Plan and our compensation committee may amend or cancel outstanding awards for purposes of satisfying changes in law or any other lawful purpose, including option repricing, but no such action may adversely affect rights under an award without the holder's consent. Certain amendments to the 2015 Stock Option Plan may require the approval of our stockholders.

No awards may be granted under the 2015 Stock Option Plan after the date that is ten years from the date of stockholder approval of the 2015 Stock Option Plan.

Other Compensation

We currently maintain broad-based benefits that are provided to all employees, including health insurance, life and disability insurance and dental insurance.

401(k) Plan

We maintain a 401(k) plan for employees. The 401(k) plan is intended to qualify under Section 401(k) of the Internal Revenue Service Code of 1986, as amended, so that contributions to the 401(k) plan by employees or by us, and the investment earnings thereon, are not taxable to the employees until withdrawn from the 401(k) plan, and so that contributions by us, if any, will be deductible by us when made. Under the 401(k) plan, employees may elect to reduce their current compensation by up to the statutorily prescribed annual limit and to have the amount of such reduction contributed to the 401(k) plan. The 401(k) plan permits us to make contributions up to the limits allowed by law on behalf of all eligible employees. Historically, we have not made any matching contributions to the 401(k) plan.

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 the director or officer. The director or officer may amend or terminate the plan in limited circumstances. Our directors and executive officers may also buy or sell additional shares of our common stock outside of a Rule 10b5-1 plan when they are not in possession of material, nonpublic information.

CERTAIN RELATIONSHIPS AND RELATED PARTY TRANSACTIONS

The following is a description of transactions since January 1, 2012 to which we have been a party, in which the amount involved exceeds $120,000, and in which any of our directors, executive officers or holders of more than 5% of our capital stock, or an affiliate or immediate family member thereof, had or will have a direct or indirect material interest. We believe the terms obtained or consideration that we paid or received, as applicable, in connection with the transactions described below were comparable to terms available or the amounts that would be paid or received, as applicable, from unaffiliated third parties.

In connection with this offering, we plan to adopt a written policy, effective upon completion of this offering, that requires all future transactions between us and any director, executive officer, holder of 5% or more of any class of our capital stock or any member of the immediate family of, or entities affiliated with, any of them, or any other related persons (as defined in Item 404 of Regulation S-K) or their affiliates, in which the amount involved is equal to or greater than $120,000, be approved in advance by our audit committee. Any request for such a transaction must first be presented to our audit committee for review, consideration and approval. In approving or rejecting any such proposal, our audit committee is to consider the relevant facts and circumstances available and deemed relevant to the audit committee, including, but not limited to, the extent of the related party's interest in the transaction, and whether the transaction is on terms no less favorable to us than terms we could have generally obtained from an unaffiliated third party under the same or similar circumstances.

All of the transactions described below were entered into prior to the adoption of this written policy but each was approved by our board of directors. Prior to our board of directors' consideration of a transaction with a related person, the material facts as to the related person's relationship or interest in the transaction were disclosed to our board of directors, and the transaction was not approved by our board of directors unless a majority of the directors approved the transaction. Our current policy with respect to approval of related person transactions is not set forth in writing.

Sales and Purchases of Securities

Series A Financing

In April 2011, we entered into a Series A convertible preferred stock purchase agreement, or the Series A purchase agreement, pursuant to which we agreed to issue and sell to investors an aggregate of 25,000,000 shares of our Series A Preferred Stock at a purchase price of $1.00 per share. These shares were to be issued in three tranches with the first tranche consisting of 10,000,000 shares and the last two tranches of 7,500,000 shares each. The first tranche of Series A Preferred Stock was issued in April 2011. In connection with the first tranche described above, certain convertible promissory notes, along with accrued but unpaid interest thereon, were automatically converted into an aggregate of 525,315 shares of our Series A Preferred Stock.

The Series A purchase agreement was subsequently amended in February 2012 to provide for the issuance of the remaining 15,000,000 shares in three tranches of 5,000,000 shares each. These tranches were issued in February 2012, March 2012 and October 2012, respectively. In January 2013, the Series A purchase agreement was further amended to provide for the issuance of an additional 15,000,000 shares of Series A Preferred Stock in three tranches. These tranches were issued in January and September of 2013.

The table below sets forth the aggregate number of shares of Series A Preferred Stock sold to our directors, executive officers or holders of more than 5% of our capital stock, or an affiliate or immediate family member thereof:

Name	Shares	Aggregate Purchase Price	
Third Rock Ventures II, L.P.	30,000,000	$	30,000,000
Beacon Bioventures Fund III Limited Partnership	10,000,000	$	10,000,000

Series B Financing

In January 2014, we issued an aggregate of 20,916,663 shares of our Series B Preferred Stock at a purchase price of $1.20 per share for aggregate consideration of $25.1 million to seven investors. The table below sets forth the number of shares of Series B Preferred Stock sold to our directors, executive officers or holders of more than 5% of our capital stock at the time of such issuance, or an affiliate or immediate family member thereof:

Name	Shares	Aggregate Purchase Price	
Third Rock Ventures II, L.P.	7,833,333	$	9,399,999.60
Beacon Bioventures Fund III Limited Partnership	2,583,333	$	3,099,999.60
David P. Schenkein 2004 Revocable Trust	41,666	$	49,999.20
Amy Schenkein 2004 Revocable Trust	41,666	$	49,999.20

Series C Financing

In November 2014, we issued an aggregate of 24,154,589 shares of our Series C Preferred Stock at a purchase price of $2.07 per share for aggregate consideration of $49.9 million to eighteen investors. The table below sets forth the number of shares of Series C Preferred Stock sold to our directors, executive officers or holders of more than 5% of our capital stock at the time of such issuance, or an affiliate or immediate family member thereof:

Name	Shares	Aggregate Purchase Price	
Third Rock Ventures II, L.P.	1,328,502	$	2,749,999.14
Beacon Bioventures Fund III Limited Partnership	483,092	$	1,000,000.44
David P. Schenkein 2004 Revocable Trust	60,386	$	124,999.02
Amy Schenkein 2004 Revocable Trust	60,386	$	124,999.02

Agreements with Stockholders

In connection with the Series C Preferred Stock financing, we entered into the Second Amended and Restated Investors' Rights Agreement, or Investor's Rights Agreement, dated as of November 7, 2014, with certain of our stockholders, including our principal stockholders and their affiliates and the Second Amended and Restated Stockholders Agreement, or Stockholders Agreement, dated as of November 7, 2014, with certain of our stockholders, including our principal stockholders and their affiliates. All of the provisions of these agreements will terminate immediately upon completion of the offering, other than the provisions relating to registration rights, which will continue in effect following completion of the offering and entitle the holders of such rights to have us register their shares of our common stock for sale in the United States. See "Description of Capital Stock — Registration Rights."

Since inception, we have received consulting and management services from Third Rock Ventures LLC, or Third Rock Ventures, which through its affiliates, has a controlling interest in us. We have paid Third Rock Ventures $3.3 million for these services, including the reimbursement of

expenses, from inception through the date of this prospectus. We do not have a written agreement in place with Third Rock Ventures with respect to the provision of consulting and management services. From time to time and at our request, partners and associates of Third Rock Ventures provide us with certain strategic and ordinary course business operations consulting services at fees mutually agreed upon in advance by us and Third Rock Ventures. For example, Third Rock Ventures provided us with the services of Entrepreneurs in Residence, who provided us with scientific leadership services and with executive services. Third Rock Ventures also provided us with the services of its partners, who provided business development advice and executive advice. The consulting and management services fees are payable to Third Rock Ventures pursuant to invoices submitted to us by Third Rock Ventures from time to time. The consulting and management services fees paid to Third Rock Ventures did not exceed 5% of the consolidated gross revenue of Third Rock Ventures during any of the past three fiscal years.

Director and Executive Officer Compensation

Please see "Executive and Director Compensation — Director Compensation" for a discussion of options granted to our non-employee directors. Please see "Executive and Director Compensation — Equity Compensation" for additional information regarding compensation of executive officers.

Employment Agreements

We have entered into offer letters with our executive officers. For more information regarding these agreements, see "Executive and Director Compensation — Employment Agreements with Our Named Executive Officers."

Indemnification Agreements and Directors' and Officers' Liability Insurance

In connection with this offering, we have entered into indemnification agreements with each of our executive officers and directors. We also maintain a general liability insurance policy which covers certain liabilities of directors and officers of our company arising out of claims based on acts or omissions in their capacities as directors or officers.

Registration Rights Agreements

We and certain holders of our convertible preferred stock have entered into an Investor's Rights Agreement pursuant to which these stockholders will have, among other things, registration rights under the Securities Act of 1933, as amended, with respect to common stock that they will hold following this offering. Upon the closing of this offering, all outstanding shares of our convertible preferred stock will be converted into common stock. See "Description of Capital Stock — Registration Rights" for a further description of the terms of these agreements.

PRINCIPAL STOCKHOLDERS

The following table sets forth information relating to the beneficial ownership of our common stock as of December 31, 2014, by:

- each person, or group of affiliated persons, known by us to beneficially own more than 5% of our outstanding shares of common stock;
- each of our directors;
- each of our named executive officers; and
- all directors and executive officers as a group.

The number of shares beneficially owned by each entity, person, director or executive officer is determined in accordance with the rules of the SEC, and the information is not necessarily indicative of beneficial ownership for any other purpose. Under such rules, beneficial ownership includes any shares over which the individual has sole or shared voting power or investment power as well as any shares that the individual has the right to acquire within 60 days of December 31, 2014 through the exercise of any stock option, warrants or other rights. Except as otherwise indicated, and subject to applicable community property laws, the persons named in the table have sole voting and investment power with respect to all shares of common stock held by that person.

The percentage of shares beneficially owned is computed on the basis of 17,686,131 shares of our common stock outstanding as of December 31, 2014, which reflects the assumed conversion of all of our outstanding shares of preferred stock into an aggregate of 15,467,479 shares of common stock. Shares of our common stock that a person has the right to acquire within 60 days of December 31, 2014 are deemed outstanding for purposes of computing the percentage ownership of the person holding such rights, but are not deemed outstanding for purposes of computing the percentage ownership of any other person, except with respect to the percentage ownership of all directors and executive officers as a group. Unless otherwise indicated below, the

address for each beneficial owner listed is c/o Blueprint Medicines Corporation, 215 First Street, Cambridge, MA 02142.

Name and address of beneficial owner(1)	Number of shares beneficially owned	Percentage of shares beneficially owned	
		Before offering	After offering
5% or greater stockholders:			
Third Rock Ventures II, L.P.(2)	7,393,059	41.80%	27.33%
Beacon Bioventures Fund III Limited Partnership(3)	2,375,711	13.43%	8.78%
Directors and named executive officers:			
Jeffrey W. Albers(4)	196,961	1.11%	*
Anthony L. Boral	—	—	—
Alexis Borisy(5)	18,181	*	*
George Demetri(6)	27,271	*	*
Christoph Lengauer(7)	184,317	1.04%	*
Stephen C. Knight	—	—	—
Kyle Kuvalanka(8)	71,856	*	*
Nicholas Lydon(9)	272,727	1.54%	1.01%
Daniel S. Lynch(10)	272,727	1.54%	1.01%
Thilo Schroeder(11)	662,054	3.74%	2.45%
All executive officers and directors as a group (10 persons)	1,706,093	9.58%	6.31%

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

(1) Unless otherwise indicated, the address for each beneficial owner is c/o Blueprint Medicines Corporation, 215 First Street, Cambridge, Massachusetts 02142.

(2) Consists of (i) 5,454,545 shares of common stock issuable upon conversion of series A convertible preferred stock held by Third Rock Ventures II, L.P. ("TRV LP"), (ii) 1,424,242 shares of common stock issuable upon conversion of series B convertible preferred stock held by TRV LP, (iii) 241,545 shares of common stock issuable upon conversion of series C convertible preferred stock held by TRV LP, and (d) 272,727 shares of common stock held by TRV LP. Each of Third Rock Ventures II GP, LP ("TRV GP"), the general partner of TRV LP, and Third Rock Ventures GP, LLC ("TRV LLC"), the general partner of TRV GP, and Mark Levin, Kevin Starr and Robert Tepper, the managers of TRV LLC, may be deemed to share voting and investment power over the shares held of record by TRV LP. The address of TRV LP is 29 Newbury Street, Suite 401, Boston, MA 02142.

(3) Consists of (i) 1,818,181 shares of common stock issuable upon conversion of series A convertible preferred stock held by Beacon Bioventures Fund III Limited Partnership ("Beacon Fund"), (ii) 469,696 shares of common stock issuable upon conversion of series B convertible preferred stock held by Beacon Fund, and (iii) 87,834 shares of common stock issuable upon conversion of series C convertible preferred stock held by Beacon Fund. Beacon Bioventures Advisors Fund III Limited Partnership ("Advisors Fund") is the general partner of Beacon Fund. Advisors Fund is solely managed by Impresa Management LLC ("Impresa"), its general partner and investment manager. Each of the individuals and entities listed above expressly disclaims beneficial ownership of the securities listed above except to the extent of any pecuniary interest therein. The address for each of the individuals and entities listed above is One Main Street, Cambridge, MA 02142.

(4) Consists of (i) 53,475 shares of common stock issuable upon exercise of stock options within 60 days of December 31, 2014, none of which are vested but are eligible for early exercise, and (ii) 143,486 shares acquired upon an early exercise and held of record by Mr. Albers, all of which are subject to a right of repurchase by us if Mr. Albers does not satisfy the option's vesting requirements. Shares acquired upon an early exercise may not be disposed of until the vesting period has been satisfied.

(5) Consists of 18,181 shares of restricted stock Mr. Borisy holds in his individual capacity.

(6) Consists of (i) 18,181 shares of restricted stock, and (ii) 9,090 options to purchase shares of common stock that are exercisable as of December 31, 2014 or will become exercisable within 60 days after such date.

