2016

ANNUAL REPORT

NASDAQ: BPMC

To our stockholders

At Blueprint Medicines, we are striving to create a blueprint for a healthier tomorrow.

We seek to create transformative medicines for genomically defined patient populations by specifically targeting the molecular drivers of disease. By leveraging our proprietary compound library and genomics expertise, we are able to rapidly move from the bench to clinical proof-of-concept. Our culture and values put patients first, and we are driven by a deep sense of urgency to develop new medicines for unserved or underserved patients. In 2016, we generated early data that show our scientific approach could be prolific and may represent a substantial opportunity for developing new and transformative drugs for cancer, rare genetic diseases and other disease areas including cancer immunology.

Powerful Precision

The year 2016 was a pivotal one, in which we accomplished all of our goals and made significant progress toward developing potentially transformative medicines for a number of rare cancers and other diseases. In the fourth quarter, we presented encouraging clinical proof-of-concept data from three Phase 1 trials evaluating BLU-285 for the treatment of unresectable gastrointestinal stromal tumors (GIST), BLU-285 for the treatment of advanced systemic mastocytosis (SM) and BLU-554 for the treatment of advanced hepatocellular carcinoma (HCC). These trials continue to enroll patients and generate important insights into the safety and clinical activity of BLU-285 and BLU-554.

In addition, we continued to advance and expand our diverse pipeline, which we believe is substantial for a company of our age. Recently, we enrolled the first patient in a Phase 1 clinical trial of BLU-667, our third clinical-stage drug candidate, which targets RET mutations and fusions. This trial is now actively enrolling patients with non-small cell lung cancer, medullary thyroid cancer and other advanced solid tumors characterized by RET alterations. BLU-667 is specifically designed to be equipotent against wild-type RET mutants and fusions as well as predicted resistant mutants. This design allows BLU-667 to potentially offer patients profound, durable responses to therapy. In addition, we entered into a strategic collaboration with Roche early last year encompassing up to five programs targeting immunokinases, which are believed to be important in cancer immunotherapy.

Jeff Albers, President and CEO

When Blueprint Medicines was founded, we established an ambitious vision to improve the lives of patients with genomically defined diseases. In 2017, this vision will come into clearer focus. We expect a cadence of data updates for BLU-285 and BLU-554 as these programs advance in the clinic. In parallel, we plan to work closely with U.S. and European regulatory authorities to determine the most efficient development path forward for both programs.

The Drive to Make Discovery Faster

Importantly, we have maintained a strong financial position to enable us to continue to advance our existing clinical programs while also investing in ongoing discovery efforts. We ended 2016 with cash, cash equivalents and investments of $268.2 million, which included net proceeds of approximately $134.5 million from our December 2016 follow-on public offering. In April 2017, we received net proceeds of approximately $215.6 million upon the closing of a subsequent follow-on public offering. Based on our current plans, we expect that our existing cash, cash equivalents and investments will be sufficient to enable us to fund our operating expenses and capital expenditure requirements into the second half of 2019.

In addition, we continue to explore a range of strategic collaboration opportunities to maximize the value of our programs and allow us to move our drug candidates more quickly toward potential approval and into the hands of patients and physicians worldwide.

A Promise to Change the Paradigm

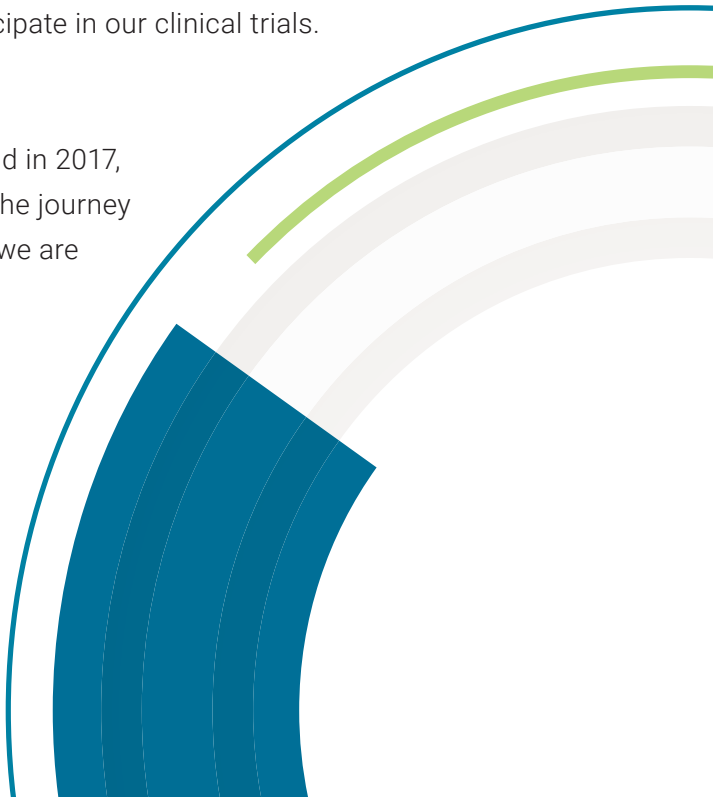
With scientific expertise, technical precision and passion, our people drive Blueprint Medicines forward. Over the past year, we rounded out our executive management team with several key appointments, including chief scientific and legal officers. In addition, we continue to hire talent across our business, while maintaining a collaborative culture defined by a sense of urgency. In fact, with the encouraging early data from our Phase 1 trials for BLU-285 and BLU-554, our team is more motivated than ever to move faster and work harder each and every day.

As we look back on all that we have accomplished, I would like to say thank you to our employees, scientific and clinical collaborators, board members and stockholders for supporting our vision to improve the lives of patients with genomically defined diseases. Most importantly, we want to thank the patients, families and physicians who participate in our clinical trials. We recognize that we could not be successful without them.

The year 2016 was transformative for Blueprint Medicines, and in 2017, we are poised to build on that momentum. Looking forward, the journey to realize the promise of our vision is still just beginning, and we are excited to share updates with you on our continued progress.

Sincerely,

Jeffrey W. Albers
President and Chief Executive Officer



Robust pipeline of diverse assets

DRUG CANDIDATE	DISCOVERY	PRECLINICAL	CLINICAL	COMMERCIAL RIGHTS
BLU-285 Inhibitor of KIT, including exon 17 mutations, and PDGFRα, including the D842V mutation			PDGFRα-DRIVEN GIST — PHASE 1	
			KIT-DRIVEN GIST — PHASE 1	
			SYSTEMIC MASTOCYTOSIS — PHASE 1	
BLU-554 Inhibitor of FGFR4			HEPATOCELLULAR CARCINOMA — PHASE 1	
BLU-667 Inhibitor of RET fusions, mutations and resistant mutants			NSCLC AND THYROID* — PHASE 1	
PRKACA Inhibitor of PRKACA fusions	FLC			
Cancer immunotherapy Immunokinases			UP TO 5 PROGRAMS, STAGE UNDISCLOSED	Roche†
Rare genetic disease			TARGET AND DEVELOPMENT STAGE UNDISCLOSED	ALEXION

*Phase 1 trial includes a basket cohort which consists of other advanced solid tumors with RET alterations.

†Blueprint Medicines has U.S. commercialization rights for up to two programs. Roche has worldwide commercialization rights for up to three programs and ex-U.S. commercialization rights for up to two programs.

FLC = Fibrolamellar carcinoma. GIST = advanced gastrointestinal stromal tumors. NSCLC = non-small cell lung cancer. All Phase 1 clinical trials are in advanced disease.

Most importantly, we want to thank the patients, families and physicians who participate in our clinical trials. We recognize that we could not be successful without them.

Therapeutic areas of focus

	PROBLEM	SOLUTION	POTENTIAL OPPORTUNITY*
Unresectable gastrointestinal stromal tumors (GIST)	Rare sarcoma of the digestive tract No current therapy addresses KIT exon 17 and PDGFRα mutations Overall survival is about 5 years in KIT-driven GIST and 15 months in PDGFRα-driven GIST	**BLU-285** is a potent and highly selective inhibitor that targets KIT, including exon 17 mutations, and PDGFRα, including the D842V mutation	**4,500** 3L patients with exon 17 mutant KIT (>90% of 3L GIST patients) **500** patients with D842V mutant PDGFRα (5-6% of GIST patients)
Systemic mastocytosis (SM)	Severe rare disease with mast cell proliferation in bone marrow and other parts of the body KIT D816V mutation is a key driver in about 90-95% of patients Overall survival is about 3 to 5 years for advanced forms of SM, and current treatments focus on symptomatic relief	**BLU-285** is a potent and highly selective inhibitor that targets the KIT D816V mutation	**4,100** patients with advanced forms of SM (including smoldering SM) who have the KIT D816V mutation **14,900** patients with indolent SM who have the KIT D816V mutation
Advanced hepatocellular carcinoma (HCC)	Liver cancer is the second leading cause of cancer death worldwide We estimate 30% of HCC patients have tumors with aberrantly activated FGFR4 signaling Current standard of care for advanced HCC (sorafenib) has about 2% response rate	**BLU-554** is a potent and highly selective inhibitor that targets FGFR4	**18,900** 1L patients with aberrantly active FGFR4 signaling **8,000** 2L patients with aberrantly active FGFR4 signaling

*Patient numbers are approximate, and based on estimated incident (GIST, HCC) or prevalent (SM) populations in major markets (US, EU5 and Japan).

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, DC 20549

Form 10-K

(Mark One)

☑ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the fiscal year ended December 31, 2016

OR

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the transition period from _____ to _____

Commission File Number: 001-37359

BLUEPRINT MEDICINES CORPORATION

(Exact name of registrant as specified in its charter)

Delaware	**26-3632015**
(State or other jurisdiction of incorporation or organization)	*(IRS Employer Identification No.)*
38 Sidney Street, Suite 200 Cambridge, MA	**02139**
(Address of principal executive offices)	*(Zip Code)*

Registrant's telephone number, including area code: **(617) 374-7580**

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

Title of Class	*Name of Exchange on Which Registered*
Common Stock, par value $0.001 per share	**NASDAQ Global Select Market**

Securities registered pursuant to Section 12(g) of the Act: **None**

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☑ No ☐

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes ☐ No ☑

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

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes ☑ No ☐

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ☐

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

Large accelerated filer ☐	Accelerated filer ☑	Non-accelerated filer ☐ (Do not check if a smaller reporting company)	Smaller reporting company ☐

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

As of June 30, 2016, the aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant, based on the last reported sales price for the registrant's common stock, par value $0.001 per share, on the NASDAQ Global Select Market on such date, was approximately $428,041,604.

Number of shares of the registrant's common stock, par value $0.001 per share, outstanding on February 28, 2017: 33,203,902

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive proxy statement for its 2017 Annual Meeting of Stockholders, which the registrant intends to file with the Securities and Exchange Commission pursuant to Regulation 14A within 120 days after the end of the registrant's fiscal year ended December 31, 2016, are incorporated by reference into Part III of this Annual Report on Form 10-K.

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Unless otherwise stated, all references to "us," "our," "Blueprint," "Blueprint Medicines," "we," the "Company" and similar designations in this Annual Report on Form 10-K refer to Blueprint Medicines Corporation and its consolidated subsidiary, Blueprint Medicines Security Corporation.

FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this Annual Report on Form 10-K 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, although not all forward-looking statements contain these identifying words.

The forward-looking statements in this Annual Report on Form 10-K include, but are not limited to, statements about:

- the initiation, timing, progress and results of our pre-clinical studies and clinical trials, including our Phase 1 clinical trials for BLU-285, BLU-554 and BLU-667, and our research and development programs;
- our ability to advance drug candidates into, and successfully complete, clinical trials;
- the timing or likelihood of regulatory filings 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 rare genetic disease collaboration with Alexion Pharma Holding and our existing cancer immunotherapy collaboration with F. Hoffmann-La Roche Ltd and Hoffmann-La Roche Inc., as well as our ability to enter into other strategic arrangements;
- the development of companion diagnostic tests for our drug candidates, including our companion diagnostic test with Ventana Medical Systems, Inc. for BLU-554 and our companion diagnostic test with QIAGEN Manchester Limited for BLU-285;
- our ability to maintain and establish collaborations;
- our financial performance; and
- developments relating to our competitors and our industry.

Any forward-looking statements in this Annual Report on Form 10-K reflect our current views with respect to future events or to our future financial performance and involve known and unknown risks, uncertainties and other 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. We have included important factors in the cautionary statements included in this Annual Report on Form 10-K, particularly in the "Risk Factors" section, that could cause actual results or events to differ materially from the forward-looking statements that we make. Given these uncertainties, you should not place undue reliance on these forward-looking statements. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make or enter into.

You should read this Annual Report on Form 10-K and the documents that we have filed as exhibits to this Annual Report on Form 10-K completely and with the understanding that our actual future results, performance or achievements may be materially different from what we expect. Except as required by law, we assume no obligation to update or revise these forward-looking statements for any reason, even if new information becomes available in the future.

This Annual Report on Form 10-K also contains estimates, projections and other information concerning our industry, our business and the markets for certain 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.

PART I

Item 1. Business.

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 diseases in genomically defined patient populations and to craft drug candidates that may provide significant and durable clinical responses for patients without adequate treatment options. This integrated biology and chemistry approach enables us to identify, characterize and design drug candidates to inhibit novel kinase targets that have been difficult to selectively inhibit. By focusing on diseases in genomically defined patient populations, we believe that we will have a more efficient development path with a greater likelihood of success. Leveraging our novel target discovery engine, we have developed a robust small molecule drug pipeline in cancer and a rare genetic disease.

Our most advanced drug candidates are BLU-285, BLU-554 and BLU-667. BLU-285 is an orally available, potent and highly selective inhibitor that targets KIT, including Exon 17 mutations, and targets PDGFRα, including the D842V mutation. These mutations abnormally activate receptor tyrosine kinases that are drivers of cancer and proliferative disorders, including gastrointestinal stromal tumors, or GIST, and systemic mastocytosis, or SM. We are currently evaluating BLU-285 in an ongoing Phase 1 clinical trial for defined subsets of patients with GIST and an ongoing Phase 1 clinical trial for advanced SM. GIST is a rare disease that is a sarcoma, or tumor of bone or connective tissue, of the gastrointestinal tract, or GI tract, and SM is a rare disorder that causes an overproduction of mast cells and the accumulation of mast cells in the bone marrow and other organs, which can lead to a wide range of debilitating symptoms and organ dysfunction and failure. BLU-554 is an orally available, potent and highly selective inhibitor that targets FGFR4, a kinase that is aberrantly activated in a defined subset of patients with hepatocellular carcinoma, or HCC, the most common type of liver cancer. We are currently evaluating BLU-554 in an ongoing Phase 1 clinical trial in patients with advanced HCC. BLU-667 targets RET, a receptor tyrosine kinase that is abnormally activated by mutations or translocations, and RET resistant mutants that we predict will arise from treatment with first generation therapies. RET is a driver of disease in non-small cell lung cancer, or NSCLC, and cancers of the thyroid, including medullary thyroid carcinoma, or MTC, and our research suggests that RET may be a driver of disease in subsets of colon cancer, breast cancer and other cancers. In December 2016, the U.S. Food and Drug Administration, or FDA, approved our Investigational New Drug, or IND, application for BLU-667 for the treatment of NSCLC, thyroid cancer and other advanced solid tumors, and we expect to initiate a Phase 1 clinical trial for BLU-667 for the treatment of NSCLC, MTC and other advanced solid tumors in the first half of 2017. In September 2015, the FDA granted orphan drug designation to BLU-554 for the treatment of HCC, and in January 2016, the FDA granted orphan drug designation to BLU-285 for the treatment of GIST and SM. In addition, in October 2016, the FDA granted fast track designation to BLU-285 for the treatment of patients with unresectable or metastatic GIST that progressed following treatment with imatinib and a second tyrosine kinase inhibitor and for the treatment of patients with unresectable or metastatic GIST with the PDGFRα D842V mutation regardless of prior therapy. We have worldwide development and commercialization rights to BLU-285, BLU-554 and BLU-667.

We also have initiated a discovery program targeting protein kinase cAMP-activated catalytic subunit alpha, or PRKACA, fusions for the treatment of fibrolamellar carcinoma, or FLC, a rare and distinct subtype of liver cancer that typically arises in young adults. PRKACA fusions are the only known recurrent genomic events in FLC and are considered to be the driver gene of the disease. Currently, there are no approved therapies for FLC, and surgery is the only available treatment option for some patients, but most patients inevitably progress. We will continue to leverage our discovery platform to systematically and reproducibly identify kinases that are drivers of diseases in genomically defined patient populations and craft drug candidates that potently and selectively target these kinases. We anticipate nominating at least one additional discovery program in 2017.

In addition to our wholly-owned clinical and pre-clinical programs, we have leveraged our discovery platform to enter into collaboration programs with Alexion Pharma Holding, or Alexion, and F. Hoffmann-La Roche Ltd and Hoffmann-La Roche Inc., which we refer to collectively as Roche. In March 2015, we entered into an agreement with Alexion to discover, develop and commercialize one or more drug candidates targeting an undisclosed rare genetic disease. In March 2016, we entered into an agreement with Roche to discover, develop and commercialize up to five small molecule therapeutics targeting kinases believed to be important in cancer immunotherapy, as single products or possibly in combination with other therapeutics. We will continue to 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 discovery platform outside of our primary strategic focus area of cancer.

Approved kinase drugs, such as imatinib, have demonstrated significant benefit to patients, and small molecule kinase drugs achieved over $22 billion in 2016 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. As of December 31, 2016, kinase drugs approved by the FDA are only directed at less than five percent of the 518 kinases that constitute the kinome. For many of the known kinases, there is a strong link between genomic 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 still unknown. Taken together, this represents a substantial opportunity for developing novel and transformative drugs for cancer, rare genetic diseases and other disease areas, including cancer immunotherapy.

To capitalize on the kinase opportunity, we built a discovery platform that integrates a novel target discovery engine and a proprietary compound library. Our novel target discovery engine 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, other than any royalties or other fees that may become payable to Roche under our cancer immunotherapy collaboration. Using this discovery platform, we have produced a drug pipeline of several promising drug candidates that target genomically defined patient subsets. We believe that our strategy will allow us to deliver transformative drugs to patients while building a fully-integrated biopharmaceutical company.

Our lead programs targeting KIT, including Exon 17 mutations, PDGFRα, including the D842V mutation, FGFR4 and RET provide strong evidence of the power of our proprietary compound library. These targets have been well characterized in the scientific literature as disease drivers, but they have been challenging to inhibit selectively with small molecules. In addition, 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 predicted RET resistant mutants.

Our Strategy

Our goal is to become a fully-integrated biopharmaceutical company capable of delivering transformative drugs to patients. The key tenets of our strategy include the following:

- ***Rapidly advance our lead drug candidates, BLU-285, BLU-554 and BLU-667, through clinical development.*** We are currently enrolling patients in our ongoing Phase 1 clinical trials for BLU-285 for the treatment of PDGFRα-driven GIST and patients with relapsed or refractory KIT-driven GIST, which we collectively refer to as advanced GIST, BLU-285 for the treatment of advanced SM and BLU-554 for the treatment of advanced HCC. In the fourth quarter of 2016, we presented preliminary data for each of these clinical trials showing that BLU-285 achieved proof-of-concept in advanced GIST and advanced SM and that BLU-554 achieved proof-of-concept in advanced HCC. We also expect to initiate a Phase 1 clinical trial for BLU-667 for the treatment of NSCLC, MTC and other advanced solid tumors in the first half of 2017. For some of our drug candidates, in order to select patients most likely to respond to our therapies and rapidly confirm mechanistic and clinical proof of concept, we may seek to develop companion diagnostic tests. We may also seek to develop assays to measure target engagement and pathway modulation, which are confirmation that a drug binds to its intended protein target *in vivo*, and we may develop measures of early response. We expect these approaches may enable earlier determination of clinical activity, allow for clear decision points for the clinical and regulatory development of our drug candidates and, for any of our drug candidates that receive marketing approval, improve patient care by identifying patients who will benefit from the

therapy. In addition, we plan to evaluate opportunities for accelerated clinical development and expedited regulatory review and approval for each of our drug candidates, including fast track designation, accelerated approval, priority review and breakthrough therapy designation. The FDA has granted fast track designation to BLU-285 for the treatment of patients with unresectable or metastatic GIST that progressed following treatment with imatinib and a second tyrosine kinase inhibitor and for the treatment of patients with unresectable or metastatic GIST with the PDGFRα D842V mutation regardless of prior therapy. In addition, the FDA has granted orphan drug designation to BLU-285 for the treatment of GIST and SM and BLU-554 for the treatment of HCC.

- ***Build a pipeline of kinase drugs for patients with genomically defined drivers of disease.*** We will continue to leverage our discovery platform to systematically and reproducibly identify kinases that are drivers of diseases in genomically defined patient populations and craft drug candidates that potently and selectively target these kinases. We anticipate nominating at least one additional discovery program in 2017.

- ***Continuously invest in our proprietary discovery 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 have continued to expand our proprietary compound library to cover a significant portion of the kinome and anticipate that as part of our discovery efforts we will continue to increase the number of compound families that inhibit each kinase target.

- ***Evaluate strategic collaborations to maximize the value of our programs and platform.*** In addition to our wholly-owned clinical and pre-clinical programs, we have leveraged our discovery platform to enter into collaboration programs with Alexion for an undisclosed rare genetic disease and with Roche for up to five small molecule therapeutics targeting kinases believed to be important in cancer immunotherapy, as single products or possibly in combination with other therapeutics. We will continue to evaluate additional collaborations that could maximize the value for our programs and allow us to leverage the expertise of strategic collaborators, including regional or global research, development, marketing or commercialization collaborations. We are also focused on engaging in collaborations to capitalize on our discovery platform outside of our primary strategic focus area of cancer.

- ***Maintain Blueprint Medicines' patient-focused and science-driven 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, innovation, hard work and an urgency for efficiently developing treatments to improve the lives of patients who have few, if any, treatment options. We plan to continue working closely with physicians and patient advocacy groups to better understand the impact that the diseases we are targeting have on patients and their families, as well as to rapidly identify and enroll patients most likely to respond to our drug candidates. 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 and passion for developing transformative drugs that have the potential to improve patients' lives. We also intend to continue fostering an environment that encourages tight integration across disciplines to ensure a seamless flow of ideas and information exchange.

Our Focus — Highly Selective Kinase Drugs for Genomically Defined Diseases

Kinases are enzymes that function in many signaling pathways to regulate critical cellular functions. Kinase-dependent signaling networks are present in multiple different cell types, including muscle cells and cells of the immune system, and deregulation of these networks can lead to disease pathology. 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 genomic 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 ABL, EGFR, B-RAF, ALK, BTK and JAK, among many others. Ongoing genomic analyses of tumor data sets continue to identify new roles for kinases as drivers of disease.

As of December 31, 2016, there were 34 FDA-approved small molecule drugs that target less than five percent of the 518 kinases, of which all but two are indicated for cancer. Kinase inhibition continues to be a fruitful approach for cancer drug development. From 2012 to 2016, 16 of 48 FDA-approved cancer drugs were kinase inhibitors.

Despite these successes, many 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 difficult-to-drug 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 have proven difficult-to-drug. 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 on-target 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 diseases in genomically defined patient populations and to craft drug candidates 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 design drug candidates to inhibit novel kinase targets. By focusing on diseases in genomically defined patient populations, 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, and 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 have continued to expand our proprietary compound library to cover a significant portion of the kinome and anticipate that as part of our discovery efforts we will continue 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, 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:

- ***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.

- ***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, including BLU-667 for RET fusions and predicted RET resistant mutants.

Our discovery platform has already yielded a robust pipeline. KIT mutations, including Exon 17 mutants, while known drivers of disease, historically, were not selectively drugged successfully. We developed BLU-285 as a selective inhibitor of KIT, including Exon 17 mutations, an effort that our proprietary compound library facilitated. 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. In addition, for our RET program, we applied our resistance mutation prediction algorithm to identify mutant forms of RET that are resistant to multi-kinase inhibitors with RET activity and utilized our proprietary compound library to develop BLU-667, a potent and selective inhibitor of RET and predicted RET resistant mutants with activity against both the wild-type and mutant enzymes. 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 discovery 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 development and commercial rights to all of our pre-clinical and clinical programs other than any drug candidates being developed in our rare genetic disease program with Alexion and our cancer immunotherapy program with Roche. The following table summarizes our most advanced drug candidates as of February 28, 2017, each of which is described in further detail below.

Drug Candidate	Initial Diseases	Genomic Drivers	Stage of Development [1]	Commercial Rights
BLU-285 *(KIT inhibitor)*	SM	KIT D816V mutation	Phase 1 enrolling	Blueprint Medicines
	GIST	D842V mutant PDGFRα	Phase 1 enrolling	
	GIST	KIT mutations, including Exon 17 mutants	Phase 1 enrolling	
BLU-554 *(FGFR4 inhibitor)*	HCC	Aberrant FGFR4 signaling	Phase 1 enrolling	Blueprint Medicines
BLU-667 *(RET inhibitor)*	NSCLC, MTC and other advanced solid tumors	RET activating mutations, fusions and predicted resistant mutants	IND accepted	Blueprint Medicines
PRKACA *(discovery program)*	FLC	PRKACA fusions	Lead optimization	Blueprint Medicines
Rare genetic disease target	Rare genetic disease	Undisclosed	Undisclosed	Alexion
Cancer immunotherapy *(up to five programs)*	Oncology	Immunokinases	Undisclosed	Blueprint Medicines [2] Roche [3]

(1) All Phase 1 clinical trials are being conducted in advanced disease.
(2) Blueprint Medicines has U.S. commercialization rights for up to two programs.
(3) Roche has worldwide commercialization rights for up to three programs and ex-U.S. commercialization rights for up to two programs.

All of our current clinical programs target patient populations with genomically defined diseases. As we advance our drug candidates through clinical development, we will enrich our Phase 1 clinical 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, with significant medical experience as oncologists and extensive drug development backgrounds. We have also entered into agreements with Ventana Medical Systems, Inc., or Ventana, to develop and commercialize a companion diagnostic test for BLU-554 that we expect to use to identify HCC patients with abberantly active FGFR4 signaling as indicated by FGF19 overexpression and QIAGEN Manchester Limited, or Qiagen, to develop and commercialize a companion diagnostic test for BLU-285 that we expect to use to identify GIST patients with the PDGFRα D842V mutation. We may collaborate with these or other third parties in the future to develop and commercialize additional companion diagnostic tests or to develop assays to measure target engagement, pathway modulation and early response.

The table below lists the initial diseases and genomic drivers targeted by BLU-285, BLU-554 and BLU-667, and for each of these diseases, the corresponding estimated number of patients in the United States, France, Germany, Italy, Spain, the United Kingdom and Japan, or the Major Markets, the estimated frequency of the targeted genomic alteration and the estimated number of patients in the Major Markets with that genomic alteration.

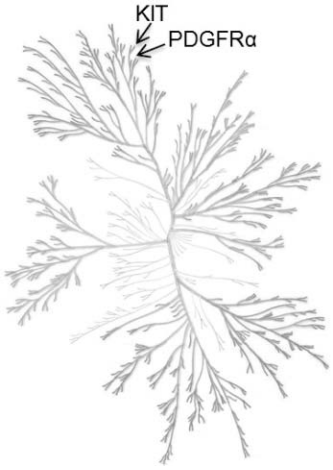
Drug Candidate	Initial Diseases	Estimated Number of Patients [1]		Genomic Drivers	Estimated Frequency of Alteration (% of Patients)	Estimated Number of Patients with Alteration in Major Markets [1]
		United States	Total Major Markets			
BLU-285	SM	1,700 advanced SM [2] 6,500 indolent SM	4,400 advanced SM [2] 16,100 indolent SM	KIT D816V mutation	90-95%	4,100 advanced SM [2] 14,900 indolent SM
	GIST [3]	3,300 first line 3,000 second line 2,400 third line	8,700 first line 7,700 second line 5,000 third line	D842V mutant PDGFRα	5-6% of primary GIST	500 total
				Exon 17 mutant KIT	<1% first line 23% second line >90% third line	100 first line 1,800 second line 4,500 third line
BLU-554	HCC [3][4]	18,000 first line 7,300 second line	63,100 first line 26,500 second line	Aberrant FGFR4 signaling	Approximately 30%	18,900 first line 8,000 second line
BLU-667	NSCLC [3]	153,900 first line 91,600 second line 37,400 third line	367,500 first line 214,200 second line 83,500 third line	RET fusions	1-2%	5,500 first line 3,200 second line 1,300 third line
	MTC [3]	480 total	990 total	RET mutations	60%	600 total

(1) Based on estimated prevalence for SM patients and MTC patients and estimated incidence for GIST, HCC and NSCLC patients.
(2) Estimate includes smoldering SM.
(3) Estimate includes metastatic and unresectable patient populations.
(4) The incidence of HCC outside of the Major Markets, including in China, South Korea, Taiwan and Singapore, represents an additional opportunity for BLU-554.

KIT Inhibitor Program

Overview

BLU-285 is an orally available, potent and highly selective inhibitor that targets KIT, including Exon 17 mutations, and targets PDGFRα, including the D842V mutation, abnormally active receptor tyrosine kinases that are drivers of cancer and proliferative disorders. BLU-285 is able to potently and selectively inhibit both KIT and PDGFRα with minimal inhibition of other kinases due to the high degree of structural similarity of the kinase domains of KIT and PDGFRα.



Kinome tree locations of KIT and PDGFRα illustrating close structural similarity between these kinases. Each branch of the dendogram represents an individual human kinase. *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.*

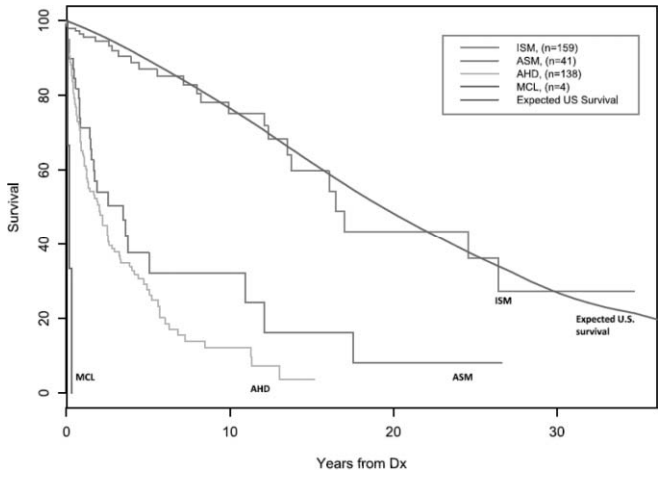
We are initially developing BLU-285 for PDGFRα-driven GIST and patients with relapsed or refractory KIT-driven GIST, which we collectively refer to as advanced GIST, and for advanced SM. In July 2015 and September 2015, respectively, the FDA accepted our IND applications for BLU-285 for the treatment of advanced GIST and BLU-285 for the treatment of advanced SM. We are currently enrolling patients in ongoing Phase 1 clinical trials for each of these indications. Based on the preliminary safety and clinical activity data from our Phase 1 clinical trial for BLU-285 for advanced SM, we plan to evaluate options to expand the clinical development of BLU-285 in other KIT-driven diseases, including possible opportunities for the treatment of indolent SM, or ISM, and KIT-mutant acute myeloid leukemia, groups of patients in need of more effective treatments.

Systemic Mastocytosis (SM)

SM Disease Background

SM is a 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. The signature of SM is the overproduction of mast cells and the accumulation of mast cells in the bone marrow and other organs. 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 ISM have a normal life expectancy. The primary burden of disease for ISM patients 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, advanced SM with an associated hematologic neoplasm, SM-AHN, and mast cell leukemia, or MCL. These 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, 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-AHN 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. In the figure above, AHD refers to SM-AHN.

Population studies, including a population-based epidemiology study that we sponsored, 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% of patients, 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 patients with the KIT D816V mutation, there are no approved therapies for SM, leaving approximately 90-95% of SM patients with limited or no treatment options. 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. However, there are no disease-modifying agents, and patients with advanced SM inevitably progress, with a three to five-year overall survival prognosis. In the Major Markets, we estimate there are approximately 4,100 patients with advanced forms of SM, including SSM, who have the KIT D816V mutation.

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 plan to evaluate options to expand the clinical development of BLU-285 for the treatment of ISM. We estimate that there are approximately 16,100 ISM patients in the Major Markets.

KIT Driver Mutations in SM

In all subtypes of SM, the mast cells of approximately 90-95% 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

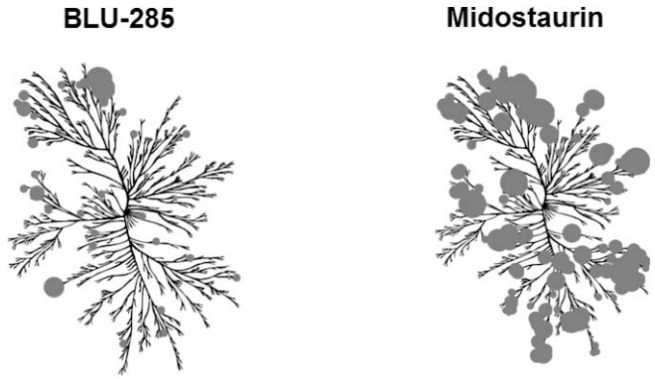
We conducted comprehensive biochemical and cellular experiments to characterize the potency and selectivity of BLU-285. BLU-285 potently inhibits KIT D816V *in vitro* (IC_{50}, or the compound concentration at which 50% of the activity is inhibited relative to control lacking compound, = 0.27 nM). In 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

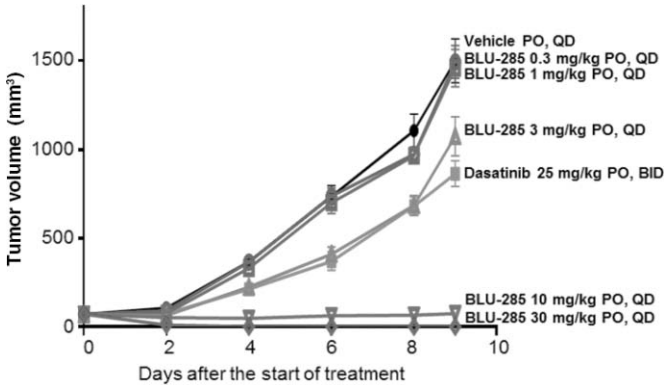
Potency of BLU-285 against KIT D816 and other Exon 17 mutations compared to imatinib. The inhibitory potencies of BLU-285 and imatinib against the KIT D816V mutant protein were evaluated in an *in vitro* enzyme activity assay. The inhibitory potencies of BLU-285 and imatinib were also evaluated in two 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 PDGFRα 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 μ M) 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 allograft 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 the 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, or BID, 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 allograft model of SM. In the figure above, QD means once a day, BID means twice a day and PO means orally.

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.

Phase 1 Clinical Trial for BLU-285 for the Treatment of Advanced SM

BLU-285 is currently being evaluated in the dose escalation stage of a Phase 1 clinical trial in patients with advanced SM, and enrollment is ongoing. In January 2016, the FDA granted orphan drug designation to BLU-285 for the treatment of SM.

In December 2016, we presented preliminary data from our ongoing Phase 1 clinical trial at the 2016 American Society of Hematology Annual Meeting. The data showed that BLU-285 was observed to be well-tolerated and achieved proof-of-concept in advanced SM. As of the data cutoff date of November 11, 2016, BLU-285 had been administered to 12 patients at three dose levels (30 mg, 60 mg and 100 mg once daily, or QD). The median age was 61.5 (ranging from 39 to 82), and the KIT D816V mutation has been confirmed in bone marrow or blood from 11 of the 12 patients. Ten of the 12 patients remained on the clinical trial as of the data cutoff date. Preliminary pharmacokinetic, or PK, analysis at all dose levels demonstrated relatively rapid absorption of BLU-285 and a mean half-life of over 19 hours, which supports QD dosing and is consistent with the initial data reported by us from the dose escalation stage of our Phase 1 clinical trial for BLU-285 in patients with advanced GIST.

Preliminary Safety Data. As of the data cutoff date of November 11, 2016, BLU-285 was observed to be well-tolerated at all doses. No patients discontinued treatment due to an adverse event, and no Grade 4 or worse treatment-related adverse events were reported. The majority of adverse events reported by investigators were Grade 1 or Grade 2, and adverse events that occurred in two or more patients included fatigue (four patients), anemia (three patients) and alkaline phosphatase elevation (three patients). All three cases of alkaline phosphatase elevation were Grade 3 but were asymptomatic and transient and occurred in the absence of transaminase or bilirubin elevations. In addition, the Grade 3 alkaline phosphatase elevations occurred in the three patients with the highest bone marrow mast cell burden at baseline, suggesting the transient alkaline phosphatase elevations may be consistent with a pharmacodynamic, or PD, effect of BLU-285 on mast cells in the bone. One of the three cases of alkaline phosphatase elevation was considered possibly treatment-related and defined as a dose-limiting toxicity at the 60 mg dose level. All three patients continued treatment with BLU-285 without a dose reduction.

Preliminary Clinical Activity Data. As of the data cutoff date of November 11, 2016, all 12 patients in the first three cohorts of the dose escalation stage of the clinical trial at doses ranging from 30 mg QD to 100 mg QD had completed at least two 28-day dosing cycles and were evaluated for signs of clinical activity.

- Investigators observed decreases in bone marrow mast cell infiltrate, measured by bone marrow biopsy, in six of the eight patients who had a bone marrow biopsy after starting treatment with BLU-285.

- Three of the six patients had a decrease of bone marrow mast infiltrate of more than 50% from baseline, including one patient with no residual mast cells in the bone marrow.

- Based on measurements at a central laboratory, serum tryptase decreased in 10 of 12 patients. The serum tryptase decrease was greater than 50% in eight patients.

- The allele burden of D816V mutant KIT decreased within the first two treatment cycles in five of six evaluable patients in circulating tumor DNA and bone marrow.

- Rash improved in five patients with urticaria pigmentosa from baseline based on investigator assessments. Urticaria pigmentosa is an allergy-mediated rash common in SM patients.

- Weight increased in 10 patients, and albumin increased in 11 patients, suggesting improvements in malabsorption.

- Ten of 12 patients remained on treatment with BLU-285, and the duration of treatment ranged from one month to 8.1 months.

Clinical Development Plans. Our Phase 1 clinical trial for BLU-285 for the treatment of advanced SM is designed to evaluate the safety and tolerability of BLU-285 in multiple ascending doses in patients with advanced SM, including ASM, SM-AHN and MCL with the goal of establishing a maximum tolerated dose, or MTD, or a recommended dose if the MTD is not achieved. The MTD for BLU-285 has not yet been established in this clinical trial, and enrollment in the dose escalation stage is ongoing. All patients will be tested retrospectively for KIT D816V mutational status. Once the MTD is reached, or a recommended dose is established, we will evaluate whether to open expansion cohorts for specific subtypes of SM. Secondary objectives for this clinical trial include assessment of the PK profile of BLU-285, assessment of response rate by the International Working Group Myeloproliferative Neoplasms Research and Treatment criteria, or IWG-MRT criteria, changes in KIT D816V mutant allele fractions in bone marrow and circulating tumor DNA, and changes in patient reported outcomes. The Phase 1 clinical trial is designed to enroll approximately 60 patients, including approximately 25 patients during dose escalation and approximately 35 additional patients in expansion cohorts, at multiple sites in the United States and the European Union.

Based on the preliminary safety profile and clinical activity observed in this clinical trial, we plan to continue to enroll patients in the dose escalation stage of this Phase 1 clinical trial until an MTD is reached or a recommended dose is established. We plan to open enrollment in expansion cohorts to evaluate BLU-285 as a single agent in advanced SM once a recommended dose for further clinical evaluation has been determined or an MTD has been reached. We expect to initiate the expansion stage of this clinical trial in 2017 and plan to enroll approximately 35 patients with advanced SM in the expansion stage. In addition, based on the preliminary safety and clinical activity data, we plan to evaluate options to expand the clinical development of BLU-285 in other KIT-driven diseases, including possible opportunities for the treatment of indolent SM and KIT-mutant acute myeloid leukemia, groups of patients in need of more effective treatments.

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 patient reported outcome tool to measure changes in total symptom burden in patients with advanced SM. In addition, we are working with patient advocacy groups relevant to SM in order to:

- raise awareness of our Phase 1 clinical trial for BLU-285 for the treatment of advanced SM;
- recruit patients to join a patient registry that we launched in December 2015 to help improve the understanding of mastocytosis from the perspective of patients and to increase participation and enrollment in clinical trials for mastocytosis that we or others may conduct in the future; and
- incorporate the SM patient perspective into our ongoing activities.

Gastrointestinal Stromal Tumors (GIST)

GIST Disease Background

GIST is a rare disease that is a sarcoma of the 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 15 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 PDGFRα 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 PDGFRα D842V mutation is found in 5-6% of frontline unresectable or metastatic GIST patients. In the Major Markets, we estimate there are approximately 500 patients with PDGFRα D842V-driven GIST.