(7) Consists of (i) 163,636 shares of restricted stock, and (ii) 20,681 options to purchase common stock that are exercisable as of December 31, 2014 or will become exercisable within 60 days after such date.

(8) Consists of (i) 38,186 options to purchase common stock that are exercisable as of December 31, 2014 or will become exercisable within 60 days after such date, and (ii) 33,670 shares acquired upon an early exercise and held of record by Mr. Kuvalanka, of which 23,148 shares are subject to a right of repurchase by us if Mr. Kuvalanka does not satisfy the option's vesting requirements. Shares acquired upon an early exercise may not be disposed of until the vesting period has been satisfied.

(9) Consists of 272,727 shares of restricted stock.

(10) Consists of 272,727 shares of restricted stock.

(11) Represents (a) 530,302 shares of common stock issuable upon conversion of Series B convertible preferred stock held by Nextech III Oncology, LPCI ("Nextech III"), and (b) 131,752 shares of common stock issuable upon conversion of Series C convertible preferred stock held by Nextech III. The general partner of Nextech III is Nextech III GP Ltd. Alfred Scheidegger and Roland Ruckstuhl are the managing members of Nextech III GP Ltd. and may be deemed to share dispositive voting and investment power over the shares held by Nextech III. Each of these individuals disclaims beneficial ownership of such shares except to the extent of his pecuniary interest therein. Mr. Schroeder, a member of our board of directors, is a partner of Nextech Invest AG, the investment advisor of Nextech III GP Ltd., and may be deemed to have voting and investment power over the shares held by Nextech III. Mr. Schroeder disclaims beneficial ownership of such shares except to the extent of any pecuniary interest therein.

DESCRIPTION OF CAPITAL STOCK

General

Upon the completion of this offering, our authorized capital stock will consist of 120,000,000 shares of common stock, par value $0.001 per share, and 5,000,000 shares of preferred stock, par value $0.001 per share, all of which will be undesignated, and there will be 25,831,965 shares of common stock outstanding and no shares of convertible preferred stock outstanding. As of March 31, 2015, we had approximately 90 record holders of our capital stock. All of our outstanding shares of convertible preferred stock will automatically convert into shares of our common stock upon the completion of this offering.

The following description of our capital stock and provisions of our amended and restated certificate of incorporation and amended and restated by-laws are summaries of material terms and provisions and are qualified by reference to our amended and restated certificate of incorporation and amended and restated by-laws, copies of which have been filed with the SEC as exhibits to the registration statement of which this prospectus is a part. The descriptions of our common stock and preferred stock reflect amendments to our amended and restated certificate of incorporation and amended and restated by-laws that will become effective immediately prior to the completion of this offering

Common Stock

Upon the completion of this offering, we will be authorized to issue one class of common stock. Holders of our common stock are entitled to one vote for each share of common stock held of record for the election of directors and on all matters submitted to a vote of stockholders. Holders of our common stock are entitled to receive dividends ratably, if any, as may be declared by our board of directors out of legally available funds, subject to any preferential dividend rights of any convertible preferred stock then outstanding. Upon our dissolution, liquidation or winding up, holders of our common stock are entitled to share ratably in our net assets legally available after the payment of all our debts and other liabilities, subject to the preferential rights of any preferred stock then outstanding. Holders of our common stock have no preemptive, subscription, redemption or conversion rights. The rights, preferences and privileges of holders of common stock are subject to, and may be adversely affected by, the rights of the holders of shares of any series of preferred stock that we may designate and issue in the future. Except as described under "Antitakeover Effects of Delaware Law and Provisions of our Amended and Restated Certificate of Incorporation and Amended and Restated By-laws" below, a majority vote of the holders of common stock is generally required to take action under our amended and restated certificate of incorporation and amended and restated by-laws.

Preferred Stock

Upon the completion of this offering, our board of directors will be authorized, without action by the stockholders, to designate and issue up to an aggregate of 5,000,000 shares of preferred stock in one or more series. Our board of directors can designate the rights, preferences and privileges of the shares of each series and any of its qualifications, limitations or restrictions. Our board of directors may authorize the issuance of preferred stock with voting or conversion rights that could adversely affect the voting power or other rights of the holders of common stock. The issuance of preferred stock, while providing flexibility in connection with possible future financings and acquisitions and other corporate purposes could, under certain circumstances, have the effect of restricting dividends on our common stock, diluting the voting power of our common stock, impairing the liquidation rights of our common stock, or delaying, deferring or preventing a change in control of our company, which might harm the market price of our common stock. See also

"Antitakeover Effects of Delaware Law and Provisions of our Amended and Restated Certificate of Incorporation and Amended and Restated By-laws — Provisions of Our Amended and Restated Certificate of Incorporation and Amended and Restated By-Laws — Undesignated Preferred Stock" below.

Our board of directors will make any determination to issue such shares based on its judgment as to our company's best interests and the best interests of our stockholders. Upon the completion of this offering, we will have no shares of preferred stock outstanding and we have no current plans to issue any shares of preferred stock following completion of this offering.

Warrants

As of December 31, 2014, warrants to purchase a total of 150,000 shares of our Series A Preferred Stock were outstanding with an exercise price of $1.00 per share. These warrants to purchase 150,000 shares of Series A Preferred Stock, which will be converted into warrants to purchase 27,272 shares of common stock upon completion of this offering, are exercisable immediately and expire on May 24, 2023. As of December 31, 2014, warrants to purchase a total of 83,333 shares of our Series B Preferred Stock were outstanding with an exercise price of $1.20 per share. These warrants to purchase 83,333 shares of Series B Preferred Stock, which will be converted into warrants to purchase 15,151 shares of common stock upon completion of this offering, are exercisable immediately and expire on November 3, 2024.

Registration Rights

We entered into a second amended and restated investors' rights agreement, dated as of November 7, 2014, or Investors' Rights Agreement, with the holders of shares of our common stock issuable upon conversion of the shares of convertible preferred stock. These shares will represent approximately 59.9% of our outstanding common stock after this offering, or 57.2% if the underwriters exercise their option to purchase additional shares in full. These shares also may be sold under Rule 144 under the Securities Act of 1933, as amended, depending on their holding period and subject to restrictions in the case of shares held by persons deemed to be our affiliates.

Under the Investors' Rights Agreement, holders of registrable shares can demand that we file a registration statement or request that their shares be included on a registration statement that we are otherwise filing, in either case, registering the resale of their shares of common stock. These registration rights are subject to conditions and limitations, including the right, in certain circumstances, of the underwriters of an offering to limit the number of shares included in such registration and our right, in certain circumstances, not to effect a requested S-1 registration within 60 days before or 180 days following any offering of our securities, including this offering or a requested S-3 registration within 30 days before or 90 days following any offering of our securities, including this offering.

Demand Registration Rights

Following the six month anniversary of the date of this prospectus, the holders of at least a majority of our registrable shares may require us to file a registration statement under the Securities Act on a Form S-1 or S-3, if available, at our expense with respect to the resale of their registrable shares, and we are required to use our best efforts to effect the registration.

Piggyback Registration Rights

If we propose to register any of our securities under the Securities Act for our own account or the account of any other holder, the holders of registrable shares are entitled to notice of such registration and to request that we include registrable shares for resale on such registration

statement, subject to the right of any underwriter to limit the number of shares included in such registration.

We will pay all registration expenses, other than underwriting discounts and commissions, related to any demand or piggyback registration. The Investors' Rights Agreement contains customary cross-indemnification provisions, pursuant to which we are obligated to indemnify the selling stockholders, in the event of misstatements or omissions in the registration statement attributable to us except in the event of fraud and they are obligated to indemnify us for misstatements or omissions attributable to them.

The registration rights will terminate upon the later of the date on which all registrable shares have been sold and the fifth anniversary of the closing date of this offering.

Stockholders Agreement

We entered into a second amended and restated stockholders agreement, dated as of November 7, 2014, or Stockholders Agreement, with all holders of our convertible preferred stock and certain holders of our common stock. This agreement provides for certain rights and obligations, such as board composition requirements and stock transfer restrictions. This agreement will terminate upon the completion of this offering; however, the lock-up provision under the Stockholders Agreement will survive termination pursuant to the terms of the agreement. The lock-up provision under the Investors' Rights Agreement will also be in effect in connection with this offering. See "Shares Eligible for Future Sales — Lock-up Agreements."

Anti-takeover Effects of Delaware Law, Our Amended and Restated Certificate of Incorporation and Our Amended and Restated By-laws

Our amended and restated certificate of incorporation and amended and restated by-laws that will take effect in connection with the closing of this offering include a number of provisions that may have the effect of encouraging persons considering unsolicited tender offers or other unilateral takeover proposals to negotiate with our board of directors rather than pursue non-negotiated takeover attempts. These provisions include the items described below.

Board Composition and Filling Vacancies

In accordance with our amended and restated certificate of incorporation, our board is divided into three classes serving three-year terms, with one class being elected each year. Our amended and restated certificate of incorporation also provides that directors may be removed only for cause and then only by the affirmative vote of the holders of 75% or more of the shares then entitled to vote at an election of directors. Furthermore, any vacancy on our board of directors, however occurring, including a vacancy resulting from an increase in the size of our board, may only be filled by the affirmative vote of a majority of our directors then in office, even if less than a quorum.

No Written Consent of Stockholders

Our amended and restated certificate of incorporation provides that all stockholder actions are required to be taken by a vote of the stockholders at an annual or special meeting, and that stockholders may not take any action by written consent in lieu of a meeting.

Meetings of Stockholders

Our amended and restated by-laws provide that only a majority of the members of our board of directors then in office may call special meetings of stockholders and only those matters set forth in the notice of the special meeting may be considered or acted upon at a special meeting of

stockholders. Our amended and restated by-laws limit the business that may be conducted at an annual meeting of stockholders to those matters properly brought before the meeting.

Advance Notice Requirements

Our amended and restated by-laws establish advance notice procedures with regard to stockholder proposals relating to the nomination of candidates for election as directors or new business to be brought before meetings of our stockholders. These procedures provide that notice of stockholder proposals must be timely given in writing to our corporate secretary prior to the meeting at which the action is to be taken. Generally, to be timely, notice must be received at our principal executive offices not less than 90 days or more than 120 days prior to the first anniversary date of the annual meeting for the preceding year. The notice must contain certain information specified in the amended and restated by-laws. These provisions may have the effect of precluding the conduct of certain business at a meeting if the proper procedures are not followed. These provisions may also discourage or deter a potential acquirer from conducting a solicitation of proxies to elect the acquirer's own slate of directors or otherwise attempting to obtain control of our company.

Amendment to By-laws and Certificate of Incorporation

As required by the Delaware General Corporation Law, any amendment of our amended and restated certificate of incorporation must first be approved by a majority of our board of directors and, if required by law or our amended and restated certificate of incorporation, thereafter be approved by a majority of the outstanding shares entitled to vote on the amendment, and a majority of the outstanding shares of each class entitled to vote thereon as a class, except that the amendment of the provisions relating to stockholder action, directors, limitation of liability, exclusive jurisdiction of Delaware Courts and the amendment of our amended and restated by-laws and amended and restated certificate of incorporation must be approved by not less than 75% of the outstanding shares entitled to vote on the amendment, and not less than 75% of the outstanding shares of each class entitled to vote thereon as a class. Our amended and restated by-laws may be amended by the affirmative vote of a majority of the directors then in office, subject to any limitations set forth in the amended and restated by-laws; and may also be amended by the affirmative vote of at least 75% of the outstanding shares entitled to vote on the amendment, or, if the board of directors recommends that the stockholders approve the amendment, by the affirmative vote of the majority of the outstanding shares entitled to vote on the amendment, in each case voting together as a single class.

Blank Check Preferred Stock

Our amended and restated certificate of incorporation provides for 5,000,000 authorized shares of preferred stock. The existence of authorized but unissued shares of preferred stock may enable our board of directors to render more difficult or to discourage an attempt to obtain control of us by means of a merger, tender offer, proxy contest or otherwise. For example, if in the due exercise of its fiduciary obligations, our board of directors were to determine that a takeover proposal is not in the best interests of us or our stockholders, our board of directors could cause shares of preferred stock to be issued without stockholder approval in one or more private offerings or other transactions that might dilute the voting or other rights of the proposed acquirer or insurgent stockholder or stockholder group. In this regard, our amended and restated certificate of incorporation grants our board of directors broad power to establish the rights and preferences of authorized and unissued shares of preferred stock. The issuance of shares of preferred stock could decrease the amount of earnings and assets available for distribution to holders of shares of common stock. The issuance may also adversely affect the rights and powers, including voting

rights, of these holders and may have the effect of delaying, deterring or preventing a change in control of us.

Section 203 of the Delaware General Corporation Law

Upon completion of this offering, we will be subject to the provisions of Section 203 of the Delaware General Corporation Law. In general, Section 203 prohibits a publicly-held Delaware corporation from engaging in a "business combination" with an "interested stockholder" for a three-year period following the time that this stockholder becomes an interested stockholder, unless the business combination is approved in a prescribed manner. A "business combination" includes, among other things, a merger, asset or stock sale or other transaction resulting in a financial benefit to the interested stockholder. An "interested stockholder" is a person who, together with affiliates and associates, owns, or did own within three years prior to the determination of interested stockholder status, 15% or more of the corporation's voting stock.

Under Section 203, a business combination between a corporation and an interested stockholder is prohibited unless it satisfies one of the following conditions:

- before the stockholder became interested, the board of directors approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder;
- upon consummation 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 commenced, excluding for purposes of determining the voting stock outstanding, shares owned by persons who are directors and also officers, and employee stock plans, in some instances; or
- at or after the time the stockholder became interested, the business combination was approved by the board of directors of the corporation and authorized at an annual or special meeting of the stockholders by the affirmative vote of at least two-thirds of the outstanding voting stock that is not owned by the interested stockholder.