For patients with KIT-driven GIST, current medical therapies slow the course of disease but progression is inevitable in most cases. 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 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 more than 90% 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. In the Major Markets, we estimate there are approximately 6,300 second line and third line patients with KIT-driven GIST. Finally, we believe frontline combinations with imatinib will have the potential to dramatically increase the duration of response. In the Major Markets, we estimate there are approximately 21,400 total patients with unresectable or metastatic GIST, including approximately 8,700 patients with unresectable or metastatic frontline GIST.

KIT and PDGFRα 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 PDGFRα. 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. The most common mutation in the PDGFRα gene is D842V, found in approximately 5-6% of frontline unresectable or metastatic GIST patients. There is currently no therapeutic option for patients with D842V mutant PDGFRα-driven GIST. PDGFRα has a very similar active site structure to KIT, and the PDGFRα D842V mutation is homologous to KIT D816V. As in the case of KIT Exon 17 mutant receptors, PDGFRα D842V mutations confer ligand-independent constitutive signaling of the mutant PDGFRα kinase.

BLU-285 Pre-clinical Development in GIST

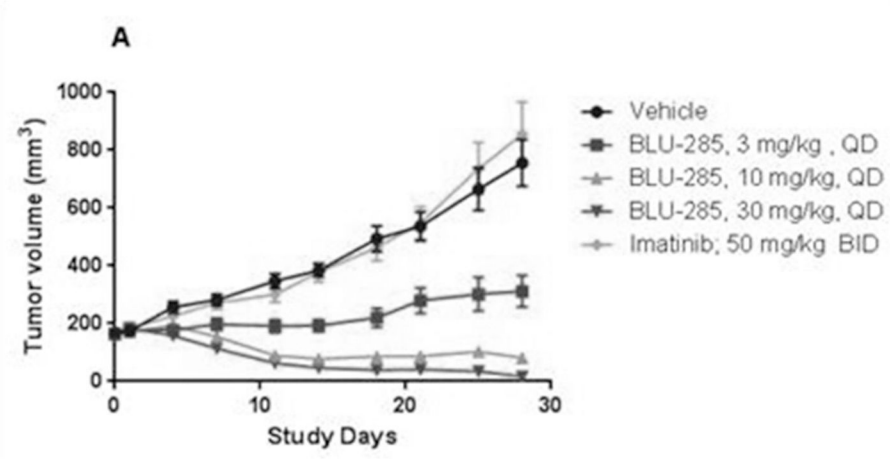
We have conducted comprehensive pre-clinical experiments to characterize the potency and selectivity of BLU-285. BLU-285 potently inhibits PDGFRα D842V *in vitro* (IC_{50} = 0.24 nM). In contrast, imatinib inhibits PDGFRα D842V at least 3,000-fold less potently (IC_{50} = 759 nM). In a cellular model driven by an activated PDGFRα D842V mutant protein, BLU-285 potently inhibits signaling of the oncogenic PDGFRα mutant protein as measured by inhibition of PDGFRα 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.

PDGFRα 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 PDGFRα D842V was evaluated in an *in vitro* enzyme activity assay and in a cellular model driven by an activated PDGFRα 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 the two highest tested doses, which were well-tolerated.



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 the figure above, QD means once a day and BID means twice a day.

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.

Phase 1 Clinical Trial for BLU-285 for Advanced GIST

BLU-285 is currently being evaluated in the dose expansion stage of a Phase 1 clinical trial in patients with advanced GIST, and enrollment is ongoing. In January 2016, the FDA granted orphan drug designation to BLU-285 for the treatment of GIST. In October 2016, the FDA granted fast track designation to BLU-285 for the treatment of patients with unresectable or metastatic GIST that progressed following treatment with imatinib and a second tyrosine kinase inhibitor and for the treatment of patients with unresectable or metastatic GIST with the PDGFRα D842V mutation regardless of prior therapy. We plan to seek regulatory guidance on potential pathways for expedited clinical development of BLU-285 for the treatment of advanced GIST.

In December 2016, we presented preliminary data from the dose escalation stage of this clinical trial in December 2016 at the 28th EORTC-NCI-AACR Symposium on Molecular Targets and Cancer Therapeutics. The data showed that BLU-285 was observed to be well-tolerated and had achieved proof-of-concept in PDGFRα-driven GIST and KIT-driven GIST. As of the data cutoff date of November 1, 2016, BLU-285 had been administered to 36 patients at seven dose levels ranging from 30 mg QD to 400 mg QD, including 18 patients with PDGFRα-driven GIST and 18 patients with KIT-driven GIST. The median age was 61 (ranging from 41 to 77), and the median number of prior treatment regimens was 3.5 (ranging from zero to 12). Preliminary PK analysis at all dose levels demonstrated relatively rapid absorption of BLU-285 and a mean half-life of over 24 hours, which supports QD dosing.

Preliminary Safety Data. As of the data cutoff date of November 1, 2016, BLU-285 was observed to be well-tolerated at all doses. No dose-limiting toxicities or treatment-related Grade 4 or 5 adverse events were reported, and no patients discontinued treatment with BLU-285 due to treatment-related adverse events. The majority of adverse events reported by investigators were Grade 1 or 2. Across all grades, adverse events reported by investigators most commonly included nausea (42%), vomiting (33%), peripheral edema (31%), fatigue (28%) and constipation (22%). Investigators reported treatment-related Grade 3 adverse events in three patients: nausea and vomiting (one patient); anemia and intratumoral hemorrhage (one patient); and hypophosphatemia (one patient), a deficiency of phosphates in the blood.

Preliminary Clinical Activity Data. As of the data cutoff date of November 1, 2016, 28 patients in the first six cohorts of the dose escalation stage of the clinical trial at doses ranging from 30 mg QD to 300 mg QD had completed at

least two 28-day dosing cycles and were evaluable for response assessment. Response assessments were based on CT and MRI imaging to measure clinical activity per Response Evaluation Criteria In Solid Tumors version 1.1, or RECIST.

- In PDGFRα-driven GIST, investigators observed radiographic tumor reduction in 14 of 15 evaluable patients with six patients achieving a partial response, or PR, by RECIST (five confirmed, one unconfirmed). For a confirmed PR, the PR was maintained through two consecutive response assessments at least four weeks apart. For the unconfirmed PR, as of the data cutoff date, a second response assessment at least four weeks after the first response assessment was not available. Tumor reduction was observed at the first dose level in the PDGFRα-driven subgroup of advanced GIST.

- In KIT-driven GIST, investigators observed radiographic tumor reduction in five of the 13 evaluable patients, including one who achieved a PR by RECIST (confirmed). At the higher dose levels (greater than or equal to 135 mg), four out of six patients had tumor reduction, including the patient with a PR, which we believe suggests increased clinical activity with increased dose. Tumor reduction was first observed at the fourth dose level in the KIT-driven subgroup of advanced GIST.

- In addition, among all 36 patients administered BLU-285 for the treatment of advanced GIST, 27 patients remained on BLU-285, including all 18 patients with PDGFRα-driven GIST. For these 36 patients, the treatment duration ranged from 0.8 months to 12.3 months. Nine patients discontinued treatment with BLU-285 due to progressive disease.

Clinical Development Plans. Our Phase 1 clinical trial for BLU-285 for the treatment of advanced GIST is designed to evaluate the safety and tolerability of BLU-285 in multiple ascending doses with the goal of establishing an MTD or a recommended dose if the MTD is not achieved. All patients will be tested retrospectively for both KIT Exon 17 and PDGFRα D842 mutational status. An MTD for BLU-285 has been established at 400 mg QD in this clinical trial, and we have initiated enrollment in the dose expansion stage. In the expansion stage, we plan to enroll cohorts for patients who have received imatinib and at least one other KIT-directed tyrosine kinase inhibitor that selects for disease with the KIT Exon 17 mutation and for patients with disease carrying a PDGFRα D842 mutation. Additional primary objectives for the dose expansion stage include determining overall response rate, or ORR, by RECIST in GIST patients who have D842V mutant PDGFRα and determining ORR by RECIST in GIST patients that have progressed following treatment with imatinib and at least one other KIT-directed tyrosine kinase inhibitor and who are not known to have D842V mutant PDGFRα. Secondary objectives include characterizing the PK of BLU-285, assessing response rate by RECIST, anti-tumor activity by Choi criteria and allelic burden using circulating tumor DNA and comparing progression free survival, or PFS, for BLU-285 with PFS for each patient's last prior anti-cancer therapy. The Phase 1 clinical trial is designed to enroll approximately 150 patients, including approximately 50 patients during dose escalation and approximately 100 additional patients in expansion cohorts, at multiple sites in the United States, European Union and Canada.

Based on the preliminary safety profile and clinical activity observed in this clinical trial, we have increased the cohort size in the expansion stage to evaluate the potential of BLU-285 as a single agent therapy in PDGFRα-driven GIST and KIT-driven GIST and to accelerate our evaluation of expanded development options for BLU-285 in GIST, including opportunities to move to earlier lines of therapy and possible combinations. In addition, in August 2016, we entered into an agreement with QIAGEN Manchester Limited to develop and commercialize an assay as a companion diagnostic test to identify GIST patients with the PDGFRα D842V mutation for use with BLU-285.

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

- raise awareness of our ongoing Phase 1 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 approximately 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, and HCC accounts 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 the European Union, the main risk factors for cirrhosis are HCV, HBV and alcohol consumption. In Asia and sub-Saharan Africa, the major risk factor is chronic HBV infection.

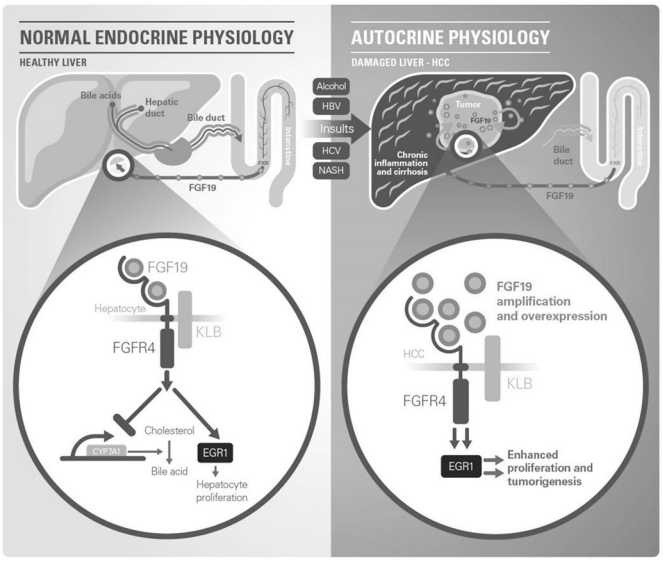
The diagnosis of HCC is typically made in adults, peaking around age 70. Disease management is complicated by concurrent liver disease, which often compromises liver function in these patients. Patients are staged depending on extent of liver disease, performance status and liver function status; these 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 molecularly 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 approximately 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 HCC patients. We estimate that more than 5% of tumors of HCC patients have this amplicon. The physiologic role of the receptor, FGFR4, and its ligand, FGF19, is to regulate bile acid metabolism in hepatocytes and liver regeneration following injury. 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-β. 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



In the figure above, HBV means hepatitis B virus, HCV means hepatitis C virus, NASH means non-alcoholic steatohepatitis and KLB means Klotho‑β.

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-β, 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 novel drug discovery platform to identify a potentially broader target responder population in addition to the FGF19-amplified patient population. We estimate that approximately 25% of HCC tumors overexpress FGF19 without amplification. We have also 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 in *Cancer Discovery* in 2015. Based on a meta-analysis of publicly available HCC genomic datasets, we estimate that approximately 30% of patients with HCC have tumors with aberrantly activated FGFR4 signaling.

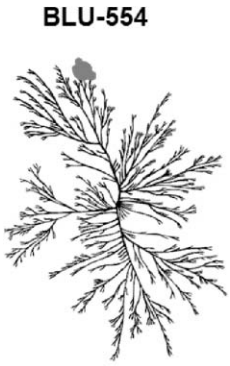
The FGFR4 signaling pathway is a promising new driver for the development of molecularly targeted therapy in HCC. In the Major Markets, we estimate there are approximately 18,900 first line and approximately 8,000 second line HCC patients with aberrantly active FGFR4 signaling, as indicated by FGF19 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 ($IC_{50} \geq 600$ 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).

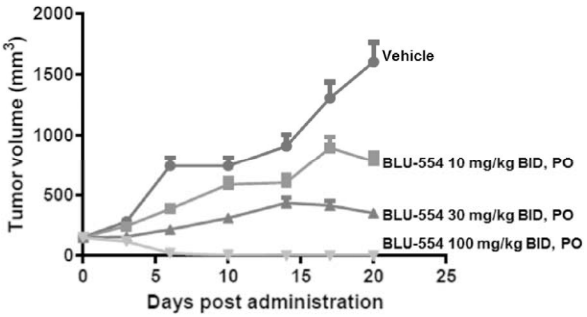
Paralog Selectivity		
FGFR4 Paralog	BLU-554	BGJ-398
FGFR4 IC_{50} (nM)	5	26
FGFR1 IC_{50} (nM)	624	<1
FGFR2 IC_{50} (nM)	1,202	<1
FGFR3 IC_{50} (nM)	2,203	<1

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.



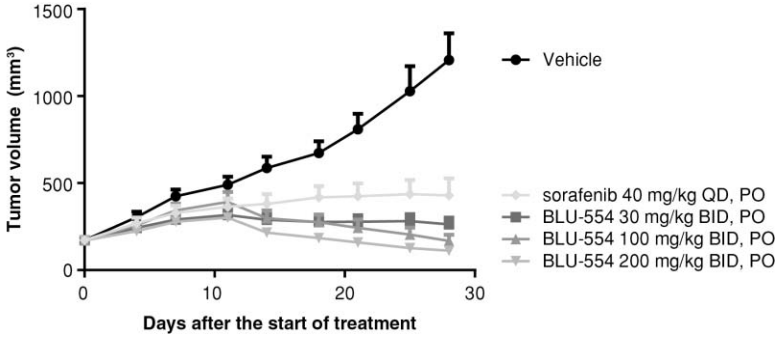
Kinome selectivity of BLU-554 as determined using the KINOME scan assay. BLU-554 was screened at 3 μM against a panel of over 450 kinases and disease-relevant mutants. Each branch of the dendogram represents an individual human kinase. Kinases bound by the compound are indicated by red circles on the 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 BID, 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 BID 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, QD means once a day, BID means twice 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 our estimate that, based on a meta-analysis of publicly available HCC genomic datasets, approximately 30% of patients with HCC have tumors with aberrantly activated FGFR4 signaling, provide critical information to identify a potential responder population and informed patient selection criteria in our Phase 1 clinical trial.

Phase 1 Clinical Trial for BLU-554 for the Treatment of Advanced HCC

BLU-554 is currently being evaluated in the dose expansion stage of a Phase 1 clinical trial in patients with advanced HCC, and enrollment is ongoing. In September 2015, the FDA granted orphan drug designation to BLU-554 for the treatment of HCC.

In November 2016, we presented preliminary data from the dose escalation stage of this ongoing clinical trial at the 28th EORTC-NCI-AACR Symposium on Molecular Targets and Cancer Therapeutics. The data showed that BLU-554 had achieved proof-of concept in this indication and an MTD had been established for BLU-554. As of the data cutoff date of November 7, 2016, BLU-554 had been administered to 25 patients in the dose escalation stage of the clinical trial at five dose levels (ranging from 140 mg QD to 900 mg QD), with the majority of patients having previously received sorafenib. Ten patients had confirmed tumor FGF19 overexpression using an investigational immunohistochemistry, or IHC, assay. PK data across all dose levels showed rapid oral absorption, a mean half-life of approximately 10 hours and exposure in the expected therapeutic range as predicted by HCC xenograft models in mice. PD data suggested that treatment with BLU-554 inhibited the FGFR4 pathway, as evidenced by effects on metabolic pathways downstream of FGFR4, with increases in the bile acid precursor C4, decreases in cholesterol and feedback upregulation of the ligand FGF19 in blood.

Preliminary Safety Data. As of the data cutoff date of November 7, 2016, the majority of adverse events reported by investigators were Grade 1 or 2 and most commonly included diarrhea (72%), nausea (44%), abdominal pain (40%), vomiting (40%), fatigue (36%), transaminase elevation (alanine aminotransferase, or ALT (32%) and aspartate aminotransferase, or AST (28%)) and decreased appetite (24%). Investigators reported Grade 3 or higher adverse events in 17 patients. Grade 3 or worse adverse events occurring in three or more patients included anemia, elevated transaminases (AST and ALT), abdominal pain and decreased lymphocytes. The MTD for BLU-554 was identified to be 600 mg QD. Two patients experienced dose-limiting toxicities at 900 mg (Grade 3 abdominal pain and Grade 3 fatigue). Only two patients discontinued treatment with BLU-554 due to treatment-related toxicities (Grade 4 increased AST and

Grade 3 hemorrhage). The case of Grade 3 hemorrhage occurred in a patient treated at 900 mg, which was above the MTD.

Preliminary Clinical Activity Data. As of the data cutoff date of November 7, 2016, 25 patients in the first five cohorts of the dose escalation stage of the clinical trial (at doses ranging from 140 mg QD to 900 mg QD) were evaluable for clinical activity.

- Investigators observed one patient with a confirmed PR, who remained on the clinical trial for eight 28-day dosing cycles, and 12 patients with stable disease, including seven who had tumor reduction but did not reach the threshold for a PR.

- Of 10 evaluable patients with FGF19 overexpression in their tumors, five had radiographic tumor reduction, including one patient with a confirmed PR. Seven of the 10 patients with FGF19 overexpression remained on the clinical trial as of the data cutoff date.

- Among all 25 evaluable patients, seven patients remained on treatment as of the data cutoff date, with treatment duration ranging from 0.8 to 7.6 months. Eighteen patients discontinued treatment with BLU-554, including 15 patients due to disease progression, two patients due to treatment-related adverse events and one patient due to the investigator's decision.

Clinical Development Plans. Our Phase 1 clinical trial for BLU-554 is designed to evaluate the safety and tolerability of BLU-554. Based on the observed mean half-life of approximately 10 hours for BLU-554 on a QD dosing schedule, we recently amended the protocol for this clinical trial to also explore a BID dosing schedule for BLU-554. For the QD dosing schedule, we have initiated enrollment of the biomarker-selected expansion cohorts for this clinical trial at the MTD of 600 mg QD. In the expansion stage for the QD dosing schedule, patients will be prospectively evaluated for tumor expression of FGF19 using an investigational IHC assay in three subsets with a range of tumors expressing FGF19. Two subsets of patients will be selected to have tumors that overexpress FGF19 (confirmed by the IHC assay), which is indicative of autocrine physiology where FGF19 is produced by the tumor cells in the liver. One of the patient subsets with tumors that overexpress FGF19 will have FGF19 gene amplification (confirmed by fluorescence in situ hybridization). The third subset of patients will be selected to have tumor FGF19 expression of less than 1% by the IHC assay, which is indicative of normal endocrine physiology, where FGF19 is produced by the intestines. For the BID dosing schedule, we plan to evaluate BLU-554 with BID dosing in multiple ascending doses with the goal of establishing an MTD for BID dosing or a recommended dose for BID dosing if the MTD for BID is not achieved. Once the MTD for BID dosing is reached, or a recommended dose for BID dosing is established, we will evaluate whether to open biomarker-selected expansion cohorts for a BID dosing schedule. Secondary objectives for this clinical trial include assessing overall response rate by RECIST criteria, the PK of BLU-554 and PD markers of BLU-554 activity. The Phase 1 clinical trial is designed to enroll approximately 130 patients, including approximately 40 patients during dose escalation for both QD and BID dosing schedules and approximately 90 additional patients in expansion cohorts for both QD and BID dosing schedules, at multiple sites in the United States, European Union and Asia.

Based on the preliminary data, we also plan to accelerate our evaluation of expanded development options for BLU-554 in HCC, including opportunities to move to earlier lines of therapy and possible combinations. In addition, in March 2015, we entered into an agreement with Ventana Medical Systems, Inc. to develop and commercialize an IHC assay as a companion diagnostic test for use with BLU-554 to identify HCC patients with aberrantly active FGFR4 signaling as indicated by FGF19 protein overexpression.

RET Program

Overview

BLU-667 is an orally available, potent selective inhibitor of the kinase RET and predicted RET resistant mutants. RET is a receptor tyrosine kinase that activates multiple downstream pathways involved in cell proliferation and survival. RET can be activated by mutation or when 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 activating mutations are implicated in MTC (approximately 60% of patients), and RET fusions are implicated in several cancers, including papillary thyroid carcinoma (approximately 10% of patients) and NSCLC (1-2% of patients). Our genomics analyses on the landscape of kinase fusions, published in *Nature Communications* in 2014, 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. In the Major Markets, we estimate there are approximately 10,000 patients with RET-driven NSCLC and approximately 600 patients with RET-driven MTC.