A Delaware corporation may "opt out" of these provisions with an express provision in its original certificate of incorporation or an express provision in its amended and restated certificate of incorporation or by-laws resulting from a stockholders' amendment approved by at least a majority of the outstanding voting shares. We have not opted out of these provisions. As a result, mergers or other takeover or change in control attempts of us may be discouraged or prevented.

Exclusive Jurisdiction of Certain Actions

Our amended and restated certificate of incorporation requires, to the fullest extent permitted by law, that derivative actions brought in our name, actions against our directors, officers and employees for breach of fiduciary duty and other similar actions may be brought only in the Court of Chancery in the State of Delaware, unless we otherwise consent. Although we believe this provision benefits us by providing increased consistency in the application of Delaware law in the types of lawsuits to which it applies, the provision may have the effect of discouraging lawsuits against our directors and officers.

NASDAQ Global Select Market Listing

Our common stock has been approved for listing on The NASDAQ Global Select Market under the trading symbol "BPMC."

Transfer Agent and Registrar

The transfer agent and registrar for our common stock will be Computershare Trust Company, N.A. The transfer agent and registrar's address is 250 Royall Street, Canton, Massachusetts, 02021.

SHARES ELIGIBLE FOR FUTURE SALE

Prior to this offering, there has been no public market for our common stock. Future sales of our common stock, including shares issued upon the exercise of outstanding options or warrants, in the public market after this offering, or the perception that those sales may occur, could cause the prevailing market price for our common stock to fall or impair our ability to raise equity capital in the future. As described below, only a limited number of shares of our common stock will be available for sale in the public market for a period of several months after completion of this offering due to contractual and legal restrictions on resale described below. Future sales of our common stock in the public market either before (to the extent permitted) or after restrictions lapse, or the perception that those sales may occur, could adversely affect the prevailing market price of our common stock at such time and our ability to raise equity capital at a time and price we deem appropriate.

Sale of Restricted Shares

Upon the closing of this offering, based on the number of shares of our common stock outstanding as of December 31, 2014, including 425,279 shares of unvested restricted stock subject to repurchase by us and 166,635 stock options that were exercised prior to vesting, and assuming (1) the conversion of our outstanding convertible preferred stock into common stock, (2) no exercise of the underwriters' option to purchase additional shares of common stock and (3) no exercise of outstanding options or warrants, we will have outstanding an aggregate of approximately 25,831,965 shares of common stock. Of these shares, all of the 8,145,834 shares of common stock to be sold in this offering, and any shares sold upon exercise of the underwriters' option to purchase 1,221,874 additional shares will be freely tradable in the public market without restriction or further registration under the Securities Act of 1933, as amended, or the Securities Act, unless the shares are held by any of our "affiliates" as such term is defined in Rule 144 of the Securities Act. All remaining shares of common stock held by existing stockholders immediately prior to the completion of this offering will be "restricted securities" as such term is defined in Rule 144. These restricted securities were issued and sold by us, or will be issued and sold by us, in private transactions and are eligible for public sale only if registered under the Securities Act or if they qualify for an exemption from registration under the Securities Act, including the exemptions provided by Rule 144 or Rule 701, which rules are summarized below.

As a result of the lock-up agreements referred to below and the provisions of Rule 144 and Rule 701 under the Securities Act, the shares of our common stock (excluding the shares sold in this offering) that will be available for sale in the public market are as follows:

Approximate Number of Shares	First Date Available for Sale into Public Market
13,294,402 shares	180 days after the date of this prospectus upon expiration of the lock-up agreements referred to below, subject in some cases to applicable volume limitations under Rule 144

Lock-up Agreements

In connection with this offering, we, our directors, our executive officers and stockholders holding substantially all of our shares of common stock outstanding as of December 31, 2014 (assuming conversion of all of our outstanding shares of convertible preferred stock), and substantially all of our option holders who are not also stockholders have agreed, subject to certain exceptions, with the underwriters not to dispose of or hedge any shares of our common stock or securities convertible into or exchangeable for shares of common stock during the period from the date of the lock-up agreement continuing through the date 180 days after the date of this

prospectus, except with the prior written consent of Goldman, Sachs & Co. and Cowen and Company, LLC, together the representatives of the underwriters. The representatives of the underwriters have advised us that they have no current intent or arrangement to release any of the shares subject to the lock-up agreements prior to the expiration of the lock-up period.

Following the lock-up periods set forth in the agreements described above, and assuming that the representatives of the underwriters do not release any parties from these agreements, all of the shares of our common stock that are restricted securities or are held by our affiliates as of the date of this prospectus will be eligible for sale in the public market in compliance with Rule 144 under the Securities Act.

In addition, pursuant to each of our second amended and restated investors' rights agreement and second amended and restated stockholders' agreement, the parties thereto have agreed that, if requested in writing by the representatives of the underwriters of the initial public offering of our securities, they will not sell, make any short sale of, grant any option for the purchase of, or otherwise dispose of any shares of our stock during the same 180-day restricted period referred to above. We expect the representatives of the underwriters to invoke this written request prior to the completion of this offering and, accordingly, that the parties to these agreements will be subject to the related transaction restrictions.

Rule 144

In general, under Rule 144, as currently in effect, once we have been subject to the public company reporting requirements of the Securities Exchange Act of 1934, as amended, or the Exchange Act, for at least 90 days, a person (or persons whose shares are required to be aggregated) who is not deemed to have been one of our "affiliates" for purposes of Rule 144 at any time during the three months preceding a sale, and who has beneficially owned restricted securities within the meaning of Rule 144 for at least six months, including the holding period of any prior owner other than one of our "affiliates," is entitled to sell those shares in the public market (subject to the lock-up agreement referred to above, if applicable) without complying with the manner of sale, volume limitations or notice provisions of Rule 144, but subject to compliance with the public information requirements of Rule 144. If such a person has beneficially owned the sales proposed to be sold for at least one year, including the holding period of any prior owner other than "affiliates," then such person is entitled to sell such shares in the public market without complying with any of the requirements of Rule 144 (subject to the lock-up agreement referred to above, if applicable). In general, under Rule 144, as currently in effect, once we have been subject to the public company reporting requirements of the Exchange Act for at least 90 days, our "affiliates," as defined in Rule 144, who have beneficially owned the shares proposed to be sold for at least six months are entitled to sell in the public market, upon expiration of any applicable lock-up agreements and within any three-month period, a number of those shares of our common stock that does not exceed the greater of:

- 1% of the number of common shares then outstanding, which will equal approximately 258,319 shares of common stock immediately after this offering (calculated on the basis of the number of shares of our common stock outstanding as of December 31, 2014, the assumptions described above and assuming no exercise of the underwriter's option to purchase additional shares and no exercise of outstanding options or warrants); or

- 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 such sale.

Such sales under Rule 144 by our "affiliates" or persons selling shares on behalf of our "affiliates" are also subject to certain manner of sale provisions, notice requirements and to the

availability of current public information about us. Notwithstanding the availability of Rule 144, the holders of substantially all of our restricted securities have entered into lock-up agreements as referenced above and their restricted securities will become eligible for sale (subject to the above limitations under Rule 144) upon the expiration of the restrictions set forth in those agreements.

Rule 701

In general, under Rule 701 as currently in effect, any of our employees, directors, officers, consultants or advisors who acquired common stock from us in connection with a written compensatory stock or option plan or other written agreement in compliance with Rule 701 under the Securities Act before the effective date of the registration statement of which this prospectus is a part (to the extent such common stock is not subject to a lock-up agreement) is entitled to rely on Rule 701 to resell such shares beginning 90 days after we become subject to the public company reporting requirements of the Exchange Act in reliance on Rule 144, but without compliance with the holding period requirements contained in Rule 144. Accordingly, subject to any applicable lock-up agreements, beginning 90 days after we become subject to the public company reporting requirements of the Exchange Act, under Rule 701 persons who are not our "affiliates," as defined in Rule 144, may resell those shares without complying with the minimum holding period or public information requirements of Rule 144, and persons who are our "affiliates" may resell those shares without compliance with Rule 144's minimum holding period requirements (subject to the terms of the lock-up agreement referred to below, if applicable).

Equity Incentive Plans

We intend to file with the SEC a registration statement under the Securities Act covering the shares of common stock that we may issue upon exercise of outstanding options reserved for issuance under the 2011 Stock Option Plan and the 2015 Plan. Such registration statement is expected to be filed and become effective as soon as practicable after the completion of this offering. Accordingly, shares registered under such registration statement will be available for sale in the open market following its effective date, subject to Rule 144 volume limitations and the lock-up agreements described above, if applicable.

MATERIAL U.S. FEDERAL INCOME TAX CONSIDERATIONS FOR NON-U.S. HOLDERS

The following is a summary of the material U.S. federal income tax consequences of the ownership and disposition of our common stock to Non-U.S. Holders, but does not purport to be a complete analysis of all the potential tax considerations relating thereto. This summary is based upon the provisions of the Internal Revenue Code of 1986, as amended (the "Code"), Treasury regulations promulgated thereunder, administrative rulings and judicial decisions, all as of the date hereof. These authorities may be changed or subject to differing interpretations, possibly with retroactive effect, so as to result in U.S. federal income tax consequences different from those set forth below. We have not sought and will not seek any ruling from the Internal Revenue Service (the "IRS"), with respect to the statements made and the conclusions reached in the following summary, and there can be no assurance that the IRS or a court will agree with such statements and conclusions.

This summary also does not address the tax considerations arising under the laws of any U.S. state or local or any non-U.S. jurisdiction, the Medicare tax on net investment income or any alternative minimum tax consequences. In addition, this discussion does not address tax considerations applicable to a Non-U.S. Holder's particular circumstances or to a Non-U.S. Holder that may be subject to special tax rules, including, without limitation:

- banks, insurance companies or other financial institutions;
- tax-exempt or government organizations;
- dealers in securities or currencies;
- traders in securities that elect to use a mark-to-market method of accounting for their securities holdings;
- persons that own, or are deemed to own, more than five percent of our capital stock;
- certain former citizens or long-term residents of the United States;
- persons who hold our common stock as a position in a hedging transaction, "straddle," "conversion transaction" or other risk reduction transaction;
- persons who do not hold our common stock as a capital asset within the meaning of Section 1221 of the Code (generally, for investment purposes);
- persons deemed to sell our common stock under the constructive sale provisions of the Code;
- real estate investment trusts or regulated investment companies;
- pension plans;
- S corporations, partnerships, or other entities or arrangements treated as partnerships for U.S. federal income tax purposes, or investors in any such entities);
- persons for whom our stock constitutes "qualified small business stock" within the meaning of Section 1202 of the Code;
- integral parts or controlled entities of foreign sovereigns;
- tax-qualified retirement plans;
- controlled foreign corporations;
- passive foreign investment companies and corporations that accumulate earnings to avoid U.S. federal income tax; or
- persons that acquire our common stock as compensation for services.

In addition, if a partnership, including any entity or arrangement classified as a partnership for U.S. federal income tax purposes, holds our common stock, the tax treatment of a partner generally

will depend on the status of the partner the activities of the partnership, and certain determinations made at the partner level. Accordingly, partnerships that hold our common stock, and partners in such partnerships, should consult their tax advisors regarding the U.S. federal income tax consequences to them of the purchase, ownership, and disposition of our common stock.

You are urged to consult your tax advisor with respect to the application of the U.S. federal income tax laws to your particular situation, as well as any tax consequences of the purchase, ownership and disposition of our common stock arising under the U.S. federal estate or gift tax rules or under the laws of any U.S. state or local or any non-U.S. or other taxing jurisdiction or under any applicable tax treaty.

Definition of a Non-U.S. Holder

For purposes of this summary, a "Non-U.S. Holder" is any beneficial owner of our common stock that is not a "U.S. person," a partnership, or an entity disregarded from its owner, each for U.S. federal income tax purposes. A U.S. person is any person that, for U.S. federal income tax purposes, is or is treated as any of the following:

- an individual who is a citizen or resident of the United States;
- a corporation (or other entity taxable as a corporation for U.S. federal income tax purposes) created or organized under the laws of the United States, any state thereof, or the District of Columbia;
- an estate, the income of which is subject to U.S. federal income tax regardless of its source; or
- a trust that (1) is subject to the primary supervision of a U.S. court and the control of one or more U.S. persons (within the meaning of Section 7701(a)(30) of the Code), or (2) has a valid election in effect to be treated as a U.S. person for U.S. federal income tax purposes.

Distributions

If we make distributions on our common stock, those payments will constitute dividends for U.S. tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. To the extent those distributions exceed both our current and our accumulated earnings and profits, they will constitute a return of capital and will first reduce a Non-U.S. Holder's basis in our common stock, but not below zero. Any excess will be treated as capital gain and will be treated as described below under "Gain on Sale or Other Disposition of Common Stock."

Subject to the discussion below on effectively connected income, any dividend paid to a Non-U.S. Holder generally will be subject to U.S. withholding tax either at a rate of 30% of the gross amount of the dividend or such lower rate as may be specified by an applicable income tax treaty. In order to receive a reduced treaty rate, a Non-U.S. Holder must provide us with an IRS Form W-8BEN (generally including a U.S. taxpayer identification number), IRS Form W-8-BEN-E or another appropriate version of IRS Form W-8 (or a successor form), in each case, certifying qualification for the reduced rate. A Non-U.S. Holder that does not timely furnish the required documentation, but that qualifies for a reduced treaty rate, may obtain a refund of any excess amounts withheld by timely filing an appropriate claim for refund with the IRS. Non-U.S. Holders should consult their tax advisors regarding their entitlement to benefits under any applicable income tax treaty.

Dividends paid to a Non-U.S. Holder that are effectively connected with the Non-U.S. Holder's conduct of a U.S. trade or business within the United States (and, if required by an applicable income tax treaty, are attributable to a permanent establishment maintained by the Non-U.S. Holder in the United States) generally are exempt from the withholding tax described above. In order to

obtain this exemption, the Non-U.S. Holder must provide the applicable withholding agent with an IRS Form W-8ECI or successor form or other applicable IRS Form W-8 certifying that the dividends are effectively connected with the Non-U.S. Holder's conduct of a trade or business within the United States. Such effectively connected dividends, although not subject to withholding tax, are taxed at the same graduated rates applicable to U.S. persons, net of certain deductions and credits, subject to an applicable income tax treaty providing otherwise. In addition, if you are Non-U.S. Holder that is a corporation, dividends you receive that are effectively connected with your conduct of a U.S. trade or business (and, if an income tax treaty applies, are attributable to a permanent establishment maintained by the you in the United States) may also be subject to a branch profits tax at a rate of 30% (or such lower rate as may be specified by an applicable income tax treaty) on such effectively connected dividends, as adjusted for certain items.

If you are eligible for a reduced rate of withholding tax pursuant to a tax treaty, you may be able to obtain a refund of any excess amounts currently withheld if you file an appropriate claim for refund with the IRS.

Gain on Sale or Other Disposition of Common Stock

Subject to the discussion below regarding backup withholding and FATCA, a Non-U.S. Holder generally will not be required to pay U.S. federal income tax on any gain realized upon the sale or other disposition of our common stock unless:

- the gain is effectively connected with the Non-U.S. Holder's conduct of a trade or business within the United States (and, if an income tax treaty applies, the gain is attributable to a permanent establishment maintained by the Non-U.S. Holder in the U.S.), in which case the Non-U.S. Holder will be required to pay tax on the net gain derived from the sale under regular graduated U.S. federal income tax rates, and for a Non-U.S. Holder that is a corporation, such Non-U.S. Holder may be subject to the branch profits tax at a 30% rate (or such lower rate as may be specified by an applicable income tax treaty) on such effectively connected dividends, as adjusted for certain items;

- the Non-U.S. Holder is an individual who is present in the United States for a period or periods aggregating 183 days or more during the calendar year in which the sale or disposition occurs and certain other conditions are met, in which case the Non-U.S. Holder will be required to pay a flat 30% tax on the gain derived from the sale, which tax may be offset by U.S. source capital losses (even though the Non-U.S. Holder is not considered a resident of the United States) (subject to applicable income tax or other treaties); or

- our common stock constitutes a U.S. real property interest by reason of our status as a "U.S. real property holding corporation" for U.S. federal income tax purposes, a USRPHC, at any time within the shorter of the five-year period preceding the disposition or the Non-U.S. Holder's holding period for our common stock. We believe we are not currently and do not anticipate becoming a USRPHC. However, because the determination of whether we are a USRPHC depends on the fair market value of our U.S. real property interests relative to the fair market value of our other business assets, there can be no assurance that we will not become a USRPHC in the future. Even if we become a USRPHC, however, gain arising from the sale or other taxable disposition by a Non-U.S. Holder of our common stock will not be subject to U.S. federal income tax as long as our common stock is regularly traded on an established securities market and such Non-U.S. Holder does not, actually or constructively, hold more than five percent of our common stock at any time during the applicable period that is specified in the Code. If the foregoing exception does not apply, then if we are or were to become a USRPHC a purchaser may be required to withhold 10% of the proceeds payable to a Non-U.S. Holder from a sale of our common stock and such Non-U.S. Holder generally will be taxed on its net gain derived from the disposition at the graduated U.S. federal income tax rates applicable to United States persons (as defined in the Code).

Backup Withholding and Information Reporting

Generally, we must file information returns annually to the IRS in connection with any dividends on our common stock paid to a Non-U.S. Holder, regardless of whether any tax was actually withheld. A similar report will be sent to the Non-U.S. Holder. Pursuant to applicable income tax treaties or other agreements, the IRS may make these reports available to tax authorities in the Non-U.S. Holder's country of residence.

Payments of dividends or of proceeds on the disposition of stock made to a Non-U.S. Holder may be subject to additional information reporting and backup withholding at a current rate of 28% unless such Non-U.S. Holder establishes an exemption, for example by properly certifying its non-U.S. status on an IRS Form W-8BEN, IRS Form W-8BEN-E, IRS Form W-8ECI, or another appropriate version of IRS Form W-8 (or a successor form). Notwithstanding the foregoing, backup withholding and information reporting may apply if either we or our paying agent has actual knowledge, or reason to know, that a holder is a U.S. person.

Backup withholding is not an additional tax; rather, the U.S. income tax liability of persons subject to backup withholding will be reduced by the amount of tax withheld. If withholding results in an overpayment of taxes, a refund or credit may generally be obtained from the IRS, provided that the required information is furnished to the IRS in a timely manner.

Foreign Account Tax Compliance Act ("FATCA")

The Foreign Account Tax Compliance Act ("FATCA") may impose withholding tax on certain types of payments made to foreign financial institutions and certain other non-U.S. entities. The legislation imposes a 30% withholding tax on dividends on, or gross proceeds from the sale or other disposition of, our common stock paid to a "foreign financial institution" or to certain "non-financial foreign entities" (each as defined in the Code), unless (i) the foreign financial institution undertakes certain diligence and reporting obligations, (ii) the non-financial foreign entity either certifies it does not have any "substantial United States owners" (as defined in the Code) or furnishes identifying information regarding each substantial United States owner, or (iii) the foreign financial institution or non-financial foreign entity otherwise qualifies for an exemption from these rules. If the payee is a foreign financial institution and is subject to the diligence and reporting requirements in (i) above, it must enter into an agreement with the U.S. Treasury requiring, among other things, that it undertake to identify accounts held by "specified United States persons" or "United States-owned foreign entities" (each as defined in the Code), annually report certain information about such accounts, and withhold 30% on payments to account holders whose actions prevent it from complying with these reporting and other requirements. If the country in which a payee is resident has entered into an "intergovernmental agreement" with the United States regarding FATCA, that agreement may permit the payee to report to that country rather than to the U.S. Department of the Treasury. Under final regulations and published guidance, the obligation to withhold from payments made to a foreign financial institution or a foreign non-financial entity under FATCA with respect to dividends on our common stock began on July 1, 2014, but with respect to the gross proceeds of a sale or other disposition of our common stock will not begin until January 1, 2017. Prospective investors should consult their tax advisors regarding FATCA.

Federal Estate Tax

Common stock owned (or treated as owned) by an individual who is not a citizen or a resident of the United States (as defined for U.S. federal estate tax purposes) at the time of death will be included in the individual's gross estate for U.S. federal estate tax purposes unless an applicable estate or other tax treaty provides otherwise, and therefore may be subject to U.S. federal estate tax.

The preceding discussion of U.S. federal tax considerations is for general information only. It is not tax advice. Each prospective investor should consult its tax advisor regarding the particular U.S. federal, state and local and non-U.S. tax consequences of purchasing, holding and disposing of our common stock, including the consequences of any proposed change in applicable laws.

UNDERWRITING

We have entered into an underwriting agreement with the underwriters named below with respect to the shares being offered. Subject to certain conditions, each underwriter has severally agreed to purchase the number of shares indicated in the following table. Goldman, Sachs & Co. and Cowen and Company, LLC are the representatives of the underwriters.

Underwriters	Number of Shares
Goldman, Sachs & Co.	3,665,626
Cowen and Company, LLC	2,647,396
JMP Securities LLC	916,406
Wedbush Securities Inc.	916,406
Total	8,145,834

The underwriters are committed to take and pay for all of the shares being offered, if any are taken, other than the shares covered by the option described below unless and until this option is exercised.

The underwriters have an option to buy up to an additional 1,221,874 shares from us to cover sales by the underwriters of a greater number of shares than the total number set forth in the table above. They may exercise that option for 30 days. If any shares are purchased pursuant to this option, the underwriters will severally purchase shares in approximately the same proportion as set forth in the table above.

The following table shows the per share and total underwriting discounts and commissions to be paid to the underwriters by us. Such amounts are shown assuming both no exercise and full exercise of the underwriters' option to purchase 1,221,874 additional shares.

Paid by the Company

	No Exercise	Full Exercise
Per Share	$1.26	$1.26
Total	$10,263,751	$11,803,312

Shares sold by the underwriters to the public will initially be offered at the initial public offering price of $18.00. Any shares sold by the underwriters to securities dealers may be sold at a discount of up to $0.756 per share from the initial public offering price. After the initial offering of the shares, the representatives may change the offering price and the other selling terms. The offering of the shares by the underwriters is subject to receipt and acceptance and subject to the underwriters' right to reject any order in whole or in part.

We and our officers, directors, and holders of substantially all of our common stock have agreed with the underwriters, subject to certain exceptions, not to dispose of or hedge any of their common stock or securities convertible into or exchangeable for shares of common stock during the period from the date of this prospectus continuing through the date 180 days after the date of this prospectus, except with the prior written consent of the representatives. This agreement does not apply to any existing employee benefit plans. See "Shares Available for Future Sale" for a discussion of certain transfer restrictions.

Prior to the offering, there has been no public market for the shares. The initial public offering price has been negotiated among us and the representatives. Among the factors to be considered in determining the initial public offering price of the shares, in addition to prevailing market

conditions, will be our historical performance, estimates of our business potential and earnings prospects, an assessment of our management and the consideration of the above factors in relation to market valuation of companies in related businesses.

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

In connection with the offering, the underwriters may purchase and sell shares of common stock in the open market. These transactions may include short sales, stabilizing transactions and purchases to cover positions created by short sales. Short sales involve the sale by the underwriters of a greater number of shares than they are required to purchase in the offering, and a short position represents the amount of such sales that have not been covered by subsequent purchases. A "covered short position" is a short position that is not greater than the amount of additional shares for which the underwriters' option described above may be exercised. The underwriters may cover any covered short position by either exercising their option to purchase additional shares or purchasing shares in the open market. In determining the source of shares to cover 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 additional shares pursuant to the option described above. "Naked" short sales are any short sales that create a short position greater than the amount of additional shares for which the option described above may be exercised. The underwriters must cover any such naked short position by purchasing 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 common stock in the open market after pricing that could adversely affect investors who purchase in the offering. Stabilizing transactions consist of various bids for or purchases of common stock made by the underwriters in the open market prior to the completion of the offering.

The underwriters may also impose a penalty bid. This occurs when a particular underwriter repays to the underwriters a portion of the underwriting discount received by it because the representatives have repurchased shares sold by or for the account of such underwriter in stabilizing or short covering transactions.

Purchases to cover a short position and stabilizing transactions, 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 our stock, and together with the imposition of the penalty bid, may stabilize, maintain or otherwise affect the market price of the common stock. As a result, the price of the common stock may be higher than the price that otherwise might exist in the open market. The underwriters are not required to engage in these activities and may end any of these activities at any time. These transactions may be effected on The NASDAQ Global Select Market, in the over-the-counter market or otherwise.

The underwriters do not expect sales to discretionary accounts to exceed five percent of the total number of shares offered.

We estimate that our share of the total expenses of the offering, excluding underwriting discounts and commissions, will be approximately $2,600,000. We have also agreed to reimburse the underwriters for certain of their expenses in an amount up to $50,000.

We have agreed to indemnify the several underwriters against certain liabilities, including liabilities under the Securities Act of 1933.

The underwriters and their respective affiliates are full service financial institutions engaged in various activities, which may include sales and trading, commercial and investment banking, advisory, investment management, investment research, principal investment, hedging, market making, brokerage and other financial and non-financial activities and services. Certain of the

underwriters and their respective affiliates have provided, and may in the future provide, a variety of these services to the issuer and to persons and entities with relationships with the issuer, for which they received or will receive customary fees and expenses.

In the ordinary course of their various business activities, the underwriters and their respective affiliates, officers, directors and employees may purchase, sell or hold a broad array of investments and actively traded securities, derivatives, loans, commodities, currencies, credit default swaps and other financial instruments for their own account and for the accounts of their customers, and such investment and trading activities may involve or relate to assets, securities and/or instruments of the issuer (directly, as collateral securing other obligations or otherwise) and/or persons and entities with relationships with the issuer. The underwriters and their respective affiliates may also communicate independent investment recommendations, market color or trading ideas and/or publish or express independent research views in respect of such assets, securities or instruments and may at any time hold, or recommend to clients that they should acquire, long and/or short positions in such assets, securities and instruments.

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), each underwriter has represented and agreed that with effect from and including the date on which the Prospectus Directive is implemented in that Relevant Member State (the Relevant Implementation Date) it has not made and will not make an offer of shares to the public in that Relevant Member State prior to the publication of a prospectus in relation to the shares that has been approved by the competent authority in that Relevant Member State or, where appropriate, approved in another Relevant Member State and notified to the competent authority in that Relevant Member State, all in accordance with the Prospectus Directive, except that it may, with effect from and including the Relevant Implementation Date, make an offer of shares to the public in that Relevant Member State at any time:

- to any legal entity that 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 representatives 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 of our common stock shall result in a requirement for the publication by us or any underwriter of a prospectus pursuant to Article 3 of the Prospectus Directive.

For the purposes of this provision, the expression an "offer of shares to the public" in relation to any shares 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 same may be varied in that Relevant Member State by any measure implementing the Prospectus Directive in that Relevant Member State and the expression Prospectus Directive means Directive 2003/71/EC (and amendments thereto, including the 2010 PD Amending Directive) and includes any relevant implementing measure in each Relevant Member State, and the expression "2010 PD Amending Directive" means Directive 2010/73/EU.

United Kingdom

Each underwriter has represented and agreed that:

- it has only communicated or caused to be communicated and will only communicate or cause to be communicated an invitation or inducement to engage in investment activity (within the meaning of Section 21 of the FSMA) received by it in connection with the issue or sale of the shares in circumstances in which Section 21(1) of the FSMA does not apply to the Issuer; and
- it has complied and will comply with all applicable provisions of the FSMA with respect to anything done by it in relation to the shares in, from or otherwise involving the United Kingdom.

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.

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:

- you confirm and warrant that you are either:
    - a "sophisticated investor" under section 708(8)(a) or (b) of the Corporations Act;

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

- 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.

Hong Kong

The shares may not be offered or sold by means of any document other than (i) in circumstances that do not constitute an offer to the public within the meaning of the Companies Ordinance (Cap. 32, Laws of Hong Kong), (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 that 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 that 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.