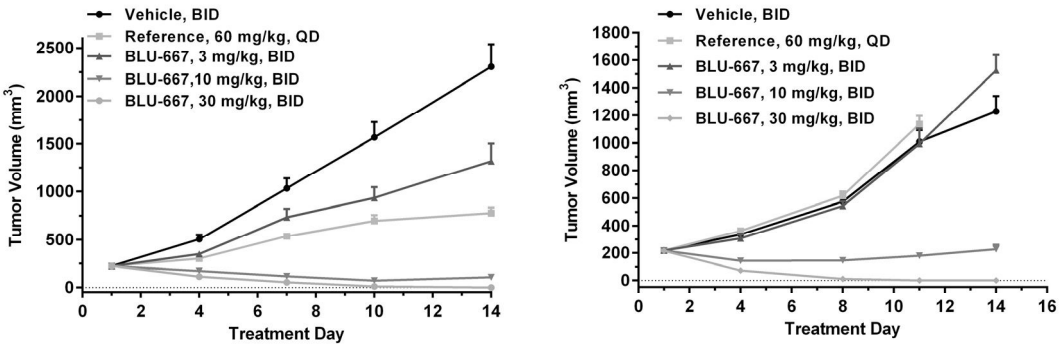
BLU-667 Pre-Clinical Development in RET

We have conducted pre-clinical experiments to characterize the potency of BLU-667 in biochemical and cellular assays. BLU-667 potently inhibits the kinase activity of both wild-type RET and predicted RET resistant mutants *in vitro* (IC_{50} of 0.4 nM and 0.3 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 resistant mutant between 1 to >1000-fold less potently than wild-type RET. In cellular models driven by either a wild-type RET fusion or resistant RET fusions, BLU-667 exhibited similar potent growth inhibitory activity in both cell lines (IC_{50} of 116.5 nM). 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.

	Biochemical			Cellular	
IC_{50}(nM)	**RET wt**	**RET Resistant Mutant**	**KDR/ VEGFR2**	**RET wt**	**RET Resistant Mutant**
BLU-667	0.4	0.3	35	16.5	15.3
Vandetanib	4	3597	4	793	9228
Cabozantinib	11	162	2	341	5582
Regorafenib	12	70	14	186	2884
Sorafenib	5.6	91	20	260	2816
Ponatinib	0.6	4	2	10	267
Lenvatinib	1.5	430	4	115	13572
Sunitinib	2.7	1.6	85	734	892

Potency of BLU-667 against wild-type RET and a predicted RET resistant mutant compared to a panel of clinically-approved multi-kinase inhibitors with RET inhibitory activity. The inhibitory potencies of BLU-667 and the multi-kinase inhibitors against wild-type RET, RET resistant mutant protein and KDR/VEGFR2 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 BLU-667 in both a wild-type RET fusion allograft and a predicted RET resistant mutant allograft. Administration of our compound orally BID for 14 days in a wild-type RET fusion allograft and for 14 days in a predicted RET resistant mutant allograft resulted in robust and dose-dependent tumor growth inhibition. At a dose of 30 mg/kg BID, a well-tolerated dose, the compound induced tumor regression in both models. 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 these models. This reference compound, dosed orally once daily at 60 mg/kg, a well-tolerated dose, inhibited tumor growth in the wild-type RET fusion allograft. At the same dose level in the RET resistant mutant allograft, this reference compound showed diminished inhibition of tumor growth.



BLU-667, a RET inhibitor, elicits dose dependent tumor growth inhibition in both a wild-type RET fusion allograft and a predicted RET resistant mutant allograft model. In the figure above, BID means twice a day, and QD means once a day.

Phase 1 Clinical Trial for BLU-667 for the Treatment of NSCLC, MTC and Other Advanced Solid Tumors

In December 2016, the FDA approved our IND application for BLU-667 for the treatment of NSCLC, thyroid cancer and other advanced solid tumors, and we expect to initiate a Phase 1 clinical trial for BLU-667 for the treatment of NSCLC, MTC and other advanced solid tumors in the first half of 2017.

Our Phase 1 clinical trial of BLU-667 in RET is designed to evaluate the safety and tolerability of BLU-667 in multiple ascending doses in patients with NSCLC, MTC and other advanced solid tumors 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 plan to open expansion cohorts for the following four patient groups: (1) NSCLC patients with a RET rearrangement who have undergone prior treatment with a tyrosine kinase inhibitor, or TKI, that inhibits RET; (2) NSCLC patients with a RET rearrangement who have never undergone treatment with a TKI that inhibits RET; (3) patients with MTC; and (4) patients with RET-altered solid tumors, other than NSCLC and MTC. Secondary objectives for this Phase 1 clinical trial include assessing the PK profile of BLU-667, assessing RET gene status in plasma and tumor tissue, characterizing the PD of BLU-667 and assessing response rate by RECIST. The Phase 1 clinical trial is designed to enroll approximately 115 patients, including approximately 35 patients during dose escalation and approximately 80 additional patients in expansion cohorts, at multiple sites in the United States and the European Union.

Collaborations and Partnerships

Alexion

In March 2015, we entered into the Alexion agreement 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, we are responsible for research and pre-clinical development activities related to drug candidates and Alexion is 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 a negotiated yearly rate per full-time equivalent for our employees' time and their 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 $250.0 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. We have recognized and received an aggregate of $3.8 million in milestone payments from Alexion through December 31, 2016. Alexion will pay us tiered royalties, ranging from 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.

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 the Alexion agreement 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.

Roche

In March 2016, we entered into the Roche agreement pursuant to which we and Roche have agreed to collaborate on the discovery, development and commercialization of up to five small molecule therapeutics targeting kinases believed to be important in cancer immunotherapy, as single products or possibly in combination with other therapeutics. The parties initiated activities for three of the collaboration programs in 2016, and the parties have agreed to work together to use our novel target discovery engine and proprietary compound library to select targets for up to two additional collaboration programs.

Under the Roche agreement, Roche is granted up to five option rights to obtain an exclusive license to exploit products derived from the collaboration programs, or licensed products, in the field of cancer immunotherapy. Such option rights are triggered upon the achievement of Phase 1 proof-of-concept. For up to three of the five collaboration programs, if Roche exercises its option, Roche will receive worldwide, exclusive commercialization rights for the licensed products. For up to two of the five collaboration programs, if Roche exercises its option, we will retain commercialization rights in the United States for the licensed products, and Roche will receive commercialization rights outside of the United States for the licensed products. We will also retain worldwide rights to any products for which Roche elects not to exercise its applicable option. Prior to Roche's exercise of an option, we will have the lead responsibility for drug discovery and pre-clinical development of all collaboration programs. In addition, we will have the lead responsibility for the conduct of all Phase 1 clinical trials other than those Phase 1 clinical trials for any product in combination with Roche's portfolio of therapeutics, for which Roche will have the right to lead the conduct of such Phase 1 clinical trials. Pursuant to the Roche agreement, the parties will share the costs of Phase 1 development for each collaboration program. In addition, Roche will be responsible for post-Phase 1 development costs for each licensed product for which it retains global commercialization rights, and we and Roche will share post-Phase 1 development costs for each licensed product for which we retain commercialization rights in the United States.

We received an upfront cash payment of $45.0 million in March 2016 upon execution of the Roche agreement, and subject to the terms of the Roche agreement, we will be eligible to receive up to approximately $965.0 million in contingent option fees and milestone payments related to specified research, pre-clinical, clinical, regulatory and sales-based milestones. Of the total contingent payments, up to approximately $215.0 million are for option fees and milestone payments for research, pre-clinical and clinical development events prior to licensing across all five potential collaboration programs, including contingent milestone payments for initiation of each of the collaboration programs for which the parties will work together to select targets. In addition, for any licensed product for which Roche retains worldwide commercialization rights, we will be eligible to receive tiered royalties ranging from low double-digits to high-teens on future net sales of the licensed product. For any licensed product for which we retain commercialization rights in the United States, we and Roche will be eligible to receive tiered royalties ranging from mid-single-digits to low double-digits on future net sales in the other party's respective territories in which it commercializes the licensed product. The upfront cash payment and any payments for milestones, option fees and royalties are non-refundable, non-creditable and not subject to set-off.

Under the Roche agreement, each party has granted the other party specified intellectual property licenses to enable the other party to perform its obligations and exercise its rights under the Roche agreement, including license grants to enable each party to conduct research, development and commercialization activities pursuant to the terms of the Roche agreement. Following Roche's exercise of its option with respect to the collaboration programs for which it will obtain worldwide rights, we will grant Roche an exclusive license under our intellectual property to develop and commercialize the licensed products generated through such collaboration program. Similarly, Roche will grant us an exclusive license under Roche's intellectual property to develop and commercialize licensed products in the United States for the collaboration programs on which we will retain rights in the United States, with Roche receiving a license under our intellectual property to develop and commercialize such licensed products outside of the United States.

Subject to the terms and conditions of the Roche agreement, we have agreed to work exclusively with Roche with respect to each collaboration target, and we have agreed to work exclusively within the field of cancer immunotherapy for a period of up to 30 months after the execution of the Roche agreement. In addition, subject to specified exceptions, Roche has a right of first negotiation in the event that we desire to grant any third party rights to develop or commercialize a licensed product under either of the collaboration programs for which we will retain commercialization rights in the United States. Roche's right of first negotiation will not apply in connection with a change of control of us, an assignment by us in accordance with the terms of the Roche agreement or certain agreements with contract research organizations, contract manufacturing organizations, academic institutions, not-for-profit third parties or distributors.

The Roche agreement will continue until the date when no royalty or other payment obligations are or will become due, unless earlier terminated in accordance with the terms of the Roche agreement. Prior to its exercise of its first option, Roche may terminate the Roche agreement at will, in whole or on a collaboration target-by-collaboration target basis, upon 120 days' prior written notice to us. Following its exercise of an option, Roche may terminate the Roche agreement at will, in whole, on a collaboration target-by-collaboration target basis, on a collaboration program-by-collaboration program basis or, if a licensed product has been commercially sold, on a country-by-country basis, (i) upon 120 days' prior written notice if a licensed product has not been commercially sold or (ii) upon 180 days' prior written notice if a licensed product has been commercially sold. Either party may terminate the Roche agreement for the other party's uncured material breach or insolvency and in certain other circumstances agreed to by the parties. In certain termination circumstances, we are entitled to retain specified licenses to be able to continue to exploit the licensed products.

Ventana

In March 2016, we entered into a master collaboration agreement and project schedules, which we refer to collectively as the Ventana agreement, with Ventana, a member of the Roche Group. Pursuant to the Ventana agreement, Ventana has agreed to develop and commercialize an assay as a companion diagnostic test to identify HCC patients with aberrantly active FGFR4 signaling as indicated by FGF19 protein overexpression for use with BLU-554. FGF19 is a ligand that activates FGFR4, a kinase that is aberrantly activated and is a driver of disease in a subset of patients with HCC. The parties anticipate using Ventana's investigational immunohistochemistry, or IHC, assay to initially develop the companion diagnostic test. IHC is a process of detecting proteins in tissue cells.

Under the Ventana agreement, Ventana is responsible for developing, and obtaining and maintaining regulatory approvals for, the companion diagnostic test in the United States, specified countries in the European Union, any other countries that recognize the CE/in vitro diagnostic self-registration process and such other countries as the parties may mutually agree. If despite using commercially reasonable efforts Ventana fails, or refuses to seek, obtain or maintain regulatory approvals for, the companion diagnostic test in any country in which Ventana is responsible for obtaining and maintaining regulatory approvals, or in the case of certain specified supply failures or failures to commercialize the companion diagnostic test in any such country, then the parties will negotiate in good faith to select, agree upon and implement one or more alternative arrangements that are reasonably acceptable to the parties for the companion diagnostic test in such country or countries.

Pursuant to the Ventana agreement, the parties will form a joint steering committee comprised of an equal number of representatives from us and Ventana. The joint steering committee will oversee the activities under the Ventana agreement and any project schedule. Upon the request of either party, the joint steering committee will form one or more of the following committees: a joint development committee, joint commercialization committee or joint patent committee.

Under the Ventana agreement, each party has granted the other party specified intellectual property licenses to enable the other party to perform its obligations and exercise its rights under the Ventana agreement, including license grants to enable Ventana to develop and commercialize companion diagnostic tests for use with any of our products that are the subject of the Ventana agreement and to enable us to develop and commercialize its products with any companion diagnostic test developed by Ventana under the Ventana agreement. Certain of the license rights granted by each party generally survive termination of the Ventana agreement. Ventana remains free to develop its companion diagnostic tests for use with a third party's therapeutic products, and we remain free to engage a third party to develop other companion diagnostic tests for use with BLU-554 and any of our other drug candidates.

Subject to the terms of the Ventana agreement, we will pay Ventana an aggregate amount of up to approximately $12.3 million over the term of the development program for the companion diagnostic test for BLU-554. In addition, we will reimburse Ventana for certain pass-through costs and will be obligated to pay Ventana up to an additional $2.0 million if we elect to have Ventana perform additional optional validation studies specified in the Ventana agreement. These amounts are subject to adjustment if the parties determine that changes in the scope of the development program are required. In addition, Ventana will retain all proceeds from the commercialization of the companion diagnostic test.

The Ventana agreement will continue until terminated by either party in accordance with its terms. If all projects under the Ventana agreement have been terminated in accordance with the terms of the Ventana agreement, either party may terminate the Ventana agreement for convenience upon 30 days' prior written notice to the other party. We are permitted to terminate any project under the Ventana agreement upon 30 days' prior written notice to Ventana in the event we cease to continue developing or commercializing the applicable product or for convenience and, under specified circumstances, payment of a termination fee and wind-down costs. Ventana is permitted to terminate any project under the Ventana agreement upon 30 or 180 days' prior written notice to us depending on the circumstances of such termination. Either party may terminate the Ventana agreement upon a material breach of the other party that is not cured within 60 days after written notice of such breach or immediately upon the bankruptcy or insolvency of the other party.

Qiagen

In August 2016, we entered into a master collaboration agreement and a project schedule, which we refer to collectively as the Qiagen agreement, with Qiagen. Pursuant to the Qiagen agreement, Qiagen has agreed to develop and commercialize an assay as a companion diagnostic test to identify GIST patients with the PDGFRα D842V mutation for use with BLU-285, one of our lead drug candidates.

Under the Qiagen agreement, Qiagen is responsible for developing, and obtaining and maintaining regulatory approvals for, the companion diagnostic test in the United States, the European Union, Canada and such other countries as the parties may mutually agree. In addition, Qiagen has agreed to use commercially reasonable efforts to manufacture the companion diagnostic test and to make the companion diagnostic test commercially available in the United States, the major European markets, Canada and such other countries as the parties may mutually agree. Under the Qiagen agreement, Qiagen has agreed to undertake specified actions to minimize the risk of an inability of supply occurring for the manufacture of the companion diagnostic test, and if Qiagen elects not to commercialize the companion diagnostic test itself in any country, Qiagen has agreed to procure alternative distribution channels or otherwise supply the companion diagnostic test to us in such quantities and upon commercially reasonable terms as necessary in order to enable us to market BLU-285 for GIST patients with the PDGFRα D842V mutation in combination with the companion diagnostic test. Qiagen remains free to develop its companion diagnostic tests for use with a third party's therapeutic products, and we remain free to engage a third party to develop other companion diagnostic tests for use with BLU-285 and any of our other drug candidates.

Subject to the terms of the Qiagen agreement and upon achievement of specified technical and development milestones, we will pay Qiagen an aggregate amount of up to approximately $6.1 million over the term of the development program for the companion diagnostic test for BLU-285. In addition, we will reimburse Qiagen for certain pass-through costs. These amounts are subject to adjustment if the parties determine that changes in the scope of the development program are required. In addition, Qiagen will retain all proceeds from the commercialization of the companion diagnostic test.

The Qiagen agreement expires on the later to occur of (i) the fifth anniversary of the Qiagen agreement and (ii) the term of any project schedule executed under the Qiagen agreement. We may terminate the Qiagen agreement or a project schedule (i) upon 30 days' prior written notice to Qiagen if such termination is due to our cessation of further development of BLU-285 or any other drug candidate covered by a project schedule executed under the Qiagen agreement and (ii) for convenience upon 120 day's prior written notice to Qiagen. Either party may terminate the Qiagen agreement or any project schedule executed under the Qiagen agreement, as applicable, upon a material breach of the other party that is not cured within 30 days after written notice of such breach or immediately upon the bankruptcy or insolvency of the other party. In the event of a termination of the Qiagen agreement by us, we will be obligated to pay Qiagen wind-down and other costs and final payments.

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, BLU-554 and BLU-667, 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 February 28, 2017, we owned seven issued U.S. patents, 20 pending U.S. patent applications, 7 pending U.S. provisional applications, 87 foreign patent applications pending in a number of jurisdictions, including Australia, Brazil, Canada, China, the European Union, Israel, India, Japan, South Korea, Mexico New Zealand, Russia, South Africa, one issued foreign patent, and six pending Patent Cooperation Treaty, or PCT, patent applications. Our pending patent applications pertain to our key research and development programs, specifically our KIT program, our FGFR4 program and our RET program; and our pipeline, specifically novel recurrent fusions. Our issued U.S. patents are projected to expire between 2033 and 2034, and any patents that may issue from our pending U.S. applications would be projected to expire between 2034 and 2037.

The intellectual property portfolios for our most advanced drug candidates as of February 28, 2017 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 just begun or is in progress. 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

The intellectual property portfolio for our KIT program contains patent applications directed to compositions of matter for BLU-285 and analogs, compositions of matter for KIT inhibitors with different compound families, as well as methods of use for these novel compounds. As of February 28, 2017, we owned three issued US patents, five pending U.S. patent applications, 28 pending foreign patent applications in a number of jurisdictions, including Argentina, Australia, Bolivia, Brazil, Canada, China, the European Union, Israel, India, Japan, South Korea, Mexico New Zealand, Pakistan, Russia, South Africa, Taiwan and Venezuela, and one pending PCT patent applications directed to our KIT program, including BLU-285. 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 February 28, 2017, we owned four issued U.S. patents, three pending U.S. patent applications, two pending U.S. provisional applications, 44 foreign patent applications in a number of jurisdictions, including Australia, Brazil, Canada, China, the European Union, Israel, India, Japan, South Korea, Mexico New Zealand, Russia, South Africa, and one issued foreign patent directed to our FGFR4 program, including BLU-554. 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, October 2034 or September 2037. Patent term adjustments or patent term extensions could result in later expiration dates.

RET

The intellectual property portfolio for our RET program contains patent applications directed to compositions of matter for BLU-667 and analogs, compositions of matter for other inhibitors of predicted RET resistant mutants and methods of use for these novel compounds. As of February 28, 2017, we owned one pending U.S. patent application, two pending PCT applications, two pending foreign patent applications filed in Argentina and Taiwan, and three pending provisional U.S. patent applications directed to our RET program, which, if issued, will have statutory expiration dates of 2036 or 2037.

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 February 28, 2017, we owned nine pending U.S. patent applications, nine pending European Union patent applications and one pending PCT patent applications directed to this technology, which, if issued, will have statutory expiration dates ranging from 2034 to 2035.

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 our discovery 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 diagnostic tests 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 our drug candidates are approved for the indications for which we are currently conducting or 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, including Exon 17 mutations, for advanced SM and GIST patients, as well as for patients with GIST with the PDGFRα 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-α 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., Deciphera Pharmaceuticals, LLC, Kolltan Pharmaceuticals, Inc., Novartis AG and Plexxikon Inc., a wholly-owned subsidiary of Daiichi Sankyo Company, Limited.

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 KIT Exon 17 mutation or the PDGFRα 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,

including by AROG Pharmaceuticals, Inc., ARIAD Pharmaceuticals, Inc., a wholly-owned subsidiary of Takeda Pharmaceutical Company Limited, Deciphera Pharmaceuticals, LLC, Kolltan Pharmaceuticals, Inc. and Plexxikon Inc., a wholly-owned subsidiary of Daiichi Sankyo Company, Limited.

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, including by AstraZeneca plc, Astellas Pharma, Inc., Bayer AG, Celgene Corporation, Eisai Inc., H3 Biomedicine Inc., Incyte Corporation, Johnson & Johnson, Novartis AG, Sanofi S.A., Taiho Pharmaceutical Co., Ltd. and Xoma Ltd.