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 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, 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.

Where the shares are subscribed or purchased under Section 275 by a relevant person that is: (a) a corporation (which is not an accredited investor) 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 (b) a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary is an accredited investor, shares, debentures and units of shares and debentures of that corporation or the beneficiaries' rights and interest in that trust shall not be transferable for 6 months after that corporation or that trust has

acquired the shares under Section 275 except: (1) to an institutional investor under Section 274 of the SFA or to a relevant person, or any person pursuant to Section 275(1A), and in accordance with the conditions, specified in Section 275 of the SFA; (2) where no consideration is given for the transfer; or (3) by operation of law.

Japan

The securities have not been and will not be registered under the Financial Instruments and Exchange Law of Japan (the Financial Instruments and Exchange Law) and each underwriter has agreed that it will not offer or sell any securities, directly or indirectly in Japan or to, or for the benefit of, any resident of Japan (which term as used herein means any person resident in Japan, including any corporation or other entity organized under the laws of Japan), or to others for re-offering or resale, directly or indirectly, in Japan or to a resident of Japan, except pursuant to an exemption from the registration requirements of, and otherwise in compliance with, the Financial Instruments and Exchange Law and any other applicable laws, regulations and ministerial guidelines of Japan.

Israel

In the State of Israel this prospectus shall not be regarded as an offer to the public to purchase shares of common stock under the Israeli Securities Law, 5728-1968, which requires a prospectus to be published and authorized by the Israel Securities Authority, if it complies with certain provisions of Section 15 of the Israeli Securities Law, 5728-1968, including, inter alia, if: (i) the offer is made, distributed or directed to not more than 35 investors, subject to certain conditions (the "Addressed Investors"); or (ii) the offer is made, distributed or directed to certain qualified investors defined in the First Addendum of the Israeli Securities Law, 5728-1968, subject to certain conditions (the "Qualified Investors"). The Qualified Investors shall not be taken into account in the count of the Addressed Investors and may be offered to purchase securities in addition to the 35 Addressed Investors. The company has not and will not take any action that would require it to publish a prospectus in accordance with and subject to the Israeli Securities Law, 5728-1968. We have not and will not distribute this prospectus or make, distribute or direct an offer to subscribe for our common stock to any person within the State of Israel, other than to Qualified Investors and up to 35 Addressed Investors.

Qualified Investors may have to submit written evidence that they meet the definitions set out in of the First Addendum to the Israeli Securities Law, 5728-1968. In particular, we may request, as a condition to be offered common stock, that Qualified Investors will each represent, warrant and certify to us and/or to anyone acting on our behalf: (i) that it is an investor falling within one of the categories listed in the First Addendum to the Israeli Securities Law, 5728-1968; (ii) which of the categories listed in the First Addendum to the Israeli Securities Law, 5728-1968 regarding Qualified Investors is applicable to it; (iii) that it will abide by all provisions set forth in the Israeli Securities Law, 5728-1968 and the regulations promulgated thereunder in connection with the offer to be issued common stock; (iv) that the shares of common stock that it will be issued are, subject to exemptions available under the Israeli Securities Law, 5728-1968: (a) for its own account; (b) for investment purposes only; and (c) not issued with a view to resale within the State of Israel, other than in accordance with the provisions of the Israeli Securities Law, 5728-1968; and (v) that it is willing to provide further evidence of its Qualified Investor status. Addressed Investors may have to submit written evidence in respect of their identity and may have to sign and submit a declaration containing, inter alia, the Addressed Investor's name, address and passport number or Israeli identification number

LEGAL MATTERS

The validity of the issuance of our common stock offered in this prospectus will be passed upon for us by Goodwin Procter LLP, Boston, Massachusetts. Certain legal matters in connection with this offering will be passed upon for the underwriters by Latham & Watkins LLP.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our financial statements at December 31, 2013 and December 31, 2014 and for each of the two years in the period ended December 31, 2014, as set forth in their report, which is included in this prospectus and elsewhere in the registration statement. 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 YOU CAN FIND MORE INFORMATION

We have filed with the SEC a registration statement on Form S-1, including exhibits and schedules, under the Securities Act that registers the shares of our common stock to be sold in this offering. This prospectus does not contain all the information contained in the registration statement and the exhibits and schedules filed as part of the registration statement. For further information with respect to us and our common stock, we refer you to the registration statement and the exhibits and schedules filed as part of the registration statement. Statements contained in this prospectus as to the contents of any contract or other document are not necessarily complete. If a contract or document has been filed as an exhibit to the registration statement, we refer you to the copies of the contract or document that has been filed. Each statement in this prospectus relating to a contract or document filed as an exhibit is qualified in all respects by the filed exhibit.

Upon the consummation of this offering, we will file annual, quarterly and current reports, proxy statements and other information with the SEC under the Exchange Act. You can read our SEC filings, including the registration statement, at the SEC's website at www.sec.gov.

You may read and copy this information at the SEC's Public Reference Room at 100 F Street, N.E., Washington D.C. 20549, at prescribed rates. You may obtain information regarding the operation of the public reference room by calling the SEC at 1-800-SEC-0330. The SEC also maintains a website (http://www.sec.gov) that contains reports, proxy and information statements and other information regarding issuers that file electronically with the SEC.

Our website address is www.blueprintmedicines.com. The information contained in, and that can be accessed through, our website is not incorporated into and is not part of this prospectus.

Blueprint Medicines Corporation
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REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

The Board of Directors and Stockholders of
Blueprint Medicines Corporation

We have audited the accompanying balance sheets of Blueprint Medicines Corporation (the "Company") as of December 31, 2013 and 2014, and the related statements of operations, convertible preferred stock and stockholders' (deficit) equity, and cash flows for the years then ended. 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 Blueprint Medicines Corporation at December 31, 2013 and 2014, and the results of its operations and its cash flows for the years then ended in conformity with U.S. generally accepted accounting principles.

/s/ Ernst & Young LLP

Boston, Massachusetts
February 19, 2015, except for Note 12B,
as to which the date is April 20, 2015

Blueprint Medicines Corporation

Balance Sheets

(in thousands, except share and per share data)

	December 31, 2013	December 31, 2014	Pro forma December 31, 2014 (unaudited)
Assets			
Current assets:			
Cash and cash equivalents	$ 1,987	$ 47,240	$ 47,240
Restricted cash	—	119	119
Prepaid expenses and other current assets	461	915	915
Total current assets	2,448	48,274	48,274
Property and equipment, net	1,404	1,482	1,482
Other assets	94	99	99
Restricted cash	189	70	70
Total assets	$ 4,135	$ 49,925	$ 49,925
Liabilities, convertible preferred stock and stockholders' (deficit) equity			
Current liabilities:			
Accounts payable	1,414	814	814
Accrued expenses	866	3,810	3,810
Deferred rent	141	138	138
Restricted stock liability	24	298	298
Current portion of term loan payable	708	1,704	1,704
Total current liabilities	3,153	6,764	6,764
Deferred rent, net of current portion	137	—	—
Restricted stock liability, net of current portion	67	29	29
Warrant liability	119	365	—
Term loan payable, net of current portion	2,155	7,338	7,338
Commitments (Note 10)			
Series A convertible preferred stock, $0.001 par value: 40,150,000 shares authorized; 40,000,000, 40,000,000 and no shares issued and outstanding at December 31, 2013, December 31, 2014 and December 31, 2014 pro forma, respectively (liquidation preference of $48,238 at December 31, 2014)	39,958	39,958	—
Series B convertible preferred stock, $0.001 par value: no shares and 20,999,996 shares authorized at December 31, 2013 and 2014, respectively; no shares, 20,916,663 and no shares issued and outstanding at December 31, 2013, December 31, 2014 and December 31, 2014 pro forma, respectively (liquidation preference of $27,075 at December 31, 2014)	—	24,985	—
Series C convertible preferred stock, $0.001 par value: no shares and 24,154,589 shares authorized at December 31, 2013 and 2014, respectively; no shares, 24,154,589 and no shares issued and outstanding at December 31, 2013, December 31, 2014 and December 31, 2014 pro forma, respectively (liquidation preference of $50,592 at December 31, 2014)	—	49,868	—
Stockholders' (deficit) equity:			
Common stock, $0.001 par value; 110,000,000 shares authorized; 2,087,808 and 2,218,652 shares issued at December 31, 2013 and 2014, respectively, and 1,221,330 and 1,626,738 shares outstanding at December 31, 2013 and 2014, respectively, and 17,686,131 and 17,094,217 shares issued and outstanding at December 31, 2014 pro forma, respectively	1	2	17
Additional paid-in capital	466	2,822	117,983
Accumulated deficit	(41,921)	(82,206)	(82,206)
Total stockholders' (deficit) equity	(41,454)	(79,382)	35,794
Total liabilities, convertible preferred stock, and stockholders' (deficit) equity	$ 4,135	$ 49,925	$ 49,925

Blueprint Medicines Corporation

Statements of Operations

(in thousands, except per share data)

	Year Ended December 31,	
	2013	**2014**
Operating expenses:		
Research and development	$ 15,928	$ 31,844
General and administrative	5,072	7,890
Total operating expenses	21,000	39,734
Other income (expense):		
Other income (expense), net	226	(98)
Interest and other expense	(138)	(453)
Total other income (expense)	88	(551)
Net loss	$ (20,912)	$ (40,285)
Convertible preferred stock dividends	(2,870)	(5,765)
Net loss applicable to common stockholders	$ (23,782)	$ (46,050)
Net loss per share applicable to common stockholders — basic and diluted	$ 23.43	$ 32.41
Weighted-average number of common shares used in net loss per share applicable to common stockholders — basic and diluted	1,015	1,421
Pro forma net loss per share applicable to common stockholders — basic and diluted (unaudited)		$ (3.07)
Pro forma weighted average number of common shares used in net loss per share applicable to common stockholders — basic and diluted (unaudited)		13,083

Blueprint Medicines Corporation

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

(in thousands, except share and per share data)

	Series A Convertible Preferred Stock		Series B Convertible Preferred Stock		Series C Convertible Preferred Stock		Common Stock		Additional Paid-in Capital	Accumulated Deficit	Stockholders' (Deficit) Equity
	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount			
Balance at December 31, 2012	25,000,000	$ 24,970	—	—	—	—	720,031	$ 1	$ 92	$ (21,009)	$ (20,916)
Issuance of Series A convertible preferred stock at $1.00 per share, net of issuance costs of $12	15,000,000	14,988	—	—	—	—	—	—	—	—	—
Issuance of common stock under stock plan	—	—	—	—	—	—	501,299	—	23	—	23
Stock-based compensation expense	—	—	—	—	—	—	—	—	351	—	351
Net loss	—	—	—	—	—	—	—	—	—	(20,912)	(20,912)
Balance at December 31, 2013	40,000,000	$ 39,958	—	$ —	—	$ —	1,221,320	$ 1	$ 466	$ (41,921)	$ (41,454)
Issuance of Series B convertible preferred stock at $1.20 per share, net of issuance costs of $115	—	—	20,916,663	24,985	—	—	—	—	—	—	—
Issuance of Series C convertible preferred stock at $2.07 per share, net of issuance costs of $131	—	—	—	—	24,154,589	49,868	—	—	—	—	—
Issuance of common stock under stock plan	—	—	—	—	—	—	405,408	1	30	—	31
Stock-based compensation expense	—	—	—	—	—	—	—	—	2,326	—	2,326
Net loss	—	—	—	—	—	—	—	—	—	(40,285)	(40,285)
Balance at December 31, 2014	40,000,000	$ 39,958	20,916,663	$ 24,985	24,154,589	$ 49,868	1,626,738	$ 2	$ 2,822	$ (82,206)	$ (79,382)
Conversion of preferred stock into common stock (unaudited)	(40,000,000)	(39,958)	(20,916,663)	(24,985)	(24,154,589)	(49,868)	15,467,479	15	114,796	—	114,811
Reclassification of warrant to purchase preferred stock to stockholders' equity (unaudited)	—	—	—	—	—	—	—	—	365	—	365
Pro forma balance at December 31, 2014 (unaudited)	—	$ —	—	$ —	—	$ —	17,094,217	$ 17	$ 117,983	$ (82,206)	$ 35,794

Blueprint Medicines Corporation

Statements of Cash Flows

(in thousands)

	Year Ended December 31,	
	2013	**2014**
Operating activities		
Net loss	$ (20,912)	$ (40,285)
Adjustments to reconcile net loss to net cash used in in operating activities:		
Depreciation and amortization	501	622
Noncash interest expense	26	85
Change in fair value of warrant liability	(4)	100
Stock-based compensation	351	2,326
Changes in assets and liabilities:		
Prepaid expenses and other current assets	16	(469)
Other assets	20	—
Accounts payable	541	(512)
Accrued expenses	550	2,873
Deferred rent	(114)	(140)
Net cash used in operating activities	(19,025)	(35,400)
Investing activities		
Purchases of property and equipment	(257)	(700)
Net cash used in investing activities	(257)	(700)
Financing activities		
Proceeds from term loan	3,000	7,000
Principal payments on loan payable	—	(750)
Proceeds from issuance of Series A convertible preferred stock, net of issuance costs	14,987	—
Proceeds from issuance of Series B convertible preferred stock, net of issuance costs	—	24,985
Proceeds from issuance of Series C convertible preferred stock, net of issuance costs	—	49,868
Debt issuance costs	(48)	(18)
Proceeds from issuance of common stock	53	268
Net cash provided by financing activities	17,992	81,353
Net (decrease) increase in cash and cash equivalents	(1,290)	45,253
Cash and cash equivalents at beginning of period	3,277	1,987
Cash and cash equivalents at end of period	$ 1,987	$ 47,240
Supplemental cash flow information		
Cash paid for interest	$ 53	$ 215
Supplemental noncash financing activity		
Issuance of warrants in connection with term loan	$ 119	$ 145

Blueprint Medicines Corporation

Notes to Financial Statements

1. Nature of Business

Blueprint Medicines Corporation (the Company), a Delaware corporation formed on October 14, 2008, is a biopharmaceutical company focused on improving the lives of patients with genomically defined diseases driven by abnormal kinase activation. The Company's approach is to systematically and reproducibly identify kinases that are drivers of genomically defined diseases and to craft drug candidates with therapeutic windows that provide significant and durable clinical response to patients.

The Company is devoting substantially all of its efforts to research and development, initial market development, and raising capital. The Company has an accumulated deficit as of December 31, 2014 of approximately $82.2 million and will require substantial additional capital for research and product development. The Company is subject to a number of risks similar to those of other early stage companies, including dependence on key individuals; the need to develop commercially viable drugs; competition from other companies, many of which are larger and better capitalized; and the need to obtain adequate additional financing to fund the development of its drugs. If the Company is unable to raise capital when needed or on attractive terms, it would be forced to delay, reduce, eliminate or out-license certain of its research and development programs or future commercialization efforts.

At December 31, 2014, the Company believes its cash and cash equivalents, totaling approximately $47.2 million, are sufficient to fund operations through at least January 1, 2016.

2. Summary of Significant Accounting Policies

Basis of Presentation

The accompanying financial statements have been prepared in accordance with United States (U.S.) generally accepted accounting principles ("U.S. GAAP") and include all adjustments necessary for the fair presentation of the Company's financial position for the periods presented.

Use of Estimates

The preparation of financial statements in conformity with U.S. generally accepted accounting principles (GAAP) requires the Company's management to make estimates and assumptions that affect the amounts reported in the financial statements and accompanying notes. Actual results could differ from those estimates. Management considers many factors in selecting appropriate financial accounting policies and in developing the estimates and assumptions that are used in the preparation of the financial statements. Management must apply significant judgment in this process. Management's estimation process often may yield a range of potentially reasonable estimates and management must select an amount that falls within that range of reasonable estimates. Estimates are used in the following areas, among others: stock-based compensation expense, including estimating the fair value of the Company's common stock (the "Common Stock"); the valuation of liability-classified warrants; accrued expenses; and income taxes.

Unaudited Pro Forma Financial Information

On February 10, 2015, the Company's board of directors authorized the management of the Company to submit on a confidential basis a registration statement with the Securities and Exchange Commission ("SEC") for the Company to sell shares of its Common Stock to the public.

Blueprint Medicines Corporation

Notes to Financial Statements (Continued)

2. Summary of Significant Accounting Policies (Continued)

Upon the closing of a qualified initial public offering, all of the Company's outstanding convertible preferred stock will automatically convert into Common Stock. The unaudited pro forma consolidated balance sheet and statement of convertible preferred stock and stockholders' (deficit) equity as of December 31, 2014 assumes the conversion of all outstanding convertible preferred stock into shares of Common Stock and the reclassification of the warrant liability to additional paid-in capital upon the completion of this proposed offering.

Comprehensive Income (Loss)

Comprehensive income (loss) is defined as the change in equity of a business enterprise during a period from transactions and other events and circumstances from non-owner sources. For the years ended December 31, 2013 and 2014, comprehensive loss was equal to net loss.

Cash Equivalents

Cash equivalents are highly liquid investments that are readily convertible into cash with original maturities of three months or less when purchased. These assets include an investment in a money market fund that invests in U.S. Treasury obligations. Cash equivalents consist of the following at December 31, 2013 and 2014 (in thousands):

	2013	2014
Money market fund	$ 1,987	$ 47,240

Fair Value of Financial Instruments

The fair value hierarchy prioritizes the inputs to valuation techniques used to measure fair value into three broad levels as follows:

Level 1 inputs are quoted prices (unadjusted) in active markets for identical assets or liabilities.

Level 2 inputs are inputs other than quoted prices included within Level 1 that are observable for the asset or liability, either directly or indirectly.

Level 3 inputs are unobservable inputs that reflect the Company's own assumptions about the assumptions market participants would use in pricing the asset or liability. Financial assets and liabilities are classified in their entirety based on the lowest level of input that is significant to the fair value measurement.

Financial instruments measured at fair value as of December 31, 2013, are classified below based on the fair value hierarchy described above:

Description	December 31, 2013	Active Markets (Level 1)	Observable Inputs (Level 2)	Unobservable Inputs (Level 3)
Money market funds, included in cash equivalents	$ 1,987	$ 1,987	$ —	$ —
Preferred stock warrants	(119)	—	—	(119)

Blueprint Medicines Corporation

Notes to Financial Statements (Continued)

2. Summary of Significant Accounting Policies (Continued)

Financial instruments measured at fair value as of December 31, 2014, are classified below based on the fair value hierarchy described above:

Description	December 31, 2014	Active Markets (Level 1)	Observable Inputs (Level 2)	Unobservable Inputs (Level 3)
Money market funds, included in cash equivalents	$ 47,240	$ 47,240	$ —	$ —
Preferred stock warrants	(365)	—	—	(365)

At December 31, 2013 and 2014, all of the Company's cash equivalents comprise of a money market account, the fair value of which is valued using Level 1 inputs. The fair value of the Company's term loan payable is determined using current applicable rates for similar instruments as of the balance sheet date. The carrying value of the Company's term loan payable approximates fair value because the Company's interest rate yield approximates current market rates. The Company's term loan payable is a Level 3 liability within the fair value hierarchy. The fair value of the preferred stock warrant liability was determined based on Level 3 inputs and utilizing the Black-Scholes option pricing model (see Note 6).

Research and Development Costs

Expenditures relating to research and development are expensed in the period incurred. Research and development expenses consist of both internal and external costs associated with the development of the Company's selective cancer therapies and building of its platform.

In certain circumstances, the Company is required to make nonrefundable advance payments to vendors for goods or services that will be received in the future for use in research and development activities. In such circumstances, the nonrefundable advance payments are deferred and capitalized, even when there is no alternative future use for the research and development, until related goods or services are provided. As of December 31, 2013 and 2014, the Company had prepaid expenses of approximately $0.1 million in each year related to nonrefundable advance payments to vendors.

Property and Equipment, Net

Property and equipment consists of lab equipment, furniture and fixtures, computer equipment, software, and leasehold improvements, all of which is stated at cost. Expenditures for maintenance and repairs are recorded to expense as incurred, whereas major betterments are capitalized as additions to property and equipment. Depreciation is recognized over the estimated useful lives of the assets using the straight-line method.

Impairment of Long-Lived Assets

The Company continually evaluates whether events or circumstances have occurred that indicate that the estimated remaining useful life of its long-lived assets may warrant revision or that the carrying value of these assets may be impaired. The Company has not recognized any impairment charges through December 31, 2014.

Blueprint Medicines Corporation

Notes to Financial Statements (Continued)

2. Summary of Significant Accounting Policies (Continued)

Warrants

The Company accounts for warrant instruments that either conditionally or unconditionally obligate the issuer to transfer assets and liabilities regardless of the timing of the redemption feature or price, even though the underlying shares may be classified as permanent or temporary equity. These warrants are subject to revaluation at each balance sheet date, and any changes in fair value are recorded as a component of other income (expense), until the earlier of their exercise or expiration or the completion of a liquidation event, including the completion of an initial public offering, at which time the warrant liability will be reclassified to stockholders' equity if the criteria for recording the warrant as an equity instrument are met. The warrant liability totaled $0.1 million and $0.4 million at December 31, 2013 and 2014, respectively (see Note 6).

Stock-Based Compensation Expense

The Company expenses the fair value of employee stock awards net of estimated forfeitures, adjusted to reflect actual forfeitures on a straight-line basis over the requisite service period, which generally is the vesting period. Compensation cost for restricted stock awards issued to employees is measured using the grant date intrinsic value of the award, net of estimated forfeitures, adjusted to reflect actual forfeitures. The Company estimates the fair value of the options granted to employees at the date of grant using the Black-Scholes option-pricing model that requires management to apply judgment and make estimates, including:

- expected volatility, which is calculated based on reported volatility data for a representative group of publicly traded companies for which historical information is available. Since the Company is privately held as of the date of these financial statements, it does not have relevant historical data to support its expected volatility. As such, the Company has used an average of expected volatility based on the volatilities of a representative group of publicly traded biopharmaceutical companies. For purposes of identifying representative companies, the Company considered characteristics such as number of drug candidates in early stages of drug development, area of therapeutic focus, length of trading history, similar vesting provisions and a similar percentage of stock options that were in-the-money. The expected volatility was determined using an average of the historical volatilities of the representative group of companies for a period equal to the expected term of the option grant. The Company intends to consistently apply this process using the same representative companies until a sufficient amount of historical information regarding the volatility of the Company's own share price becomes available or until circumstances change, such that the identified entities are no longer representative companies. In the latter case, more suitable, similar entities whose share prices are publicly available would be utilized in the calculation;

- risk-free interest rate, which is based on the U.S. Treasury yield curve in effect at the time of grant commensurate with the expected life assumption;

- expected term, which the Company calculates using the simplified method, as prescribed by the Securities and Exchange Commission Staff Accounting Bulletin No. 107, *Share-Based Payment,* as the Company has insufficient historical information regarding stock options to provide a basis for an estimate;

Blueprint Medicines Corporation

Notes to Financial Statements (Continued)

2. Summary of Significant Accounting Policies (Continued)

- fair value of the underlying common shares, which is determined using the option-pricing method (OPM) or a hybrid of the probability-weighted expected return method, or PWERM, and the OPM, and was approved by our board of directors; and

- dividend yield which is zero based on the fact that the Company never paid cash dividends and does not expect to pay any cash dividends in the foreseeable future.

The amount of stock-based compensation expense recognized during a period is based on the fair value of the portion of the awards that are ultimately expected to vest. Forfeitures are estimated at the time of grant and revised, if necessary, in subsequent periods if actual forfeitures differ from those estimates. The term "forfeitures" is distinct from "cancellations" or "expirations" and represents only the unvested portion of the surrendered option. The Company evaluates its forfeiture rate at each reporting period. Ultimately, the actual expense recognized over the vesting period will be for only those options that vest.

Stock-based awards issued to non-employees, including directors for non-board-related services, are accounted for based on the fair value of such services received or of the intrinsic value of equity instruments issued, whichever is more reliably measured. These stock-based awards are revalued at each vesting date and period-end. Stock-based awards subject to service-based vesting conditions are expensed on a straight-line basis over the vesting period.

Income Taxes

The Company recognizes deferred tax assets and liabilities for the expected future tax consequences of events that have been recognized in the Company's financial statements or tax returns. Under this method, deferred tax assets and liabilities are determined based on differences between the financial statement carrying amounts and the tax bases of the assets and liabilities using the enacted tax rates in effect in the years in which the differences are expected to reverse. A valuation allowance against deferred tax assets is recorded if, based on the weight of the available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized. The Company accounts for uncertain tax positions using a more-likely-than-not threshold for recognizing and resolving uncertain tax positions. The evaluation of uncertain tax positions is based on factors including, but not limited to, changes in the law, the measurement of tax positions taken or expected to be taken in tax returns, the effective settlement of matters subject to audit, new audit activity, and changes in facts or circumstances related to a tax position.

Concentrations of Credit Risk and Off-Balance-Sheet Risk

The Company has no significant off-balance-sheet risk such as foreign exchange contracts, option contracts, or other foreign hedging arrangements. Financial instruments that potentially expose the Company to concentrations of credit risk primarily consist of cash and cash equivalents. The Company maintains its cash and cash equivalents in a custodian account at a high quality financial institution, and consequently, the Company believes that such funds are subject to minimal credit risk.

Blueprint Medicines Corporation

Notes to Financial Statements (Continued)

2. Summary of Significant Accounting Policies (Continued)

Segment and Geographic Information

Operating segments are identified as components of an enterprise about which separate discrete financial information is available for evaluation by the chief operating decision maker, or decision making group, in making decisions on how to allocate resources and assess performance. The Company's chief operating decision maker is the chief executive officer. The Company and the chief operating decision maker view the Company's operations and manage its business as one operating segment. The Company operates only in the United States.

Net Loss per Share Applicable to Common Stockholders

Basic net loss per share applicable to common stockholders is calculated by dividing net loss applicable to common stockholders by the weighted average shares outstanding during the period, without consideration for common stock equivalents. Net loss applicable to common stockholders is calculated by adjusting the net loss of the Company for cumulative preferred stock dividends. Diluted net loss per share applicable to common stockholders is calculated by adjusting weighted average shares outstanding for the dilutive effect of common stock equivalents outstanding for the period. For purposes of the dilutive net loss per share applicable to common stockholders calculation, convertible preferred stock, warrants, stock options, and unvested restricted stock are considered to be common stock equivalents but are excluded from the calculation of diluted net loss per share applicable to common stockholders, as their effect would be anti-dilutive; therefore, basic and diluted net loss per share applicable to common stockholders were the same for all periods presented. The following common stock equivalents were excluded from the calculation of diluted net loss per share applicable to common stockholders for the periods indicated because including them would have had an anti-dilutive effect.

	Years ended December 31,	
	2013	2014
Convertible preferred stock	7,272,726	15,467,479
Warrants	27,272	42,423
Stock options	385,250	1,501,912
Unvested restricted stock	836,712	425,279
Total	8,521,960	17,437,093

Unaudited pro forma net loss per share applicable to common stockholders is computed using the weighted-average number of common shares outstanding after giving effect to the conversion of all convertible preferred stock into shares of the Common Stock as if such conversion had occurred at the beginning of the period presented, or the date of original issuance, if later. Accordingly, the pro forma basic and diluted net loss per share applicable to stockholders does not include the effects of the cumulative preferred stock dividends. Additionally, the changes in the fair value of the warrants to purchase convertible preferred stock have been excluded from the determination of unaudited pro forma net loss as those re-measurements would not be required when the warrants to purchase convertible preferred stock become warrants to purchase Common Stock. Shares to be sold in the offering are excluded from the unaudited pro forma basic and diluted loss per share applicable to common stockholders calculations.