BLU-667

The development of BLU-667 will focus on patients with the kinase RET, RET fusions and predicted RET resistant mutants. There are no approved medical therapies for RET, but there are several approved multi-kinase inhibitors with RET activity being evaluated in clinical trials, including alectinib, apatinib, cabozantinib, dovitinib, lenvatinib, ponatinib, sorafenib, sunitinib and vandetinib. In addition, there are potentially competitive drug candidates in development, including by Ignyta, Inc., Loxo Oncology, Inc. and Mirati Therapeutics.

Commercialization Plans

Our goal is to become a fully-integrated biopharmaceutical company capable 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 currently own worldwide commercial rights to all of our oncology focused drug candidates. Subject to obtaining regulatory approval, we believe that we may be able to commercialize one or more of our drug candidates in as little as five years. However, we may never obtain regulatory approval for our drug candidates or be able to develop or commercialize a marketable drug. In addition, subject to regulatory approval, 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.

Under the terms of our agreements related to the development and commercialization of companion diagnostic tests, Ventana is responsible for the commercialization of the companion diagnostic test for BLU-554 that we expect to use to identify HCC patients with abberantly active FGFR4 signaling as indicated by FGF19 overexpression, and Qiagen is responsible for the commercialization of the companion diagnostic test for BLU-285 that we expect to use to identify GIST patients with the PDGFRα D842V mutation.

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, BLU-554 and BLU-667 for our pre-clinical and 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, BLU-554 and BLU-667 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 developing drug candidates that can be produced cost-effectively at contract manufacturing facilities.

Under the terms of our agreements related to the development and commercialization of companion diagnostic tests, we will rely on each of Ventana for the manufacture of the companion diagnostic test for BLU-554 that we expect to use to identify HCC patients with abberantly active FGFR4 signaling as indicated by FGF19 overexpression and Qiagen for the manufacture of the companion diagnostic test for BLU-285 that we expect to use to identify GIST patients with the PDGFRα D842V mutation. We generally expect to rely on third parties for the manufacture of any other companion diagnostic tests we may seek to 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, 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.

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, debarment, 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 non-clinical tests, sometimes referred to as pre-clinical laboratory tests, pre-clinical animal studies and formulation studies 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 actively maintained, including by submitting annual reports;
- 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 study sites 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 pre-clinical data, 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 and/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 for oncology indications generally involve a small number of disease-affected patients who are treated with the drug candidate in escalating dose cohorts. The primary purpose of these clinical trials is to determine the MTD, or a recommended dose if the MTD is not achieved, assess the PK profile, pharmacologic action, side effect tolerability and safety of the drug. Phase 1 clinical trials for oncology indications may also evaluate preliminary evidence of clinical activity. 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 PK and PD 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.

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 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. In addition, 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. In addition, 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 fiscal year 2017 fee schedule, effective through September 30, 2017, the user fee for an application requiring clinical data, such as an NDA, is $2,038,100. PDUFA also imposes an annual product fee for human drugs ($97,750) and an annual establishment fee ($512,000) 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. In addition, 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 by inspecting the sponsor or clinical trial sites 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 requirements 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 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 based on pre-clinical or preliminary clinical data 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. 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 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 and priority review. 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, 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. Development program candidates designated as orphan drugs are exempt from the above requirements. 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 of 2010, or collectively, the Affordable Care Act. 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, voluntary recalls, 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 voluntary 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. In addition, 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 diagnostic tests, are medical devices, often *in vitro* devices, which provide information that is essential for the safe and effective use of a corresponding drug. For example, we have entered into agreements with Ventana to develop and commercialize a companion diagnostic test for BLU-554 that we expect to use to identify HCC patients with abberantly active FGFR4 signaling as indicated by FGF19 overexpression and Qiagen to develop and commercialize a companion diagnostic test for BLU-285 that we expect to use to identify GIST patients with the PDGFRα D842V mutation. 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, pre-clinical 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 test 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, pre-clinical, 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 test 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 test 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 the European Union, 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 the European Union are subject to significant regulatory controls. Although the current EU Clinical Trials Directive 2001/20/EC, or Clinical Trials Directive, 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.

In April 2014, the European Union adopted a new Clinical Trials Regulation (EU) No 536/2014, or the Clinical Trials Regulation, which is set to replace the Clinical Trials Directive. It is expected that the new Clinical Trials Regulation will apply by October 2018. The Clinical Trials Regulation will overhaul the current system of approvals for clinical trials in the European Union. Specifically, the new legislation, which will be directly applicable in all member states, aims at simplifying and streamlining the approval of clinical trials in the European Union. For instance, the new Clinical Trials Regulation provides for a streamlined application procedure via a single entry point and strictly defined deadlines for the assessment of clinical trial applications.

European Drug Review and Approval

In the European Economic Area, or EEA, (which is comprised of the 28 Member States of the European Union 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 State 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 the European Union, 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 European Union 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. In addition, 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 is 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 Affordable Care Act, enacted in March 2010, has had a significant impact on the health care industry. The Affordable Care Act expanded coverage for the uninsured while at the same time containing overall healthcare costs. With regard to pharmaceutical products, the Affordable Care Act, 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 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 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 2025 unless additional Congressional action is taken. On January 2, 2013, then 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 January 2017, Congress voted to adopt a budget resolution for fiscal year 2017, that while not a law, is widely viewed as the first step toward the passage of legislation that would repeal certain aspects of the Affordable Care Act. Further, on January 20, 2017, U.S. President Donald Trump signed an Executive Order directing federal agencies with authorities and responsibilities under the Affordable Care Act to waive, defer, grant exemptions from, or delay the implementation of any provision of the Affordable Care Act that would impose a fiscal burden on states or a cost, fee, tax, penalty or regulatory burden on individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. Congress also could consider subsequent legislation to replace elements of the Affordable Care Act that are repealed. Thus, in light of the stated policies of the new U.S. presidential administration, there is uncertainty with respect to the impact, if any, on the provisions of the Affordable Care Act affecting us. While any legislative and regulatory changes will likely take time to develop, and may or may not have an impact on the regulatory regime to which we are subject, we cannot predict the ultimate content, timing or effect of any healthcare reform legislation or the impact of potential legislation on us.

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 paying 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.

In addition, 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 Affordable Care Act, 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 are required to submit annual reports to the Centers for Medicare & Medicaid Services, which publicly posts the data on its website. 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 February 28, 2017, we had 106 full-time employees, including 41 employees with M.D. or Ph.D. degrees. Of these full-time employees, 80 employees are engaged in research and development activities, and 26 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.

Corporate Information

We were incorporated in the State of 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 38 Sidney Street, Suite 200, Cambridge, Massachusetts 02139, and our telephone number is (617) 374-7580.

Information Available on the Internet

Our Internet website address is http://www.blueprintmedicines.com. The information contained on, or that can be accessed through, our website is not a part of or incorporated by reference in this Annual Report on Form 10-K. We have included our website address in this in this Annual Report on Form 10-K solely as an inactive textual reference. We make available free of charge through our website our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and amendments to those reports filed or furnished pursuant to Sections 13(a) and 15(d) of the Exchange Act. We make these reports available through the "Investors—SEC Filings" section of our website as soon as reasonably practicable after we electronically file such reports with, or furnish such reports to, the Securities and Exchange Commission, or SEC. We also make available, free of charge on our website, the reports filed with the SEC by our executive officers, directors and 10% stockholders pursuant to Section 16 under the Exchange Act as soon as reasonably practicable after copies of those filings are provided to us by those persons. You can find, copy and inspect information we file at the SEC's public reference room, which is located at 100 F Street, N.E., Room 1580, Washington, DC 20549. Please call the SEC at 1-800-SEC-0330 for more information about the operation of the SEC's public reference room. You can review our electronically filed reports and other information that we file with the SEC on the SEC's website at http://www.sec.gov.

Item 1A. Risk Factors

The following risk factors and other information included in this Annual Report on Form 10-K should be carefully considered. The risks and uncertainties described below are not the only ones we face. Additional risks and uncertainties not presently known to us or that we presently deem less significant may also impair our business operations. Please see page 1 of this Annual Report on Form 10-K for a discussion of some of the forward-looking statements that are qualified by these risk factors. If any of the following risks occur, our business, financial condition, results of operations and future growth prospects could be materially and adversely affected.

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 investors can base an 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 and commencing Phase 1 clinical trials for our most advanced drug candidates, BLU-285, BLU-554 and BLU-667.

We are currently evaluating BLU-285 in an ongoing Phase 1 clinical trial for defined subsets of patients with gastrointestinal stromal tumors, or GIST, and an ongoing Phase 1 clinical trial for advanced systemic mastocytosis, or SM and BLU-554 in an ongoing Phase 1 clinical trial in patients with advanced hepatocellular carcinoma, or HCC. In addition, in December 2016, the U.S. Food and Drug Administration, or FDA, approved our Investigational New Drug, or IND, application for BLU-667 for the treatment of non-small cell lung cancer, or NSCLC, thyroid cancer and other advanced solid tumors, and we expect to initiate a Phase 1 clinical trial for BLU-667 for NSCLC, medullary thyroid cancer, or MTC, and other advanced solid tumors in the first half of 2017. In September 2015, the FDA granted orphan drug designation to BLU-554 for the treatment of HCC, and in January 2016, the FDA granted orphan drug designation to BLU-285 for the treatment of GIST and SM. In addition, in October 2016, the FDA granted fast track designation to BLU-285 for the treatment of patients with unresectable or metastatic GIST that progressed following treatment with imatinib and a second tyrosine kinase inhibitor and for the treatment of patients with unresectable or metastatic GIST with the PDGFRα D842V mutation regardless of prior therapy. 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 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. 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. To date, we have financed our operations primarily through public offerings of our common stock, private placements of our convertible preferred stock, collaborations and a debt financing. Through December 31, 2016, we have received an aggregate of $501.3 million from such transactions, including $312.4 million in aggregate gross proceeds from the sale of common stock in our May 2015 initial public offering and December 2016 follow-on underwritten public offering, $115.1 million in gross proceeds from the issuance of convertible preferred stock, $18.8 million of upfront and milestone payments from Alexion Pharma Holding, or Alexion, a $45.0 million upfront payment from F. Hoffmann-La Roche Ltd and Hoffmann-La Roche Inc., which we refer to collectively as Roche, and $10.0 million in gross proceeds from the debt financing.

We have incurred net losses in each year since our inception, and as of December 31, 2016, we had an accumulated deficit of $207.5 million. Our net losses were $72.5 million, $52.8 million and $40.3 million for the years ended December 31, 2016, 2015 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 continuing our existing clinical trials and beginning additional clinical trials. In addition, if we obtain marketing approval for our drug candidates, we will incur significant sales, marketing and outsourced-manufacturing expenses. We have incurred and will continue to 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 pharmaceuticals, 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, BLU-554 and BLU-667, and we 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, BLU-667 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;
- establish commercial manufacturing capabilities or make arrangements with third party manufacturers for clinical supply and commercial manufacturing;
- 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.

We may 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 pharmaceuticals is capital-intensive. We are currently advancing our lead drug candidates, BLU-285, BLU-554 and BLU-667, through clinical development. We expect our expenses to increase in connection with our ongoing activities, particularly as we continue the research and development of, initiate or continue 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, Roche or other collaborators. We may also need to raise additional funds sooner if we choose to pursue additional indications or geographies for our drug candidates or otherwise expand more rapidly than we presently anticipate. Furthermore, we expect to continue 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.

As of December 31, 2016, we had cash, cash equivalents and investments of $268.2 million. Based on our current plans, we expect that our existing cash, cash equivalents and investments, excluding any potential option fees and milestone payments under our existing collaborations, will be sufficient to enable us to fund our operating expenses and capital expenditure requirements into at least late 2018. 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 costs of producing drug substance and drug product material for use in pre-clinical studies, clinical trials and for use as commercial supply;
- the scope, prioritization and number of our research and development programs;
- the success of our collaborations with Alexion and Roche;
- the success of our current or future companion diagnostic test collaborations, including our companion diagnostic test with Ventana Medical Systems, Inc., or Ventana, for BLU-554 and our companion diagnostic test with QIAGEN Manchester Limited, or Qiagen, for BLU-285;
- 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 development activities and 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 development and 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, 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 public and private equity offerings, debt financings, collaborations, strategic alliances and licensing arrangements. We do not have any committed external source of funds, other than our collaborations with Alexion and Roche, each of which is limited in scope and duration, and funds already borrowed under the loan and security agreement that we entered into with Silicon Valley Bank in May 2013. To the extent that we raise additional capital through the sale of common stock or securities convertible or exchangeable into common stock, the ownership interest of our stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that materially adversely affect the rights of our common stockholders. 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.

Risks Related to Drug Development and Regulatory Approval

We are very early in our development efforts with only three drug candidates, BLU-285, BLU-554 and BLU-667, in clinical development. All of our other drug candidates are currently in pre-clinical or earlier stages of development. If we are unable to advance our other drug candidates to clinical development, obtain regulatory approval for our lead drug candidates or other drug candidates and ultimately commercialize our lead drug candidates or other drug candidates, or experience significant delays in doing so, our business will be materially harmed.

We are very early in our development efforts with only three drug candidates, BLU-285, BLU-554 and BLU-667, in clinical development. All of our other drug candidates are currently in pre-clinical or earlier stages of development. 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, BLU-554 and BLU-667. 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 or 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 diagnostic tests, which are assays or tests to identify an appropriate patient population. For example, we have entered into agreements with Ventana to develop and commercialize a companion diagnostic test for BLU-554 that we expect to use to identify HCC patients with abberantly active FGFR4 signaling as indicated by FGF19 overexpression and Qiagen to develop and commercialize a companion diagnostic test for BLU-285 that we expect to use to identify GIST patients with the PDGFRα D842V mutation. Companion diagnostic tests are subject to regulation as medical devices and must themselves be approved for marketing by the FDA or certain other foreign regulatory agencies before we may commercialize our drug candidates. The success of our lead drug candidates and other drug candidates will depend on several factors, including the following:

- successful enrollment in, and completion of, clinical trials, including our current Phase 1 clinical trials for BLU-285 and BLU-554 and our anticipated Phase 1 clinical trial for BLU-667;
- successful completion of pre-clinical studies for our other drug candidates;
- approval of INDs for future clinical trials for our other drug candidates;
- successful development of companion diagnostic tests for use with our drug candidates, including the development of a companion diagnostic test for BLU-554 for identifying HCC patients with FGF19 signaling and BLU-285 for identifying GIST patients with the PDGFRα D842V mutation;
- 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.

Each of our lead drug candidates, BLU-285, BLU-554 and BLU-667, is in clinical development, and all of our other drug candidates are in pre-clinical development. The risk of failure for our lead drug candidates and other drug candidates 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, current Phase 1 clinical trials and future clinical trials may not be successful.

We are currently enrolling patients in our ongoing Phase 1 clinical trials for BLU-285 for the treatment of advanced GIST, BLU-285 for the treatment of advanced SM and BLU-554 for the treatment of advanced HCC. We expect to initiate a Phase 1 clinical trial for BLU-667 for the treatment of NSCLC, MTC and other advanced solid tumors in the first half of 2017.

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 the European Union for each drug candidate and, consequently, the ultimate approval and commercial marketing of BLU-285, BLU-554, BLU-667 and our other drug candidates. We do not know whether any of our clinical trials for our lead drug candidates will 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.

We may choose not to develop a potential product candidate, or we may suspend or terminate one or more discovery programs or pre-clinical drug candidates or programs.

At any time and for any reason, we may determine that one or more of our discovery programs or pre-clinical drug candidates or programs does not have sufficient potential to warrant the allocation of resources toward such program or drug candidate. Accordingly, we may choose not to develop a potential drug candidate or elect to suspend or terminate one or more of our discovery programs or pre-clinical drug candidates or programs. For example, we have determined to suspend our discovery program for inhibitors of neurotrophic tyrosine receptor kinase, or NTRK, and predicted NTRK resistant mutants. If we suspend or terminate a program or drug candidate in which we have invested significant resources, we will have expended resources on a program that will not provide a full return on our investment and may have missed the opportunity to have allocated those resources to potentially more productive uses, including existing or future programs or drug candidates.

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 diseases in genomically defined patient populations, 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 size of the target patient population;
- the eligibility criteria for the clinical trial;
- 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.

Because the target patient populations for our drug candidates are relatively small, it may be difficult to successfully identify patients, which may lead to delays in enrollment for our trials. If the market opportunities for our drug candidates are smaller than we believe they are, our product revenues may be adversely affected and our business may suffer.

We focus our research and product development on treatments for cancer and rare genetic diseases, including genomically defined cancer and diseases driven by abnormal kinase activation. Because the target patient populations for our drug candidates are relatively small it may be difficult to successfully identify patients. We have entered into an agreements with Ventana to develop and commercialize a companion diagnostic test for BLU-554 in order to identify HCC patients with aberrantly active FGFR4 signaling as indicated by FGF19 overexpression and with Qiagen to develop and commercialize a companion diagnostic test for BLU-285 in order to identify GIST patients with the PDGFRα D842V mutation. We may engage third parties to develop companion diagnostic tests for use in some of our other current or future clinical trials. However, Ventana, Qiagen or other third parties may not be successful in developing such companion diagnostic tests, furthering the difficulty in identifying patients for our clinical trials. Our inability to enroll a sufficient number of patients in 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. If we are unable to include patients with the driver of the disease, including the applicable genomic alteration for diseases in genomically defined patient populations, 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. In addition, 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. These estimates may prove to be incorrect, and new studies may reduce the estimated incidence or prevalence of these diseases. The number of patients in the United States, European Union and elsewhere may turn out to be lower than expected, may not be otherwise amenable to treatment with our products or patients may become increasingly difficult to identify and access, all of which would adversely affect our business, prospects and ability to achieve or sustain profitability.

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 diagnostic tests, 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 diagnostic tests, including the companion diagnostic tests that we are developing with Ventana for BLU-554 in order to identify HCC patients with aberrantly active FGFR4 signaling as indicated by FGF19 overexpression and with Qiagen for BLU-285 in order to identify GIST patients with the PDGFRα D842V mutation, 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 diagnostic tests, including the companion diagnostic tests that we are developing with Ventana for BLU-554 and with Qiagen for BLU-285. We have not received approval to market any of our drug candidates or related companion diagnostic tests from regulatory authorities in any jurisdiction and it is possible that none of our drug candidates or any drug candidates or related companion diagnostic tests 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 for a drug candidate, Pre-Market Approval, or PMA, application for a companion diagnostic test 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 test 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 diagnostic tests, 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 diagnostic tests, 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. As is the case with all oncology drugs, it is likely that there may be side effects associated with the use of our drug candidates. 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.

In October 2016, the FDA granted fast track designation to BLU-285 for the treatment of patients with unresectable or metastatic GIST that progressed following treatment with imatinib and a second tyrosine kinase inhibitor and for the treatment of patients with unresectable or metastatic GIST with the PDGFRα D842V mutation regardless of prior therapy. We may also seek fast track designation for some of our other 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 though we have received fast track designation for BLU-285 for treatment of patients with unresectable or metastatic GIST that progressed following treatment with imatinib and a second tyrosine kinase inhibitor and for the treatment of patients with unresectable or metastatic GIST with the PDGFRα D842V mutation regardless of prior therapy, or even if we receive fast track designation for our other drug candidates, 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.

While we have received orphan drug designation for two of our lead drug candidates, BLU-285 and BLU-554, for specified indications, we may seek orphan drug designation for some of our other drug candidates. However, we may be unsuccessful in obtaining or may be unable to maintain the benefits associated with orphan drug designation, including the potential for market exclusivity.

In September 2015, the FDA granted orphan drug designation to BLU-554 for the treatment of HCC, and in January 2016, the FDA granted orphan drug designation to BLU-285 for the treatment of GIST and SM. As part of our business strategy, we may seek orphan drug designation for some of our other drug candidates, and we may be unsuccessful. Regulatory authorities in some jurisdictions, including the United States and the European Union, 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 the European Union, 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 the European Union 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). In addition, 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 the European Union would be

sufficient to justify the necessary investment in developing the drug. In the European Union, 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 the European Union. The European Union 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 designated 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 other drug candidates in addition to BLU-554 for the treatment of HCC and BLU-285 for the treatment of GIST and SM, we may never receive such designations. Even if we receive orphan drug designation for any of our drug candidates, 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. In addition, 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 marketing 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 discovery 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 of diseases in genomically defined patient populations 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, HCC and RET-driven NSCLC and MTC 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 in the United States, France, Germany, Italy, Spain, the United Kingdom and Japan, or the Major Markets, there are approximately: (i) 4,100 patients with advanced forms of SM, including smoldering SM, who have the KIT D816V mutation; (ii) 500 patients with PDGFRα D842V-driven GIST; (iii) 6,300 second line and third line patients with KIT-driven GIST; (iv) 18,900 first line and approximately 8,000 second line HCC patients with aberrantly active FGFR4 signaling, as indicated by FGF19 overexpression; and (iv) 10,000 patients with RET-driven NSCLC and approximately 600 patients with RET-driven MTC.