Blueprint Medicines Corporation

Notes to Financial Statements (Continued)

2. Summary of Significant Accounting Policies (Continued)

Unaudited pro forma net loss per share applicable to common stockholders is computed as follows (in thousands except for share and per share information):

	Year Ended December 31, 2014
Net loss	$ (40,285)
Add back: remeasurement of warrant to purchase convertible preferred stock	100
Net loss per share applicable to common stockholders — basic and diluted	$ (40,185)
Pro forma weighted average common shares outstanding:	
Weighted average common shares outstanding	1,420,518
Adjustment for assumed conversion of convertible preferred stock	11,662,970
Pro forma weighted average common shares outstanding — basic and diluted	13,083,488
Pro forma basic and diluted loss per share applicable to common stockholders	$ (3.07)

Recent Accounting Pronouncements

In 2014, the FASB issued new guidance on management's responsibility in evaluating whether or not there is substantial doubt about a company's ability to continue as a going concern within one year from the date the financial statements are issued each reporting period. This new accounting guidance is effective for annual periods ending after December 15, 2016. Early adoption is permitted. The Company is in process of evaluating the new guidance and determining the expected effect on its financial statements.

In June 2014, the FASB issued Accounting Standards Update ("ASU") 2014-10, Development Stage Entities (Topic 915) ("ASU 2014-10"), which removes the definition of a development stage entity from the ASC, thereby removing the financial reporting distinction between development stage entities and other reporting entities. Accordingly, ASU 2014-10 eliminates the requirements for development stage entities to (1) present inception-to-date information in the statements of operations, cash flows and shareholder equity, (2) label financial statements as those of a development stage entity, (3) disclose a description of the development stage activities in which the entity is engaged and (4) disclose in the first year in which the entity is no longer a development stage entity that in prior years it had been in the development stage. ASU 2014-10 is effective for public business entities for annual periods beginning after December 15, 2014, and interim reporting periods beginning after December 15, 2015, with early adoption permitted. The Company early adopted the provisions of ASU 2014-10 in these financial statements.

Blueprint Medicines Corporation

Notes to Financial Statements (Continued)

3. Restricted Cash

At December 31, 2013 and 2014, $0.2 million of the Company's cash is restricted by a bank. As of December 31, 2014, $0.1 million of the restricted cash is included in current assets as collateral for a stand-by letter of credit issued by the Company to its landlord in connection with the lease of the Company's corporate headquarters. As of December 31, 2014, $0.1 million of the restricted cash is included in long-term assets related to the Company's corporate credit card agreement.

4. Property and Equipment, Net

Property and equipment and related accumulated depreciation are as follows (in thousands):

	Estimated Useful Life (Years)	December 31	
		2013	2014
Lab equipment	5	$ 1,719	$ 2,000
Furniture and fixtures	4	285	326
Computer equipment	3	275	369
Leasehold improvements	Term of lease	—	191
Software	3	49	142
		2,328	3,028
Less: accumulated depreciation and amortization		(924)	(1,546)
Total property and equipment, net		$ 1,404	$ 1,482

Depreciation expense for the years ended December 31, 2013 and 2014 was $0.5 million and $0.6 million, respectively.

5. Accrued Expenses

Accrued expenses consist of the following (in thousands):

	December 31	
	2013	2014
Employee compensation	$ 278	$ 623
External research and pre-clinical development	91	2,034
Severance	150	330
Consulting	108	216
License fees	100	—
Interest	28	150
Other	111	457
	$ 866	$ 3,810

Blueprint Medicines Corporation

Notes to Financial Statements (Continued)

6. Term Loan

In May 2013, the Company entered into a loan and security agreement (Loan and Security Agreement) with Silicon Valley Bank. Under the terms of the agreement, the Company may borrow up to $5.0 million. Loan advances accrue interest at a fixed rate of 2% above the Prime Rate. In June 2013, the Company drew the first loan advance of $1.0 million under the Loan and Security Agreement and was required to make interest-only payments until April 1, 2014, and consecutive monthly payments of principal, plus accrued interest, over the remaining term through March 2017. In September 2013, the Company drew the second loan advance of $2.0 million under the Loan and Security Agreement and was required to make interest-only payments until April 1, 2014, and consecutive monthly payments of principal, plus accrued interest, over the remaining term through March 2017. In June 2014, the Company drew the remaining $2.0 million advance under the Loan and Security Agreement and is required to make interest-only payments until January 1, 2015, and consecutive monthly payments of principal, plus accrued interest, over the remaining term through December 2017. In November 2014, the Company amended the Loan and Security Agreement to allow the Company to borrow an additional $5.0 million. The Company accounted for the amendment as a modification to the existing Loan and Security Agreement. The Company immediately drew the additional $5.0 million and is required to make interest-only payments until December 1, 2015, and consecutive monthly payments of principal, plus accrued interest, over the remaining term through November 2018. The Company is required to pay a fee of 4.00% of the total loan advances at the end of the term of the loan. The fee is being accreted to interest expense over the term of the loan. In the event of prepayment, the Company is obligated to pay 1% to 2% of the amount of the outstanding principal depending upon the timing of the prepayment.

The term loan is collateralized by a blanket lien on all corporate assets, excluding intellectual property, and by a negative pledge of the Company's intellectual property. The term loan contains customary default provisions that include material adverse events, as defined therein. The Company has determined that the risk of subjective acceleration under the material adverse events clause is remote and therefore has classified the outstanding principal in current and long-term liabilities based on scheduled principal payments.

The Company assessed all terms and features of the term loan in order to identify any potential embedded features that would require bifurcation. As part of this analysis, the Company assessed the economic characteristics and risks of the term loan, including put and call features. The Company determined that all features of the term loan are clearly and closely associated with a debt host and do not require bifurcation as a derivative liability, or the fair value of the feature is immaterial to the Company's financial statements. The Company will continue to reassess the features on a quarterly basis to determine if they require separate accounting.

Scheduled monthly principal payments on the term loan, as of December 31, 2014, are as follows (in thousands):

2015	$	1,806
2016		3,333
2017		2,583
2018		1,528
Total	$	9,250

Blueprint Medicines Corporation

Notes to Financial Statements (Continued)

6. Term Loan (Continued)

In connection with the Loan and Security Agreement, the Company issued a warrant to Silicon Valley Bank to purchase 150,000 shares of Series A Convertible Preferred Stock at an exercise price of $1.00 per share. In connection with the amendment to the Loan and Security Agreement, the Company issued a warrant to Silicon Valley Bank to purchase 83,333 shares of Series B Convertible Preferred Stock at an exercise price of $1.20 per share. Both warrants were exercisable immediately and have a ten-year life. No portion of the warrants have been exercised as of December 31, 2014.

The warrants are classified as a liability and are re-measured to the-then current fair value at each balance sheet date. Re-measurement gains or losses are recorded in other income (expense) in the statements of operations. The following table sets forth a summary of changes in the fair value of the warrants which represents a recurring measurement that is classified within Level 3 of the fair value hierarchy wherein fair value is estimated using significant unobservable inputs (in thousands):

	Year Ended	
	December 31, 2013	December 31, 2014
Beginning balance	$ —	$ 119
Issuance of warrant at fair value	123	146
Change in fair value	(4)	100
Ending balance	$ 119	$ 365

The Company valued the warrants for the purchase of Series A and B Convertible Preferred Stock ("Series A and Series B Warrants") at issuance and at the balance sheet dates using the Black-Scholes option pricing model. The significant assumptions used in estimating the fair value of the warrants include the volatility of the stock underlying the warrant, risk-free interest rate, estimated fair value of the preferred stock underlying the warrant, and the estimated term of the warrant. The fair value of the preferred stock underlying the warrants was estimated using the implied value from the Company's Common Stock valuations on those dates. The Company used the following weighted-average assumptions in its Black-Scholes option pricing model:

	Series A Warrant			Series B Warrant	
	Issuance	December 31, 2013	December 31, 2014	Issuance	December 31, 2014
Fair value of underlying instrument	$ 1.00	$ 1.00	$ 1.69	$ 1.97	$ 1.97
Expected volatility	80.70%	89.00%	89.98%	87.18%	87.38%
Expected term (in years)	10.0	9.5	8.4	10.0	9.8
Risk-free interest rate	2.58%	3.05%	2.15%	2.36%	2.24%
Expected dividend yield	—%	—%	—%	—%	—%

The Company recorded a debt discount upon issuance of the warrants, which is being accreted as interest expense over the remaining term of the loan. The Company also recorded a

Blueprint Medicines Corporation

Notes to Financial Statements (Continued)

6. Term Loan (Continued)

warrant liability that is classified as a long-term liability in the accompanying balance sheets. The Company recorded interest expense related to the Series A and Series B Warrants of less than $0.1 million in each of the years ended December 31, 2013 and 2014.

7. Stockholders' (Deficit) Equity

Series A Convertible Preferred Stock

In January and September 2013, the Company issued 10,000,000 and 5,000,000 shares, respectively, of Series A Convertible Preferred Stock at a price of $1.00 per share, resulting in net proceeds of $15.0 million.

Series B Convertible Preferred Stock Financing

In January 2014, the Company issued a total of 20,916,663 shares of Series B Convertible Preferred Stock at $1.20 per share for net proceeds of $25.0 million.

Series C Convertible Preferred Stock Financing

In November 2014, the Company issued a total of 24,154,589 shares of Series C Convertible Preferred Stock at $2.07 per share for net proceeds of $49.9 million.

Convertible Preferred Stock

The rights, preferences, and privileges of the Preferred Stock are listed below:

Conversion

Shares of Preferred Stock are convertible without payment of any additional consideration into such number of fully paid and non-assessable shares of Common Stock as determined by dividing the original issuance price by the conversion price at the time in effect. The conversion price is the original price, or $5.50 per share for Series A, $6.60 per share for Series B and $11.38 per share for Series C, subject to adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization with respect to the Preferred Stock.

Conversion is at the option of the Preferred Stockholders, although conversion is automatic upon the earlier of the consummation of an initial public offering resulting in gross proceeds to the Company of at least $40 million and at a price of at least $12.52 per share of Common Stock or the vote or written consent of the majority of outstanding shares of Series A, B and C Convertible Preferred Stock.

Dividends

Holders of the Preferred Stock are entitled to receive, before any cash is paid out or set aside for any Common Stock, dividends at the annual rate of 8% of the original purchase price per share, subject to adjustment for stock splits; stock dividends; or, in certain circumstances, the sale of Common Stock at a price below the original issue price of the Preferred Stock. The dividends are cumulative, and are payable only when and if declared by the board of directors of the Company.

Blueprint Medicines Corporation

Notes to Financial Statements (Continued)

7. Stockholders' (Deficit) Equity (Continued)

No dividends have been declared since inception. Aggregate cumulative dividends at December 31, 2014 were $10.8 million.

Liquidation Preference

Holders of Series C Convertible Preferred Stock and Series B Convertible Preferred stock have preference in the event of a liquidation, dissolution, sale, or winding up of the Company equal to the greater of $11.38 per share for Series C and $6.60 per share for Series B, plus any accrued but unpaid dividends whether or not declared, plus any dividends declared but unpaid thereon or such amount per share as would have been payable had all shares of Series C Convertible Preferred Stock and Series B Convertible Preferred Stock been converted into Common Stock immediately prior to such liquidation.

After the payment of all liquidation preferences to holders of Series C and Series B Convertible Preferred Stock, holders of the Series A Preferred Stock have preference in the event of a liquidation, dissolution, sale, or winding up of the Company equal to the greater of $5.50 per share, plus any accrued but unpaid dividends whether or not declared, plus any dividends declared but unpaid thereon or such amount per share as would have been payable had all shares of Series A Convertible Preferred Stock been converted into Common Stock immediately prior to such liquidation.

Thereafter, if assets remain in the Company, the holders of the Common Stock shall receive all of the remaining assets of the Company pro rata based on the number of shares of Common Stock held by each. If the assets of the Company are insufficient to pay the full preferential amounts to the preferred stockholders, the assets shall be distributed ratably among such holders in proportion to their aggregate liquidation preference amounts.

As the Preferred Stock may become redeemable upon an event that is outside of the control of the Company, the Preferred Stock has been classified outside of stockholders' (deficit) equity. Since the Preferred Stock is not initially redeemable and it is not probable that it will become redeemable, the carrying value of the Preferred Stock has not been adjusted.

Voting Rights

Holders of the Series A, Series B and Series C Convertible Preferred Stock are entitled to vote as a single class with the holders of Common Stock and shall have one vote for each equivalent common share into which the preferred stock is convertible. A majority vote of the Series A Preferred Stockholders, Series B Preferred Stockholders and Series C Preferred Stockholders is required in order to amend the Certificate of Incorporation or By-Laws; reclassify Common Stock or establish another class of stock; create or authorize additional shares of preferred stock; effect a sale, liquidation, or merger of the Company; repurchase or redeem any capital stock; or engage in any action that would adversely affect the holders of the preferred stock.

The Company assessed the Series A, B and C Convertible Preferred Stock for any beneficial conversion features or embedded derivatives, including the conversion option, that would require bifurcation from the Series A, B and C Convertible Preferred Stock and receive separate accounting treatment. Based on the Company's determination that the Preferred Stock is an "equity host," the Company determined that all features of the Preferred Stock are clearly and closely related to the

Blueprint Medicines Corporation

Notes to Financial Statements (Continued)

7. Stockholders' (Deficit) Equity (Continued)

equity host, and do not require bifurcation as a derivative liability. On the date of issuance, the fair value of Common Stock into which the Series A, B and C Convertible Preferred Stock was convertible was less than the effective conversion price of the Series A, B and C Convertible Preferred Stock, and as such, there was no intrinsic value of the conversion option at the commitment date.

Common Stock

The holders of the Company's Common Stock are entitled to one vote for each share held. Common stockholders are not entitled to receive dividends, unless declared by the board of directors.