The total addressable market opportunity for BLU-285 for the treatment of patients with SM and GIST, BLU-554 for the treatment of HCC patients with aberrantly active FGFR4 signaling and BLU-667 for the treatment of patients with NSCLC and MTC will ultimately depend upon, among other things, the diagnosis criteria included in the final label for each of BLU-285, BLU-554 and BLU-667, 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, including the number of addressable patients in those markets, 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 GIST patients with the PDGFRα D842V mutation, it may face competition from other drug candidates in development for these indications, including drug candidates in development by AB Science S.A., AROG Pharmaceuticals, Inc., ARIAD Pharmaceuticals, Inc., a wholly-owned subsidiary of Takeda Pharmaceutical Company Limited, Deciphera Pharmaceuticals, LLC, Kolltan Pharmaceuticals, Inc., Novartis AG and Plexxikon Inc., a wholly-owned subsidiary of Daiichi Sankyo Company, Limited. 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, BLU-554 may face competition from other drug candidates in development by AstraZeneca plc, Bayer AG, Celgene Corporation, Eisai Inc., H3 Biomedicine Inc., Incyte Corporation, Johnson & Johnson, Novartis AG, Sanofi S.A., Taiho Pharmaceutical Co., Ltd. and Xoma Ltd. If BLU-667 receives marketing approval for patients with RET or mutations, it may face competition from other drug candidates in development, including drug candidates in development by ARIAD Pharmaceuticals, Inc., a wholly-owned subsidiary of Takeda Pharmaceutical Company Limited, AstraZeneca plc, Eisai Inc., Exelixis, Inc., GlaxoSmithKline plc, Ignyta, Inc., Loxo Oncology, Inc., Mirati Therapeutics, Inc., Novartis AG, Pfizer Inc. and Roche.

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 diagnostic tests 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 later-stage 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, including Ventana and Qiagen, are unable to successfully develop and commercialize companion diagnostic tests 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 diagnostic tests. There has been limited success to date industrywide in developing and commercializing these types of companion diagnostic tests. To be successful, we need to address a number of scientific, technical and logistical challenges. We have entered into agreements to develop and commercialize companion diagnostic tests with Ventana for BLU-554 in order to identify HCC patients with aberrantly active FGFR4 signaling as indicated by FGF19 overexpression and with Qiagen for BLU-285 in order to identify GIST patients with the PDGFRα D842V mutation. However, we have not yet initiated development and commercialization of these companion diagnostic tests or companion diagnostic tests for any of our other programs. We have little experience in the development and commercialization of companion diagnostic tests and may not be successful in developing and commercializing appropriate companion diagnostic tests to pair with any of our drug candidates that receive marketing approval. Companion diagnostic tests 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 companion diagnostic tests, we expect to rely on Ventana and Qiagen to design, manufacture, obtain regulatory approval for and commercialize the companion diagnostic tests for BLU-554 and BLU-285, respectively, and we expect to rely in whole or in part on other third parties to design, manufacture, obtain regulatory approval for and commercialize any other companion diagnostic tests for our drug candidates. We and our collaborators, including Ventana and Qiagen, may encounter difficulties in developing and obtaining approval for the companion diagnostic tests, including issues relating to selectivity/specificity, analytical validation, reproducibility, or clinical validation. In addition, our collaborators for any companion diagnostic test that we may seek to develop, our collaborators, including Ventana and Qiagen:

- may not perform their respective obligations as expected or as required under our agreements with them;
- may not pursue commercialization of a companion diagnostic test even if it receives any required regulatory approvals;
- may elect not to continue the development of a companion diagnostic test based on changes in their or other third parties' strategic focus or available funding, or external factors such as an acquisition, that divert resources or create competing priorities;
- may not commit sufficient resources to the marketing and distribution of the a companion diagnostic test; and
- may terminate their relationship with us.

Any delay or failure by us or our collaborators, including Ventana and Qiagen, to develop or obtain regulatory approval of the companion diagnostic tests could delay or prevent approval of our drug candidates. If we, or any third parties that we engage to assist us, including Ventana and Qiagen, are unable to successfully develop and commercialize companion diagnostic tests 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, including Ventana and Qiagen, may encounter production difficulties that could constrain the supply of the companion diagnostic tests, and both they and we may have difficulties gaining acceptance of the use of the companion diagnostic tests in the clinical community. If such companion diagnostic tests 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 test 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 diagnostic tests or additional pricing pressures.

In January 2017, Congress voted to adopt a budget resolution for fiscal year 2017, that while not a law, is widely viewed as the first step toward the passage of legislation that would repeal certain aspects of the Affordable Care Act. Further, on January 20, 2017, U.S. President Donald Trump signed an Executive Order directing federal agencies with authorities and responsibilities under the Affordable Care Act to waive, defer, grant exemptions from, or delay the implementation of any provision of the Affordable Care Act that would impose a fiscal burden on states or a cost, fee, tax, penalty or regulatory burden on individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. Congress also could consider subsequent legislation to replace elements of the Affordable Care Act that are repealed.

Healthcare reforms stemming from the repeal of, and potential replacement for, the Affordable Care Act may result in more rigorous coverage criteria and lower reimbursement among regulated third-party payors, and in additional downward pressure on the prices that we receive for sales of our products, if approved. Any reduction in reimbursement from Medicare or other government-funded federal programs, including the Veterans Health Administration, or state healthcare programs could lead to a similar reduction in payments from private commercial payors. The implementation of cost containment measures or other healthcare reforms may thus prevent us from being able to generate revenue or attain profitability.

We are currently unable to predict what additional legislation or regulation, if any, relating to the health care industry may be enacted in the future or what effect recently enacted federal legislation or any such additional legislation or regulation would have on our business. The pendency or approval of such proposals or reforms could result in a decrease in our stock price or limit our ability to raise capital or to enter into collaboration agreements for the further development and potential commercialization of our products.

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 or 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 countries in the European Union, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a 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 materially harmed. In addition, the recent United Kingdom referendum on its membership in the European Union resulted in a majority of United Kingdom voters voting to exit the European Union, often referred to as Brexit. Brexit has already and may continue to adversely affect European and/or worldwide regulatory conditions. Brexit could lead to legal uncertainty and potentially divergent national laws and regulations, including those related to the pricing of prescription pharmaceuticals, as the United Kingdom determines which European Union laws to replicate or replace. If the United Kingdom were to significantly alter its regulations affecting the pricing of prescription pharmaceuticals, we could face significant new costs. As a result, Brexit could impair our ability to transact business in the European Union and the United Kingdom.

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 collaborations with Alexion and Roche, as well as 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 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 rely on medical institutions, clinical investigators, CROs, contract laboratories and other third parties to conduct or otherwise support clinical trials for our drug candidates. We rely heavily on these parties for execution of clinical trials for our drug candidates and control only certain aspects of their activities. Nevertheless, we are 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 are 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 our current or future clinical trials 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 current or 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 clinical trials, and we expect to continue to do so for 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, BLU-554 and BLU-667, 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 patents 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 inhibitors with different compound families, composition of matter for FGFR4 inhibitors with multiple compound families, 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 has a statutory expiration date in 2034, the issued patent directed to BLU-285 composition of matter has a statutory expiration date in 2034 and any patents issuing from our pending patent applications are projected to expire between 2034 and 2037.

As of February 28, 2017, we owned three issued U.S. patents, five pending U.S. patent applications, 28 foreign patent applications in a number of jurisdictions, including Australia, Argentina, Brazil, Bolivia, Canada, China, the European Union, Hong Kong, Israel, India, Iraq, Japan, Lebanon, Mexico, New Zealand, Pakistan, Paraguay, Philippines, Russia, Singapore, South Africa, South Korea, Taiwan, Uruguay and Venezuela, and one pending Patent Cooperation Treaty, or PCT, patent applications directed to our KIT program, including BLU-285. 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 February 28, 2017, we owned four issued U.S. patents, three pending U.S. patent applications, two pending U.S. provisional applications, and 44 pending foreign patent applications in a number of jurisdictions, including Argentina, Australia, Bolivia, Brazil, Canada, China, Egypt, the European Union, Hong Kong, Israel, India, Indonesia, Iraq, Japan, South Korea, Lebanon, Mexico New Zealand, Pakistan, Paraguay, Philippines, Russia, Singapore, South Africa, Taiwan, Thailand, Uruguay and Venezuela, directed to our FGFR4 program, including BLU-554. 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, October 2034 or September 2037. Patent term adjustments or patent term extensions could result in later expiration dates.

As of February 28, 2017, we owned one pending U.S. patent application, two pending PCT applications, two pending foreign patent applications filed in Argentina and Taiwan, and three pending provisional U.S. patent applications directed to our RET program, which, if issued, will have statutory expiration dates of 2036 or 2037. Patent term adjustments or patent term extensions could result in later expiration dates.

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 February 28, 2017, we owned nine U.S. patent applications, nine European Union patent applications and one pending PCT patent application directed to this technology, which, if issued, will have statutory expiration dates ranging from 2034 to 2035

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. For example, we are aware of a U.S. patent owned by a third party that has generic composition of matter claims that cover BLU-554. If the claims of this third party patent are asserted against us, we do not believe BLU-554 or our proposed activities related to BLU-554 would be found to infringe any valid claim of this patent. While we may decide to initiate proceedings to challenge the validity of this patent in the future, we may be unsuccessful, and courts or patent offices in the United States and abroad could uphold the validity of any such patent. If we were to challenge the validity of any issued United States patent in court, we would need to overcome a statutory presumption of validity that attaches to every United States patent. This means that in order to prevail, we would have to present clear and convincing evidence as to the invalidity of the patent's claims.

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. For example, we are aware of a U.S. patent owned by a third party that has generic composition of matter claims that cover BLU-554. If the claims of this third party patent are asserted against us, we do not believe BLU-554 or our proposed activities related to BLU-554 would be found to infringe any valid claim of this patent. While we may decide to initiate proceedings to challenge the validity of this patent in the future, we may be unsuccessful, and courts or patent offices in the United States and abroad could uphold the validity of any such patent. If we were to challenge the validity of any issued United States patent in court, we would need to overcome a statutory presumption of validity that attaches to every United States patent. This means that in order to prevail, we would have to present clear and convincing evidence as to the invalidity of the patent's claims.

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. In addition, 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. In addition, 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, business development, financial and legal expertise of Jeffrey W. Albers, our President and Chief Executive Officer, Anthony L. Boral, our Chief Medical Officer, Marion Dorsch, our Chief Scientific Officer, Kathryn Haviland, our Chief Business Officer, Michael Landsittel, our Vice President of Finance, and Tracey McCain, our Chief Legal Officer, as well as the other principal members of our management, scientific and clinical team. Although we have entered into employment agreements with our executive officers, other than Mr. Landsittel, each of our executive officers 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.

We expect to continue hiring qualified development personnel. Recruiting and retaining qualified scientific, clinical, manufacturing and sales and marketing personnel will 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 key employees and executive officers 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 February 28, 2017, we had 106 full-time employees, and in connection with operating as 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. In addition, Brexit has already and may continue to adversely affect European and/or worldwide economic or market, political or regulatory conditions and may contribute to instability in the global financial markets, political institutions and regulatory agencies. The long-term impact of Brexit, including on our business and our industry, will depend on the terms that are negotiated in relation to the United Kingdom's future relationship with the European Union. 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 have adopted 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. In addition, 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

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

As a public company, we have incurred and expect to continue to incur, particularly after we are no longer an "emerging growth company," 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, or SEC, 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 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 has been and may in the future be volatile and fluctuate substantially.

Our stock price has been and in the future may be subject to substantial volatility. In addition, the stock market in general, and NASDAQ listed and biopharmaceutical companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. For example, our stock traded within a range of a high price of $38.33 and a low price of $13.04 per share for the period beginning on April 30, 2015, our first day of trading on The NASDAQ Global Select Market, through February 28, 2017. As a result of this volatility, our stockholders could incur substantial losses. In addition, 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.

These and other market and industry factors may cause the market price and demand for our common stock to fluctuate substantially, regardless of our actual operating performance, which may limit or prevent investors from readily selling their shares of common stock and may otherwise negatively affect the liquidity of our common stock. In the past, when the market price of a stock has been volatile, holders of that stock have instituted securities class action litigation against the company that issued the stock. If any of our stockholders brought a lawsuit against us, we could incur substantial costs defending the lawsuit. Such a lawsuit could also divert the time and attention of our management.

An active trading market for our common stock may not be sustained, and investors may not be able to resell their shares at or above the price they paid.

Although we have listed our common stock on The NASDAQ Global Select Market, an active trading market for our shares may not be sustained. 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 price at which they acquired their shares or at the time that they would like to sell. An inactive trading market may also impair our ability to raise capital to continue to fund operations by selling shares and may impair our ability to acquire other companies or technologies by using our shares as consideration.

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

The trading market for our common stock relies in part on the research and reports that equity research analysts publish about us or our business. We do not control these analysts. 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 common stock, the price of our common stock could decline. If one or more of these analysts cease to cover our common stock, we could lose visibility in the market for our common stock, which in turn could cause our common stock price to decline.

Our executive officers, directors, principal stockholders and their affiliates maintain the ability to exercise significant influence over our company and all matters submitted to stockholders for approval.

The holdings of our executive officers, directors and stockholders who own more than 5% of our outstanding common stock, together with their affiliates and related persons, represent beneficial ownership, in the aggregate, of approximately 44% of our common stock, based on the number of shares of our common stock outstanding as of

December 31, 2016. As a result, these stockholders, if they choose to 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. This concentration of voting power could delay or prevent an acquisition of our company on terms that other stockholders may desire.

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.

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.

Future sales of our common stock, including by us or our directors and executive officers or shares issued upon the exercise of currently outstanding options, could cause our stock price to decline.

A substantial portion of our outstanding common stock can be traded without restriction at any time. In addition, a portion of our outstanding common stock is currently restricted as a result of federal securities laws, but can be sold at any time subject to applicable volume limitations. As such, sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares intend to sell shares, by us or others, could reduce the market price of our common stock or impair our ability to raise adequate capital through the sale of additional equity securities. In addition, we have a significant number of shares that are subject to outstanding options. The exercise of these options and the subsequent sale of the underlying common stock could cause a further decline in our stock price. These sales also might make it difficult for us to sell equity securities in the future at a time and at a price that we deem appropriate. We cannot predict the number, timing or size of future issuances or the effect, if any, that any future issuances may have on the market price for our common stock.

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) December 31, 2020; (ii) the last day of the fiscal year in which we have total annual gross revenues of $1 billion or more; (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 SEC, 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;
- 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.

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 the sole source of gain for our stockholders.

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. In addition, under the loan and security agreement with Silicon Valley Bank, 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 the sole source of gain for our stockholders 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 shifts in our stock ownership, some of which are outside our control. As of December 31, 2016, we had federal net operating loss carryforwards of approximately $179.8 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 us.

Item 1B. Unresolved Staff Comments.

None.

Item 2. Properties.

Our headquarters are located in Cambridge, Massachusetts where we occupy approximately 38,500 rentable square feet of office and laboratory space pursuant to a lease agreement that we entered into on February 12, 2015. The lease term commenced June 15, 2015 and ends on October 31, 2022. We have an option to extend the lease term for five additional years. We believe that this 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.

Item 3. Legal Proceedings.

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

Item 4. Mine Safety Disclosures.

Not applicable.

PART II

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

Certain Information Regarding the Trading of Our Common Stock

Our common stock trades under the symbol "BPMC" on the NASDAQ Global Select Market and has been publicly traded since April 30, 2015. Prior to this time, there was no public market for our common stock. The following table sets forth the high and low sales prices of our common stock as reported on the NASDAQ Global Market for the periods indicated:

Year Ended December 31, 2015:	**High**	**Low**
Second Quarter (beginning April 30, 2015)	$ 37.17	$ 18.00
Third Quarter	$ 33.10	$ 19.39
Fourth Quarter	$ 27.00	$ 19.08
Year Ended December 31, 2016:		
First Quarter	$ 25.99	$ 13.04
Second Quarter	$ 22.48	$ 13.27
Third Quarter	$ 29.90	$ 19.51
Fourth Quarter	$ 38.33	$ 25.08

Holders

As of February 28, 2017, there were approximately 48 holders of record of our common stock. This number does not include beneficial owners whose shares are held by nominees in street name.

Dividends

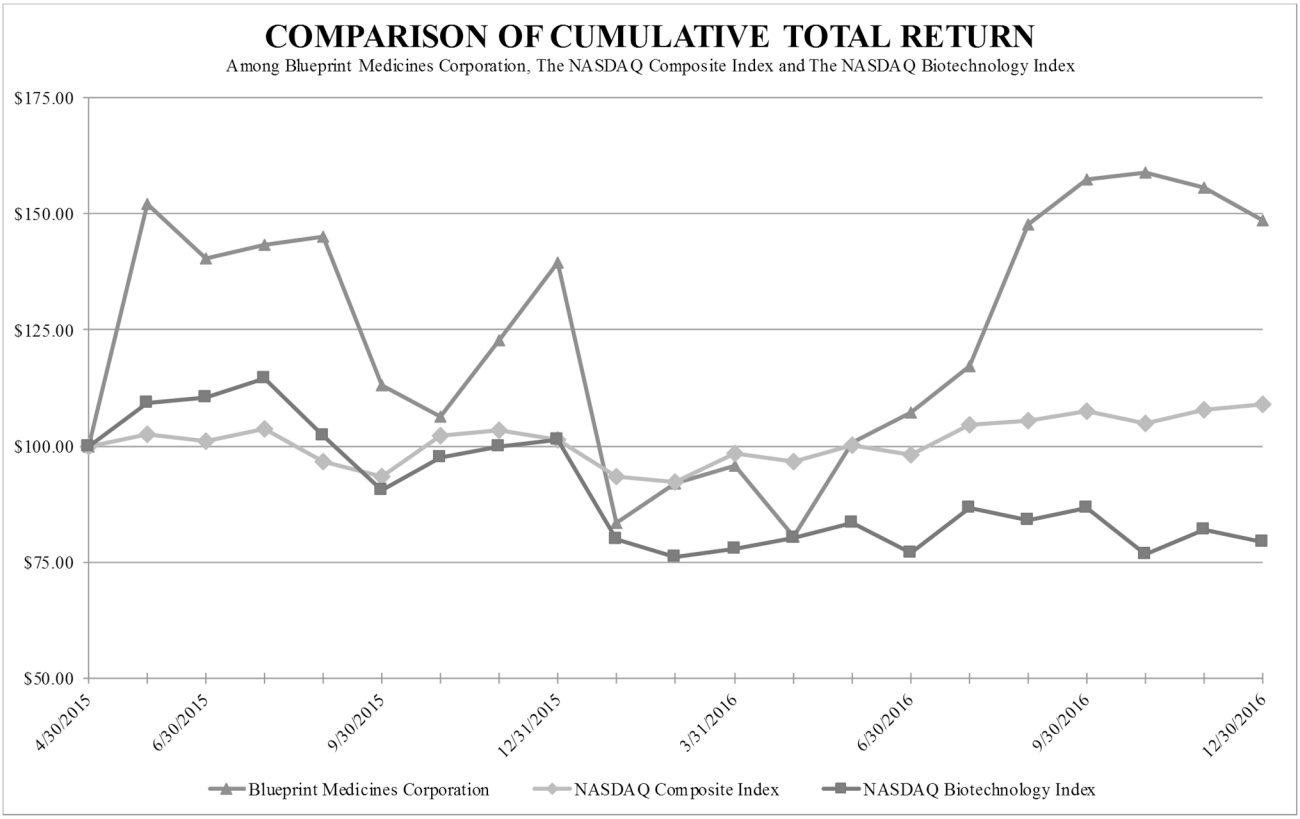
We have never declared or paid cash dividends on our capital stock. We currently intend to retain all available funds and any future earnings, if any, to fund the development and expansion of our business, and we do not anticipate paying any cash dividends in the foreseeable future. In addition, pursuant 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.

Stock Performance Graph

The following performance graph and related information shall not be deemed to be "soliciting material" or to be "filed" with the Securities and Exchange Commission, or SEC, for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, or the Exchange Act, nor shall such information be incorporated by reference into any future filing under the Exchange Act or Securities Act of 1933, as amended, or the Securities Act, except to the extent that we specifically incorporate it by reference into such filing.

The following performance graph compares the performance of our common stock to the NASDAQ Composite Index and to the NASDAQ Biotechnology Index from April 30, 2015 (the first date that shares of our common stock were publicly traded) through December 31, 2016. The comparison assumes $100 was invested in our common stock

and in each of the foregoing indices after the market closed on April 30, 2015, and it assumes reinvestment of dividends, if any. The stock price performance included in this graph is not necessarily indicative of future stock price performance.



Issuer Purchases of Equity Securities

The following table provides information relating to our repurchase of shares of our common stock during the three months ended December 31, 2016.

Period	Total Number of Shares Purchased (1)	Average Price Paid per Share ($) (2)	Total Number of Shares Purchased as Part of Publicly Announced Plans or Programs (3)	Maximum Number (or Approximate Dollar Value) of Shares that May Yet be Purchased Under the Plans or Programs (3)
October 1 - October 31	—	$ —	—	—
November 1 - November 30	—	—	—	—
December 1 - December 31	38	0.06	—	—
Total	38	$ 0.06	—	—

(1) All repurchases were made in connection with the forfeiture of shares of common stock by the recipient of such equity incentive awards in connection with the termination of the recipient's employment or other service relationship with us.

(2) The repurchase price for all shares of common stock was equal to the price per share initially paid by the recipient.

(3) We presently have no publicly announced share repurchase plan or program.

Use of Proceeds from Initial Public Offering of Common Stock

On May 5, 2015, we completed an initial public offering, or IPO, of our common stock, which resulted in the sale of 9,367,708 shares, including 1,221,874 shares sold by us pursuant to the exercise in full by the underwriters of their option to purchase additional shares in connection with the offering, at a price to the public of $18.00 per share. The offer and sale of all of the shares in our IPO was registered under the Securities Act pursuant to a registration statement on Form S-1 (File No. 333-202938), which was declared effective by the SEC on April 29, 2015. Following the sale of the shares in connection with the closing of our IPO, the offering terminated. The offering did not terminate until the sale of all of the shares offered. Goldman, Sachs & Co. and Cowen and Company acted as joint book-running managers for the offering. JMP Securities acted as a co-manager for the offering. Wedbush PacGrow also acted as a co-manager for the offering.

We received approximately $154.8 million in net proceeds, after deducting underwriting discounts and commissions and offering costs paid by us. As of December 31, 2016, we estimate that we have used approximately $117.8 million of the net proceeds from the offering as follows: approximately $28.4 million of external costs to fund our Phase 1 clinical trials; approximately $30.2 million of external costs for new and ongoing research activities; approximately $22.6 million of internal research and development costs and approximately $36.6 million for working capital and other general corporate purposes. None of the offering expenses consisted of direct or indirect payments made by us to directors, officers or persons owning 10% or more of our common stock or to their associates, or to our affiliates, and we have not used any of the net proceeds from the offering to make payments, directly or indirectly, to any such persons. There has been no material change in the planned use of the net proceeds from our IPO as described in our final prospectus filed with the SEC on April 30, 2015 pursuant to Rule 424(b)(4) under the Securities Act. We have invested the unused proceeds from the offering in cash equivalents and investments in accordance with our investment policy.

Item 6. Selected Financial Data.

You should read the following selected consolidated financial data together with our financial statements and the related notes appearing at the end of this Annual Report on Form 10-K and Item 7 "Management's Discussion and Analysis of Financial Condition and Results of Operations" section of this Annual Report on Form 10-K. We have derived the consolidated statement of operations data for the years ended December 31, 2016, 2015 and 2014 and the consolidated balance sheet data as of December 31, 2016 and 2015 from our audited consolidated financial statements included elsewhere in this Annual Report on Form 10-K. We have derived the consolidated statement of operations data for the year ended December 31, 2013 and the consolidated balance sheet data as of December 31, 2014 and 2013 from our audited consolidated financial statements and related notes not included in this Annual Report on Form 10-K. The selected historical financial information in this section is not intended to replace our financial statements and the related notes thereto. Our historical results for any prior period are not necessarily indicative of results to be expected in any future period.

	Year Ended December 31,			
	2016	2015	2014	2013
	(in thousands, except per share data)			
Statements of Operations Data:				
Collaboration revenue	$ 27,772	$ 11,400	$ —	$ —
Operating expenses:				
Research and development	81,131	48,588	31,844	15,928
General and administrative	19,218	14,456	7,890	5,072
Total operating expenses	100,349	63,044	39,734	21,000
Other income (expense):				
Other income (expense), net	551	(429)	(98)	226
Interest and other expense	(469)	(696)	(453)	(138)
Total other income (expense)	82	(1,125)	(551)	88
Net loss	$ (72,495)	$ (52,769)	$ (40,285)	$ (20,912)
Convertible preferred stock dividends	—	(3,153)	(5,765)	(2,870)
Net loss applicable to common stockholders	$ (72,495)	$ (55,922)	$ (46,050)	$ (23,782)
Net loss per share applicable to common stockholders — basic and diluted(1)	$ (2.64)	$ (3.07)	$ (32.41)	$ (23.43)
Weighted-average number of common shares used in net loss per share applicable to common stockholders — basic and diluted(1)	27,492	18,236	1,421	1,015

(1) See Note 12, "Net Loss per Share" in the accompanying notes to our audited consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K for further details on the calculation of basic and diluted net loss per share applicable to common stockholders.

	As of December 31,			
	2016	2015 (1)	2014	2013
	(in thousands)			
Balance Sheet Data:				
Cash and cash equivalents	52,069	$ 162,707	$ 47,240	$ 1,987
Investments	216,149	—	—	—
Working capital(2)	191,913	151,776	41,510	(705)
Total assets	282,795	178,898	49,925	4,135
Deferred revenue	47,235	13,640	—	—
Term loan payable	4,069	7,338	9,042	2,863
Warrant liability	—	—	365	119
Convertible preferred stock	—	—	114,811	39,958
Total stockholders' equity (deficit)	213,078	143,979	(79,382)	(41,454)

(1) Upon the closing of our IPO in May 2015, all outstanding shares of our convertible preferred stock were converted into 15,467,479 shares of common stock, and warrants exercisable for convertible preferred stock were automatically converted into warrants exercisable for 42,423 shares of common stock.

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

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

The following discussion and analysis of our financial condition and results of operations should be read in conjunction with our audited consolidated financial statements and related notes appearing elsewhere in this Annual Report on Form 10-K. Some of the information contained in this discussion and analysis or set forth elsewhere in this Annual Report on Form 10-K, including information with respect to our plans and strategy for our business, 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 Annual Report on Form 10-K, our actual results or timing of certain events could differ materially from the results or timing described in, or implied by, these forward-looking statements.

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 diseases in genomically defined patient populations and to craft drug candidates that may provide significant and durable clinical responses for patients without adequate treatment options. This integrated biology and chemistry approach enables us to identify, characterize and design drug candidates to inhibit novel kinase targets that have been difficult to selectively inhibit. By focusing on diseases in genomically defined patient populations, we believe that we will have a more efficient development path with a greater likelihood of success. Leveraging our novel target discovery engine, we have developed a robust small molecule drug pipeline in cancer and a rare genetic disease.

Our most advanced drug candidates are BLU-285, BLU-554 and BLU-667. BLU-285 is an orally available, potent and highly selective inhibitor that targets KIT, including Exon 17 mutations, and targets PDGFRα, including the D842V mutation. These mutations abnormally activate receptor tyrosine kinases that are drivers of cancer and proliferative disorders, including gastrointestinal stromal tumors, or GIST, and systemic mastocytosis, or SM. We are currently evaluating BLU-285 in an ongoing Phase 1 clinical trial for defined subsets of patients with GIST and an ongoing Phase 1 clinical trial for advanced SM. GIST is a rare disease that is a sarcoma, or tumor of bone or connective tissue, of the gastrointestinal tract, or GI tract, and SM is a rare disorder that causes an overproduction of mast cells and the accumulation of mast cells in the bone marrow and other organs, which can lead to a wide range of debilitating symptoms and organ dysfunction and failure. BLU-554 is an orally available, potent and highly selective inhibitor that targets FGFR4, a kinase that is aberrantly activated in a defined subset of patients with hepatocellular carcinoma, or HCC, the most common type of liver cancer. We are currently evaluating BLU-554 in an ongoing Phase 1 clinical trial in patients with advanced HCC. BLU-667 targets RET, a receptor tyrosine kinase that is abnormally activated by mutations or translocations, and RET resistant mutants that we predict will arise from treatment with first generation therapies. RET is a driver of disease in non-small cell lung cancer, or NSCLC, and cancers of the thyroid, including medullary thyroid carcinoma, or MTC, and our research suggests that RET may be a driver of disease in subsets of colon

cancer, breast cancer and other cancers. In December 2016, the U.S. Food and Drug Administration, or FDA, approved our Investigational New Drug, or IND, application for BLU-667 for the treatment of NSCLC, thyroid cancer and other advanced solid tumors, and we expect to initiate a Phase 1 clinical trial for BLU-667 for the treatment of NSCLC, MTC and other advanced solid tumors in the first half of 2017. In September 2015, the FDA granted orphan drug designation to BLU-554 for the treatment of HCC, and in January 2016, the FDA granted orphan drug designation to BLU-285 for the treatment of GIST and SM. In addition, in October 2016, the FDA granted fast track designation to BLU-285 for the treatment of patients with unresectable or metastatic GIST that progressed following treatment with imatinib and a second tyrosine kinase inhibitor and for the treatment of patients with unresectable or metastatic GIST with the PDGFRα D842V mutation regardless of prior therapy. We have worldwide development and commercialization rights to BLU-285, BLU-554 and BLU-667.

We also have initiated a discovery program targeting protein kinase cAMP-activated catalytic subunit alpha, or PRKACA, fusions for the treatment of fibrolamellar carcinoma, or FLC, a rare and distinct subtype of liver cancer that typically arises in young adults. PRKACA fusions are the only known recurrent genomic events in FLC and are considered to be the driver gene of the disease. Currently, there are no approved therapies for FLC, and surgery is the only available treatment option for some patients, but most patients inevitably progress. We will continue to leverage our discovery platform to systematically and reproducibly identify kinases that are drivers of diseases in genomically defined patient populations and craft drug candidates that potently and selectively target these kinases. We anticipate nominating at least one additional discovery program in 2017.

In addition to our wholly-owned clinical and pre-clinical programs, we have leveraged our discovery platform to enter into collaboration programs with Alexion Pharma Holding, or Alexion, and F. Hoffmann-La Roche Ltd and Hoffmann-La Roche Inc., which we refer to collectively as Roche.

Since inception, our operations have focused on organizing and staffing our company, business planning, raising capital, establishing our intellectual property, building our discovery 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 clinical trials, conducting pre-clinical studies, including GLP toxicology studies and commencing clinical development activities. We do not have any drugs approved for sale and have not generated any revenue from drug sales.

To date, we have financed our operations primarily through public offerings of our common stock, private placements of our convertible preferred stock, collaborations and a debt financing. Through December 31, 2016, we have received an aggregate of $501.3 million from such transactions, including $312.4 million in aggregate gross proceeds from the sale of common stock in our May 2015 initial public offering, or IPO, and December 2016 follow-on underwritten public offering, $115.1 million in gross proceeds from the issuance of convertible preferred stock, $18.8 million of upfront and milestone payments from Alexion, a $45.0 million upfront payment from Roche and $10.0 million in gross proceeds from the debt financing.

Since inception, we have incurred significant operating losses. Our net losses were $72.5 million, $52.8 million and $40.3 million for the years ended December 31, 2016, 2015 and 2014. As of December 31, 2016, we had an accumulated deficit of $207.5 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, particularly as we:

- continue the planned clinical development activities for two of our lead drug candidates, BLU-285 and BLU-554, commence the planned clinical development activities for our other lead drug candidate, BLU-667;
- continue to produce drug substance and drug product material for use in pre-clinical studies and clinical trials;
- continue to discover, validate and develop additional drug candidates;
- conduct research and development activities under our collaborations with Alexion and Roche;

- conduct development and commercialization activities for companion diagnostic tests, including our companion diagnostic tests with Ventana Medical Systems, Inc., or Ventana, for BLU-554 and with QIAGEN Manchester Limited, or Qiagen, for BLU-285;

- 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.

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. Our revenue consists of collaboration revenue under the Alexion agreement and Roche agreement, including amounts that are recognized related to upfront payments, milestone payments and amounts due to us for research and development services. In the future, revenue may include additional milestone payments and royalties on any net product sales under the respective collaboration agreements. We expect that any revenue we generate will fluctuate from quarter to quarter as a result of the timing and amount of license fees, research and development reimbursements, payments for manufacturing services, and milestone and other payments.

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, clinical activities and manufacturing on our behalf;

- the cost of consultants;

- the cost of lab supplies and acquiring, developing and manufacturing pre-clinical study and clinical trial 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 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. In addition, future commercial and regulatory factors beyond our control will impact our clinical development programs and plans.

A significant portion of our research and development expenses have been external expenses, which we track on a program-by-program basis following nomination as a development candidate. Our internal research and development expenses are primarily personnel-related expenses, including stock-based compensation expense. 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 for the years ended December 31, 2016 and 2015. Pre-development candidate expenses, unallocated expenses and internal research and development expenses have been classified separately.

	Year Ended December 31,		
	2016	2015	2014
		(in thousands)	
BLU-285 external expenses	$ 10,653	$ 6,338	5,290
BLU-554 external expenses	13,160	5,134	3,437
BLU-667 external expenses	6,599	—	—
External pre-development candidate expenses and unallocated expenses	32,232	23,104	13,855
Internal research and development expenses	18,487	14,012	9,262
Total research and development expenses	$ 81,131	$ 48,588	$ 31,844

We expect that our research and development expenses will increase in future periods as we expand our operations and incur additional costs in connection with our clinical trials. These increases will likely include the costs related to the implementation and expansion of clinical trial sites and related patient enrollment, monitoring, program management and drug product and drug substance manufacturing expenses. In addition, we expect that our research and development expenses will increase in future periods as we incur additional costs in connection with research and development activities under our collaborations with Alexion and Roche and development activities for companion diagnostic tests, including our companion diagnostic tests with Ventana and Qiagen.

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 expect that our general and administrative expenses will increase in the future to support continued research and development activities, including as we continue our existing clinical trials and initiate additional clinical trials, as well as pre-commercial development activities. These increases will likely include increased costs related to the hiring of additional personnel, legal, auditing and filing fees and general compliance and consulting expenses, among other expenses. We have incurred and will continue to incur additional costs associated with operating as a public company.

Other Income (Expense)

Other income (expense) consists primarily of income earned on cash equivalents and investments and the re-measurement gain or loss associated with the change in the fair value of the convertible preferred stock warrant liability in periods prior to our IPO.

Interest Expense

Interest expense consists primarily of interest expense on amounts outstanding under a loan and security agreement that we entered into with Silicon Valley Bank in May 2013 and amortization of debt discount.

Critical Accounting Policies and Estimates

Our management's discussion and analysis of our financial condition and results of operations are based on our consolidated financial statements, which have been prepared in accordance with U.S. generally accepted accounting principles. The preparation of these consolidated 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 consolidated 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 consolidated financial statements prospectively from the date of change in estimates.

Our critical accounting policies are those policies that require the most significant judgments and estimates in the preparation of our financial statements. Management has determined that our most critical accounting policies are those relating to revenue recognition, accrued research and development expenses, available-for-sale investments and stock-based compensation.

Available-for-Sale Investments

We classify marketable securities with a remaining maturity when purchased of greater than three months as available-for-sale. Marketable securities with a remaining maturity date greater than one year are classified as non-current. Available-for-sale securities are maintained by an investment manager and may consist of U.S. Treasury securities and U.S. government agency securities. Available-for-sale securities are carried at fair value with the unrealized gains and losses included in other comprehensive income (loss) as a component of stockholders' equity until realized. Any premium or discount arising at purchase is amortized and/or accreted to interest income and/or expense over the life of the instrument. Realized gains and losses are determined using the specific identification method and are included in other income (expense). If any adjustment to fair value reflects a decline in value of the investment, we consider all available evidence to evaluate the extent to which the decline is "other-than-temporary" and, if so, mark the investment to market through a charge to our statement of operations and comprehensive loss.

Revenue Recognition

We recognize revenue from license and collaboration agreements in accordance with Financial Accounting Standards Board, or FASB, Accounting Standards Codification, or ASC, Topic 605, *Revenue Recognition,* or ASC 605. Accordingly, revenue is recognized when all of the following criteria are met:

- persuasive evidence of an arrangement exists;
- delivery has occurred or services have been rendered;
- the seller's price to the buyer is fixed or determinable; and
- collectability is reasonably assured.

Amounts received prior to satisfying the revenue recognition criteria are recognized as deferred revenue in our balance sheets. Amounts expected to be recognized as revenue within the 12 months following the balance sheet date are classified as deferred revenue, current portion. Amounts not expected to be recognized as revenue within the 12 months following the balance sheet date are classified as deferred revenue, net of current portion.

Our revenue is currently generated through our collaboration agreements with Alexion and Roche. During the year ended December 31, 2016, we recognized revenue under the Alexion agreement of $23.3 million, which represents $14.6 million of reimbursable research and development costs, $1.8 million in milestone payments that were recognized upon achievement, as well as a portion of the $15.0 million upfront payment and the $1.8 million non-substantive milestone payment previously received. During the year ended December 31, 2016, we received $14.2 million related to reimbursable research and development costs under the Alexion agreement. As of December 31, 2016, we have recorded unbilled accounts receivable of $3.6 million related to reimbursable research and development costs under the Alexion agreement for activities performed during the fourth quarter of 2016. During the year ended December 31, 2016, we recognized revenue under the Roche agreement of $4.5 million, which represents a portion of the $45.0 million upfront payment.

The terms of these agreements contain multiple elements, or deliverables, including exclusive license granted by us to Alexion and Roche to research, develop, manufacture and commercialize the licensed products and the compounds in the field in the territory, as well as research and development activities to be performed by us on behalf of Alexion and Roche related to the licensed product candidates. In addition, the terms of these agreements include payments to us of one or more of the following: a nonrefundable, upfront payment; contingent milestone payments related to specified pre-clinical milestones, development milestones and sales-based commercial milestones; fees for research and development services rendered; and royalties on commercial sales of licensed product candidates, if any. To date, we have received the upfront payment upon execution of the Alexion agreement, the upfront payment upon execution of the Roche agreement, payments for the achievement of the certain pre-clinical milestones under the Alexion agreement and payments for certain research and development services under the Alexion agreement. We are eligible to earn additional milestone payments under both agreements. We have not earned royalty revenue as a result of product sales.

When evaluating multiple element arrangements, we consider whether the deliverables under the arrangement represent separate units of accounting. This evaluation requires subjective determinations and requires management to make judgments about the individual deliverables and whether such deliverables are separable from the other aspects of the contractual relationship. In determining the units of accounting, management evaluates certain criteria, including whether the deliverables have standalone value, based on the consideration of the relevant facts and circumstances for each arrangement. The consideration received is allocated among the separate units of accounting using the relative selling price method, and the applicable revenue recognition criteria are applied to each of the separate units. Deliverables are considered separate units of accounting provided that: (i) the delivered item(s) has value to the customer on a stand-alone basis and (ii) if the arrangement includes a general right of return relative to the delivered item(s), delivery or performance of the undelivered item(s) is considered probable and substantially in our control. In assessing whether an item has stand-alone value, we consider factors such as the research, manufacturing and commercialization capabilities of the collaboration partner and the availability of the associated expertise in the general marketplace. In addition, we consider whether the collaboration partner can use the other deliverable(s) for their intended purpose without the receipt of the remaining element(s), whether the value of the deliverable is dependent on the undelivered

item(s) and whether there are other vendors that can provide the undelivered element(s). Our collaboration agreements with Alexion and Roche do not contain a general right of return relative to the delivered item(s).

Arrangement consideration that is fixed or determinable is allocated among the separate units of accounting using the relative selling price method. Then, the applicable revenue recognition criteria in ASC 605-25 are applied to each of the separate units of accounting in determining the appropriate period and pattern of recognition. We determine the selling price of a unit of accounting following the hierarchy of evidence prescribed by ASC 605-25. Accordingly, we determine the estimated selling price for units of accounting within each arrangement using vendor-specific objective evidence, or VSOE, of selling price, if available, third-party evidence, or TPE, of selling price if VSOE is not available, or best estimate of selling price, or BESP, if neither VSOE nor TPE is available. We typically use BESP to estimate the selling price, since it generally does not have VSOE or TPE of selling price for its units of accounting. Determining the BESP for a unit of accounting requires significant judgment. In developing the BESP for a unit of accounting, we consider applicable market conditions and relevant entity-specific factors, including factors that were contemplated in negotiating the agreement with the customer and estimated costs. We validate the BESP for units of accounting by evaluating whether changes in the key assumptions used to determine the BESP will have a significant effect on the allocation of arrangement consideration between multiple units of accounting.