The Company has reserved the following shares of Common Stock for the potential conversion of Preferred Stock and the issuance of Common Stock in connection with stock options:

	December 31	
	2013	2014
Series A Convertible Preferred Stock	7,272,726	7,272,726
Series B Convertible Preferred Stock	—	3,803,024
Series C Convertible Preferred Stock	—	4,391,729
Warrants	27,272	42,423
Stock options	555,221	1,775,481
	7,855,219	17,285,383

8. Stock Awards

The Company grants restricted stock awards, incentive stock options (ISO), and nonstatutory stock options (NSO) under the Blueprint Medicines Corporation 2011 Stock Option and Grant Plan (the Plan), as amended and restated. At December 31, 2014, there were 273,350 shares available for future grant under the Plan. ISOs may not be granted at less than fair value on the date of the grant. Furthermore, the exercise price of ISOs granted to an employee, who at the time of grant is a 10% shareholder, may not be less than 110% of the fair value on the date of grant.

Terms of restricted stock awards and stock option agreements, including vesting requirements, are determined by the board of directors, subject to the provisions of the Plan. Options and restricted stock awards granted by the Company generally vest ratably over four years, with a one-year cliff for new employee awards, and are exercisable from the date of grant for a period of ten years. For options and restricted stock awards granted to date, the exercise price equaled the estimated fair value of the Common Stock as determined by the board of directors on the date of grant. The dates of the Company's contemporaneous valuations have not always coincided with the dates of the stock option grants. For financial reporting purposes, the Company performed common stock valuations with the assistance of a third-party specialist, as of January 6, 2014, July 30, 2014 and November 10, 2014 to determine stock-based compensation expense.

Blueprint Medicines Corporation

Notes to Financial Statements (Continued)

8. Stock Awards (Continued)

During the year ended December 31, 2013, the Company issued 124,252 and 110,906 shares of Common Stock to employees and non-employees, respectively. The shares were issued under the terms of the Plan, and allow the Company, at its discretion, to repurchase unvested shares if the employees terminate their relationship with the Company. The shares vest over a one-year or four-year term. The shares are recorded in stockholders' (deficit) equity as they vest. The Company did not issue any shares of Common Stock to employees or non-employees during the year ended December 31, 2014.

A summary of the Company's unvested restricted stock and related information follows:

	Shares	Weighted-Average Grant Date Fair Value
Unvested at December 31, 2013	836,712	$ 0.42
Granted	—	—
Vested	(398,792)	0.36
Repurchased	(12,641)	0.31
Unvested at December 31, 2014	425,279	0.46

The Company has granted restricted stock to non-employees which contain both performance-based and service-based vesting criteria. Stock-based compensation expense associated with these performance-based awards is recognized if the performance condition is considered probable of achievement using management's best estimates. During the year ended December 31, 2014 management concluded that the milestones associated with 181,818 shares of performance-based restricted stock were probable of achievement, and the Company began to record stock-based compensation expense using the accelerated attribution method, accordingly. The Company recorded $0.9 million of stock-based compensation expense for non-employee performance-based awards in the year ended December 31, 2014. A summary of the Company's stock option activity and related information follows:

	Shares	Weighted-Average Exercise Price	Remaining Contractual Life (in Years)	Aggregate Intrinsic Value(3) (in thousands)
Outstanding at December 31, 2013	385,250	$ 1.48	9.81	$ 148
Granted	1,226,103	2.14		
Exercised	(10,521)	1.48		
Canceled	(98,920)	1.51		
Outstanding at December 31, 2014(1)	1,501,912	$ 2.02	9.42	$ 7,704
Exercisable at December 31, 2014	171,700	$ 1.68	8.99	$ 940
Vested and expected to vest at December 31, 2014(2)	1,442,277	$ 2.02	9.42	$ 7,399

(1) Includes 166,635 unvested shares of common stock related to early exercises of stock options.

Blueprint Medicines Corporation

Notes to Financial Statements (Continued)

8. Stock Awards (Continued)

(2) Represents the number of vested options as of December 31, 2014, plus the number of unvested options expected to vest as of December 31, 2014.

(3) Intrinsic value represents the amount by which the fair market value as of December 31, 2014 of the underlying common stock exceeds the exercise price of the option.

The fair value of stock options is estimated on the grant date using the Black-Scholes option-pricing model based on the following weighted average assumptions:

	Year Ended	
	December 31, 2013	December 31, 2014
Risk-free interest rate	1.70% - 2.84%	1.70% - 2.14%
Expected dividend yield	0.00%	0.00%
Expected term (years)	6.1	6.1
Expected stock price volatility	88.96%	92.99%

The weighted-average grant date fair value of options granted in the years ended December 31, 2013 and 2014 was $1.18 and $3.46, respectively. The total intrinsic value of options exercised in the year ended December 31, 2014 was $0.1 million. There were no options exercised in the year ended December 31, 2013.

Total stock-based compensation expense recognized for all stock-based compensation awards in the statements of operations is as follows (in thousands):

	Year Ended December 31	
	2013	2014
Research and development	$ 224	$ 1,052
General and administrative	127	1,274
Total stock-based compensation expense	$ 351	$ 2,326

At December 31, 2014, there was $4.7 million of total unrecognized compensation cost related to nonvested stock awards, which is expected to be recognized over a weighted-average period of 2.84 years. Due to an operating loss, the Company does not record tax benefits associated with stock-based compensation or option exercises. Tax benefit will be recorded when realized.

Blueprint Medicines Corporation

Notes to Financial Statements (Continued)

9. Income Taxes

A reconciliation of the U.S. statutory income tax rate to the Company's effective tax rate is as follows for the years ended December 31, 2013 and 2014:

	Year Ended December 31,	
	2013	2014
Federal income tax (benefit) at statutory rate	34.00%	34.00%
Permanent differences	0.38	(1.87)
Federal research and development credits	2.08	1.30
State income tax, net of federal benefit	5.16	4.93
Other	1.46	0.70
Change in valuation allowance	(43.08)	(39.06)
Effective income tax rate	0.00%	0.00%

The Company had net losses in all periods presented and therefore has not recognized any federal or state income tax expense.

The Company's deferred tax assets and liabilities consist of the following:

	December 31	
	2013	2014
Deferred tax assets:		
Net operating loss carryforwards	$ 15,993	$ 30,603
Research and development credit carryforwards	1,123	1,949
Accrued expenses and other	294	628
Deferred rent	109	54
Total gross deferred tax asset	17,519	33,234
Deferred tax liability	(139)	(85)
Debt discount	(41)	(74)
Valuation allowance	(17,339)	(33,075)
Net deferred tax asset	$ —	$ —

Management has evaluated the positive and negative evidence bearing upon the realizability of its deferred tax assets, and has determined that it is more likely than not that the Company will not recognize the benefits of its federal and state deferred tax assets, and as a result, a valuation allowance of $17.3 million and $33.0 million has been established at December 31, 2013 and 2014, respectively. The change in the valuation allowance was $9.0 million and $15.7 million for the years ended December 31, 2013 and 2014, respectively. The Company has incurred net operating losses (NOL) since inception. At December 31, 2014, the Company had federal and state NOL carryforwards of $78.1 million and $76.6 million, respectively, which expire beginning in 2030. As of December 31, 2014, the Company had federal and state research and development tax credit carryforwards of $1.5 million and $0.7 million, respectively, which expire beginning in 2025. The

Blueprint Medicines Corporation

Notes to Financial Statements (Continued)

9. Income Taxes (Continued)

Company does not have any NOL carryforwards associated with deductible stock option exercises as of December 31, 2013 or 2014.

The Internal Revenue Code of 1986, as amended (the "Code"), provides for a limitation of the annual use of net operating losses and other tax attributes (such as research and development tax credit carryforwards) following certain ownership changes (as defined by the Code) that could limit the Company's ability to utilize these carryforwards. At this time, the Company has not completed a study to assess whether an ownership change under Section 382 of the Code has occurred, or whether there have been multiple ownership changes since the Company's formation. The Company may have experienced ownership changes, as defined by the Code, as a result of past financing transactions. Accordingly, the Company's ability to utilize the aforementioned carryforwards may be limited. Additionally, U.S. tax laws limit the time during which these carryforwards may be applied against future taxes. Therefore, the Company may not be able to take full advantage of these carryforwards for federal or state income tax purposes.

Interest and penalty charges, if any, related to unrecognized tax benefits would be classified as income tax expense in the accompanying statements of operations. As of December 31, 2013 and 2014, the Company has no accrued interest related to uncertain tax positions. Interest and penalty charges, if any, related to unrecognized tax benefits would be classified as income tax expense in the accompanying statements of operations In many cases, the Company's uncertain tax positions are related to years that remain subject to examination by relevant tax authorities. Since the Company is in a loss carryforward position, it is generally subject to examination by the U.S. federal, state, and local income tax authorities for all tax years in which a loss carryforward is available.

10. Commitments

Operating Lease

The Company leases its corporate headquarters under an operating lease that expires on November 1, 2015. In March 2014, the Company amended its existing lease agreement to expand the size of the original premises by 4,422 square feet. The rent per square foot for the additional space is $52.00. All other terms of the lease remain materially unchanged. On February 1, 2015, the Company's option to extend the term of the lease for an additional three-year period expired. The Company did not exercise its option. The Company's lease agreement has escalating rent payments. The Company recorded $0.6 million and $0.8 million of rent expense for the years ended December 31, 2013 and 2014, respectively. The Company records rent expense on a straight-line basis. The lease agreement required the Company to pay a security deposit of $0.1 million, which is included in restricted cash in the accompanying balance sheet.

The minimum aggregate future lease commitments at December 31, 2014, are as follows (in thousands):

2015	$ 875

Blueprint Medicines Corporation

Notes to Financial Statements (Continued)

11. Related-Party Transactions

The Company has received consulting and management services from one of its investors, Third Rock Ventures LLC (Third Rock Ventures). The Company paid Third Rock Ventures $0.4 million for these services during each of the years ended December 31, 2013 and 2014. At December 31, 2013, $0.1 million due to Third Rock Ventures was included in accrued expenses. All amounts owed to Third Rock Ventures for services rendered in the year ended December 31, 2014 were paid by December 31, 2014.

12A. Subsequent Events — Lease Agreement and Amendment to 2011 Stock Option and Grant Plan

Lease Agreement

On February 12, 2015, the Company entered into a lease for approximately 38,500 rentable square feet of office and laboratory space in Cambridge, Massachusetts, with a lease term commencing June 15, 2015 and ending on October 31, 2022, assuming occupancy in October 2015. The Company has an option to extend the lease for five additional years. The lease agreement requires the Company to pay a security deposit of $1.3 million, which will be recorded in restricted cash on the Company's balance sheet. The lease has a total committment of $17.9 million over the seven year term.

Amendment to 2011 Stock Option and Grant Plan

In February 2015, the Company amended the Blueprint Medicines Corporation 2011 Stock Option and Grant Plan to increase the number of shares available for grant to 3,590,927.

12B. Subsequent Events — Collaboration Agreement and Reverse Stock Split

Collaboration Agreement

In March 2015, the Company entered into a research, development and commercialization agreement, with Alexion Pharma Holding, or Alexion, to research, develop and commercialize drug candidates for an undisclosed activated kinase target, which is the cause of a rare genetic disease. Under the terms of this agreement, the Company will be responsible for research and pre-clinical development activities related to drug candidates and Alexion will be responsible for all clinical development, manufacturing and commercialization activities related to drug candidates.

Alexion is responsible for funding 100% of the Company's research and development costs incurred under the research plan, including pass-through costs and the Company's employees' time devoted to the research plan at a negotiated yearly rate per full-time equivalent for its employees' time and associated overhead expenses. The Company received a $15.0 million non-refundable upfront payment in March 2015 upon execution of the Alexion agreement and is eligible to receive over $250 million in payments upon the successful achievement of pre-specified pre-clinical, clinical, regulatory and commercial milestones as follows: (i) up to $6.0 million in pre-clinical milestone payments for the first licensed product, (ii) up to $83.0 million and $61.5 million in development milestone payments for the first and second licensed products, respectively, and (iii) up to $51.0 million in commercial milestone payments for each of the first and second licensed products. Alexion will pay the Company tiered royalties, ranging from the mid-single to low-double digit percentages royalties, on a country-by-country and licensed

Blueprint Medicines Corporation

Notes to Financial Statements (Continued)

12B. Subsequent Events — Collaboration Agreement and Reverse Stock Split (Continued)

product-by-licensed product basis, on worldwide net product sales of licensed products. The royalty term for each licensed product in each country is the period commencing with first commercial sale of such licensed product in such country and ending on the later of (i) the expiration of the last-to-expire valid claim of specified patents covering such licensed product, (ii) the expiration of the applicable regulatory exclusivity period, and (iii) 10 or 15 years from specified commercial sales, whichever comes earlier.

Alexion has the right to terminate the Alexion agreement due to the Company's uncured breach or insolvency, industry transaction involving the Company, or voluntarily upon 90 days prior written notice. The Company has the right to terminate the Alexion agreement due to Alexion's uncured breach or insolvency, or certain other events agreed to by the parties.

Reverse Stock Split

In connection with preparing for its initial public offering, the Company effected a 1-for-5.5 reverse stock split of the Company's common stock. The reverse stock split became effective on April 10, 2015. All share and per share amounts in the financial statements and notes thereto have been retroactively adjusted for all periods presented to give effect to this reverse stock split, including reclassifying an amount equal to the reduction in par value of common stock to additional paid-in capital.

8,145,834 Shares

Blueprint Medicines Corporation

Common Stock

Goldman, Sachs & Co. **Cowen and Company**

JMP Securities

Wedbush PacGrow

Through and including May 24, 2015 (the 25th day after the date of this prospectus), all dealers effecting transactions in these securities, whether or not participating in this offering, may be required to deliver a prospectus. This is in addition to a dealer's obligation to deliver a prospectus when acting as an underwriter and with respect to an unsold allotment or subscription.