In the event that an element of a multiple element arrangement does not represent a separate unit of accounting, we recognize revenue from the combined element over the period over which we expect to fulfill its performance obligations or as undelivered items are delivered, as appropriate, if all of the other revenue recognition criteria in ASC 605-25 are met. If the pattern of performance in which the service is provided to the customer can be determined and objectively measurable performance measures exist, then we recognize revenue under the arrangement using the proportional performance method. If there is no discernible pattern of performance and/or objectively measurable performance measures do not exist, then we recognize revenue under the arrangement on a straight-line basis over the period we are expected to complete our performance obligations. Revenue recognized is limited to the lesser of the cumulative amount of payments received or the cumulative amount of revenue earned, as determined using the straight-line method or proportional performance method, as applicable, as of the period ending date.

Our multiple-element revenue arrangements may include the following:

Exclusive Licenses

The deliverables under our collaboration agreements may include exclusive licenses to research, develop, manufacture and commercialize licensed products. To account for this element of an arrangement, management evaluates whether an exclusive license has stand-alone value from the undelivered elements based on the consideration of the relevant facts and circumstances of the arrangement, including the research and development capabilities of the collaboration partner. We may recognize the arrangement consideration allocated to licenses upon delivery of the license if facts and circumstances indicate that the license has stand-alone value from the undelivered elements, which generally include research and development services. We defer arrangement consideration allocated to licenses if facts and circumstances indicate that the delivered license does not have stand-alone value from the undelivered elements.

When management believes a license does not have stand-alone value from the other deliverables to be provided in the arrangement, we recognize revenue attributed to the license on a proportional basis over our contractual or estimated performance period, which is typically the term of our research and development obligations. If management cannot reasonably estimate when our performance obligation ends, then revenue is deferred until management can reasonably estimate when the performance obligation ends. The periods over which revenue should be recognized are subject to estimates by management and may change over the course of the research and development and licensing agreement. Such a change could have a material impact on the amount of revenue we record in future periods.

Research and Development Services

The deliverables under our collaboration agreements may include research and development services to be performed by us on behalf of the partner. Payments or reimbursements resulting from our research and development efforts are recognized as the services are performed and presented on a gross basis because we are the principal for such efforts, so long as there is persuasive evidence of an arrangement, the fee is fixed or determinable, and collection of the related amount is reasonably assured.

Milestone Revenue

Our collaboration agreements may include contingent milestone payments related to specified pre-clinical milestones, development milestones and sales-based commercial milestones.

At the inception of an arrangement that includes milestone payments, we evaluate whether each milestone is substantive and at risk to both parties on the basis of the contingent nature of the milestone. This evaluation includes an assessment of whether:

- the consideration is commensurate with either our performance to achieve the milestone or the enhancement of the value of the delivered item(s) as a result of a specific outcome resulting from the our performance to achieve the milestone;
- the consideration relates solely to past performance; and
- the consideration is reasonable relative to all of the deliverables and payment terms within the arrangement.

We evaluate factors such as the scientific, clinical, regulatory, commercial and other risks that must be overcome to achieve the respective milestone and the level of effort and investment required to achieve the respective milestone in making this assessment. There is considerable judgment involved in determining whether a milestone satisfies all of the criteria required to conclude that a milestone is substantive. Milestones that are not considered substantive are accounted for as license payments and recognized over the remaining period of performance from the date of achievement of the milestone. Milestones that are considered substantive will be recognized in their entirety upon successful accomplishment of the milestone, assuming all other revenue recognition criteria are met.

Royalty Revenue

We will recognize royalty revenue in the period of sale of the related product(s), based on the underlying contract terms, provided that the reported sales are reliably measurable, and we have no remaining performance obligations, assuming all other revenue recognition criteria are met.

Accrued Research and Development Expenses

As part of the process of preparing our consolidated 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. Prior to April 30, 2015, we were a privately-held company and lacked company-specific historical and implied volatility information. As such, we have used an average of expected volatility based on the volatilities of a representative group of publicly traded biopharmaceutical companies for a period equal to the expected term of the option grant. Beginning in the fourth quarter of 2015, we began to include our own volatility into the average calculation. 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;

- prior to becoming a public company, fair value estimates of the underlying shares of common stock, which were determined using the option-pricing method, or OPM, or a hybrid of the probability-weighted expected return method and the OPM and were approved by our board of directors. Upon becoming a public company, the fair value of the underlying shares of common stock equals the closing price of our stock on The NASDAQ Global Select Market on the date of grant; 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, 2016	December 31, 2015	December 31, 2014
Risk-free interest rate	1.55 %	1.66 %	1.92 %
Expected dividend yield	— %	— %	— %
Expected term (years)	6.0	6.0	6.1
Expected stock price volatility	75.94 %	85.43 %	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.

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.

Subject to certain conditions, as an EGC, we intend to rely on certain exemptions and reduced reporting requirements available under the JOBS Act, 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) December 31, 2020; (ii) the last day of the fiscal year in which we have total annual gross revenues of $1 billion or more; (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, 2016 and 2015

The following table summarizes our results of operations for the years ended December 31, 2016 and 2015, together with the changes in those items in dollars and as a percentage:

	Year Ended December 31,			
	2016	2015	Dollar Change	% Change
	(in thousands)			
Collaboration revenue	$ 27,772	$ 11,400	$ 16,372	144 %
Operating expenses:				
Research and development	81,131	48,588	32,543	67
General and administrative	19,218	14,456	4,762	33
Total operating expenses	100,349	63,044	37,305	59
Other income (expense):				
Other income, net	551	(429)	980	(228)
Interest expense	(469)	(696)	227	33
Total other income (expense)	82	(1,125)	1,207	107
Net loss	$ (72,495)	$ (52,769)	$ (19,726)	(37)%

Collaboration Revenue

Collaboration revenue increased by $16.4 million from $11.4 million for the year ended December 31, 2015 to $27.8 million for the year ended December 31, 2016. Collaboration revenue for the year ended December 31, 2016 was related to the Alexion and Roche agreements. Collaboration revenue under the Alexion agreement began in March 2015 upon the execution of the Alexion agreement, and we recorded $23.3 million in collaboration revenue under the Alexion agreement for the year ended December 31, 2016. The increase in collaboration revenue from the year ended December 31, 2015 under the Alexion agreement of $11.9 million was primarily related to increased reimbursable research and development costs, increased recognition of portions of the $15.0 million upfront payment and $1.8 million in milestone payments received from Alexion and increased milestone payments recognized upon achievement during the year ended December 31, 2016. We entered into the Roche agreement in March 2016 and recorded $4.5 million in collaboration revenue under the Roche agreement for the year ended December 31, 2016.

Research and Development Expense

Research and development expense increased by $32.5 million from $48.6 million for the year ended December 31, 2015 to $81.1 million for the year ended December 31, 2016. The increase in research and development expense was primarily related to the following:

- approximately $10.3 million in increased expenses for external clinical activities as we advanced two of our lead drug candidates, BLU-285 and BLU-554, in Phase 1 clinical trials;
- approximately $9.5 million in increased expenses associated with clinical manufacturing activities;
- approximately $6.5 million in increased personnel expense primarily due to a 33% increase in headcount, which was primarily driven by growth in the clinical and non-clinical organizations as we advanced two of our lead drug candidates, BLU-285 and BLU-554, in Phase 1 clinical trials, including an increase in stock-based compensation expense;
- approximately $4.4 million in increased expenses associated with continuing to build our discovery platform and advance our discovery pipeline, including expenses related to the Alexion agreement; and
- approximately $1.8 million in increased expenses associated with IND-enabling pre-clinical toxicology studies, primarily related to BLU-667 and the Alexion agreement.

General and Administrative Expense

General and administrative expense increased by $4.7 million from $14.5 million for the year ended December 31, 2015 to $19.2 million for the year ended December 31, 2016. The increase in general and administrative expense was primarily related to the following:

- approximately $2.7 million in increased personnel expenses primarily due to an increase of 57% in general and administrative headcount to support our overall growth as a publicly traded company, including an increase in stock-based compensation expense; and

- approximately $1.6 million in increased professional fees, including external legal fees, insurance premiums and market research expenses.

Other Income (Expense), Net

Other income (expense), net, increased by $1.0 million from $0.4 million of expense for the year ended December 31, 2015 to $0.6 million of income for the year ended December 31, 2016. The increase in other income (expense), net, was primarily related to an increase in investment income during the year ended December 31, 2016 due to our investing in marketable securities beginning in 2016. Also contributing to the increase in other income (expense) was the impact of the re-measurement associated with the change in the fair value of the convertible preferred stock warrant liability included in the year ended December 31, 2015. Upon the closing of our IPO, all outstanding warrants exercisable for convertible preferred stock were automatically converted into warrants exercisable for shares of common stock, and we reclassified the warrants as an equity instrument. Accordingly, there were no related fair value adjustments in 2016.

Interest Expense

Interest expense decreased by $0.2 million from $0.7 million for the year ended December 31, 2015 to $0.5 million for the year ended December 31, 2016. The decrease was primarily related to a decrease in the average outstanding principle balance for the year ended December 31, 2016 under the loan and security agreement with Silicon Valley Bank. We expect that interest expense will continue to decrease in subsequent periods as the principal amount under the loan decreases.

Comparison of Years Ended December 31, 2015 and 2014

The following table summarizes our results of operations for the years ended December 31, 2015 and 2014, together with the changes in those items in dollars and as a percentage:

	Year Ended December 31,			
	2015	2014	Dollar Change	% Change
	(in thousands)			
Collaboration revenue	$ 11,400	$ —	$ 11,400	100 %
Operating expenses:				
Research and development	48,588	31,844	16,744	53
General and administrative	14,456	7,890	6,566	83
Total operating expenses	63,044	39,734	23,310	59
Other income (expense):				
Other income (expense), net	(429)	(98)	(331)	(338)
Interest expense	(696)	(453)	(243)	(54)
Total other income (expense)	(1,125)	(551)	(574)	(104)
Net loss	$ (52,769)	$ (40,285)	$ (12,484)	(31)%

Collaboration Revenue

Collaboration revenue was $11.4 million for the year ended December 31, 2015 under the Alexion agreement. We did not record any collaboration revenue during the year ended December 31, 2014.

Research and Development Expense

Research and development expense increased by $16.7 million from $31.8 million for the year ended December 31, 2014 to $48.6 million for the year ended December 31, 2015. The increase in research and development expense was primarily related to the following:

- approximately $6.0 million in increased personnel expense primarily due to a 49% increase in headcount, largely driven by growth in the clinical and non-clinical organizations as we advanced two of our lead drug candidates, BLU-285 and BLU-554, into clinical trials, as well as higher stock-based compensation expense;

- approximately $6.0 million in external clinical activities as we advanced two of our lead drug candidates, BLU-285 and BLU-554, into clinical trials; and

- approximately $5.4 million as we continued to build our discovery platform and advance our discovery pipeline forward, including expenses associated with development of BLU-667 and expenses related to the Alexion agreement.

These increases were partially offset by $0.7 million of lower external IND-enabling pre-clinical and toxicology studies as well as manufacturing activities primarily due to timing associated with toxicology studies for BLU-285 and BLU-554 during the year ended December 31, 2014.

General and Administrative Expense

General and administrative expense increased by $6.6 million from $7.9 million for the year ended December 31, 2014 to $14.5 million for the year ended December 31, 2015. The increase in general and administrative expense was primarily related to the following:

- approximately $3.5 million in increased personnel expenses primarily due to an increase of 113% in general and administrative headcount to support our overall growth as a publicly traded company as well as an increase in stock-based compensation expense; and

- approximately $2.5 million increase in professional fees, including external legal and audit fees, insurance premiums, public relations fees and recruiting costs and fees paid to members of our board of directors.

Other Income (Expense), Net

Other income (expense), net, increased by $0.3 million from $0.1 million for the year ended December 31, 2014 to $0.4 million for the year ended December 31, 2015. The increase in other income (expense), net, was primarily related to the impact of the re-measurement associated with the change in the fair value of the convertible preferred stock warrant liability.

Interest Expense

Interest expense increased by $0.2 million from $0.5 million for the year ended December 31, 2014 to $0.7 million for the year ended December 31, 2015. The increase in interest expense was primarily related to a higher outstanding principal balance under the loan and security agreement with Silicon Valley Bank for the year ended December 31, 2015.

Liquidity and Capital Resources

Sources of Liquidity

To date, we have financed our operations primarily through public offerings of our common stock, private placements of our convertible preferred stock, collaborations and a debt financing. Through December 31, 2016, we have received an aggregate of $501.3 million from such transactions, including $312.4 million in aggregate gross proceeds from the sale of common stock in our May 2015 IPO and December 2016 follow-on underwritten public offering, $115.1 million in gross proceeds from the issuance of convertible preferred stock, $18.8 million of upfront and milestone payments from Alexion, a $45.0 million upfront payment from Roche and $10.0 million in gross proceeds from the debt financing.

As of December 31, 2016, we had cash, cash equivalents and investments of $268.2 million.

Cash Flows

The following table provides information regarding our cash flows for the years ended December 31, 2016, 2015 and 2014:

	Year Ended December 31,		
(in thousands)	**2016**	**2015**	**2014**
Net cash used in operating activities	$ (24,513)	$ (31,676)	$ (35,400)
Net cash used in investing activities	(218,702)	(6,079)	(700)
Net cash provided by financing activities	132,577	153,222	81,353
Net (decrease) increase in cash and cash equivalents	$ (110,638)	$ 115,467	$ 45,253

Net Cash Used in Operating Activities. Net cash used in operating activities was $24.5 million during the year ended December 31, 2016 compared to net cash used in operating activities of $31.7 million during year ended December 31, 2015. The decrease in net cash used in operating activities was primarily due to changes in deferred

revenue related to the timing and amount of upfront payments from Alexion and Roche, partially offset by an increase in net loss of $19.7 million for the year end December 31, 2016 as compared to the year ended December 31, 2015. In the year ended December 31, 2016, we received a $45.0 million upfront payment from Roche, and in the year ended December 31, 2015, we received a $15.0 million upfront payment from Alexion.

Net cash used in operating activities was $31.7 million during the year ended December 31, 2015 compared to net cash used in operating activities of $35.4 million during year ended December 31, 2014. The decrease in cash used in operating activities was primarily due to the receipt of a $15.0 million upfront payment from Alexion, partially offset by an increase in net loss of $12.5 million for the year end December 31, 2015 as compared to the year ended December 31, 2014.

Net Cash Used in Investing Activities. Net cash used in investing activities was $218.7 million during the year ended December 31, 2016 compared to net cash used in investing activities of $6.1 million during the year ended December 31, 2015. Net cash used in investing activities for the year ended December 31, 2016 consisted primarily of purchases and maturities of investments. We classify these investments as available-for-sale and record them at fair value in the accompanying condensed consolidated balance sheets. Net cash used in investing activities for the year ended December 31, 2015 consisted primarily of purchases of property and equipment.

Net cash used in investing activities was $6.1 million during the year ended December 31, 2015 compared to net cash used in investing activities of $0.7 million during the year ended December 31, 2014. Net cash used in investing activities for the year ended December 31, 2015 consisted of purchases of property and equipment as well as a security deposit payment for our new office lease agreement. Net cash used in investing activities for the year ended December 31, 2014 consisted of purchases of property and equipment.

Net Cash Provided by Financing Activities. Net cash provided by financing activities was $132.6 million during the year ended December 31, 2016 compared to net cash provided by financing activities of $153.2 million during the year ended December 31, 2015. Net cash provided by financing activities for the year ended December 31, 2016 was primarily due to $135.0 million in net proceeds from our December 2016 follow-on underwritten public offering, after deducting underwriting discounts and commissions and estimated offering expenses payable by us, partially offset by $3.3 million of principal payments on term loan payable. Net cash provided by financing activities for the year ended December 31, 2015 was primarily due to $154.8 million of net proceeds from our IPO, after deducting underwriting discounts and commissions and offering expenses payable by us, partially offset by $1.8 million of principal payments on term loan payable.

Net cash provided by financing activities was $153.2 million during the year ended December 31, 2015 compared to net cash provided by financing activities of $81.4 million during the year ended December 31, 2014. Net cash provided by financing activities for the year ended December 31, 2015 was primarily due to $154.8 million in net proceeds from our IPO, after deducting underwriting discounts and commissions and offering expenses payable by us, partially offset by $1.8 million of principal payments on term loan payable. The cash provided by financing activities for the year ended December 31, 2014 was primarily due to $74.9 million of net proceeds received from the private placement of our Series B and Series C convertible preferred stock and $6.3 million of proceeds from our term loan, net of principal payments.

Borrowings

In May 2013, we entered into the loan and security agreement with Silicon Valley Bank. 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. During the year ended December 31, 2015, we paid principal payments of $1.8 million on the first $10.0 million of advances and during the year ended December 31, 2016, we paid principal payments of $3.3 million. We are required to pay a fee of 4% of the total loan advances at the end of the term of the loan. There are no financial covenants associated with the loan and security agreement. As of December 31, 2016, we had $4.1 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.

See Note 9, "Term Loan," in the accompanying notes to our audited consolidated financial statements for additional information.

Funding Requirements

We expect our expenses to increase in connection with our ongoing activities, particularly as we continue the research and development of, continue and initiate clinical trials of, and seek marketing approval for, our 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, we expect to continue 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.

As of December 31, 2016, we had cash, cash equivalents and investments of $268.2 million. Based on our current plans, we expect that our existing cash, cash equivalents and investments, excluding any potential option fees and milestone payments under our existing collaborations, will be sufficient to enable us to fund our operating expenses and capital expenditure requirements into at least late 2018. 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 costs of producing drug substance and drug product material for use in pre-clinical studies, clinical trials and for use as commercial supply;
- the scope, prioritization and number of our research and development programs;
- the success of our collaborations with Alexion and Roche;
- the success of our current or future companion diagnostic test collaborations, including our companion diagnostic test with Ventana for BLU-554 and our companion diagnostic test with Qiagen for BLU-285;
- 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 development activities and 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 studies 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. At this time, we do not have any committed external source of funds outside of those to be earned in connection with our agreements with Alexion and Roche. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our common stockholders. 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, 2016:

	Payments Due by Period				
(in thousands)	**Total**	**Less than 1 Year**	**1 to 3 Years**	**3 to 5 Years**	**More than 5 Years**
Operating lease commitments (1)	$ 15,024	$ 2,396	$ 5,010	$ 5,315	$ 2,303
Debt repayments (2)	4,302	2,734	1,568	-	-
Total	$ 19,326	$ 5,130	$ 6,578	$ 5,315	$ 2,303

(1) Represents future minimum lease payments under our non-cancelable operating lease, which expires in October 2022, for our offices located at 38 Sidney Street, Cambridge, MA. 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 with Silicon Valley Bank. As of December 31, 2016, we had $4.1 million in outstanding principal under the loan and security agreement with Silicon Valley Bank.

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 generally cancelable at any time by us upon less than 180 days' prior written notice. Certain of these agreements require us to pay milestones to such third parties upon achievement of certain development, regulatory or commercial milestones. Amounts related to contingent milestone payments are not considered contractual obligations as they are contingent on the successful achievement of certain development, regulatory approval and commercial milestones, which may not be achieved.

We also have obligations to make future payments to third parties that become due and payable on the achievement of certain milestones. We have not included these commitments on our balance sheet or in the table above

because the achievement and timing of these milestones is not fixed and determinable. These commitments include the following:

- In March 2016, we entered into the Ventana agreement pursuant to which Ventana has agreed to develop and commercialize the companion diagnostic for BLU-554 that we expect to use to identify HCC patients with aberrantly active FGFR4 signaling as indicated by FGF19 overexpression. Subject to the terms of the Ventana agreement, we will pay Ventana an aggregate amount of up to approximately $12.3 million over the term of the development program for the companion diagnostic test for BLU-554 plus pass-through costs and certain other specified amounts. See "Item 1. Business—Collaborations and Partnerships—Ventana" of this Annual Report on Form 10-K for additional information on the Ventana agreement.

- In August 2016, we entered into the Qiagen agreement pursuant to which Qiagen has agreed to develop and commercialize the companion diagnostic for BLU-285 that we expect to use to identify GIST patients with the PDGFRα D842V mutation. Subject to the terms of the Qiagen agreement and upon achievement of specified technical and development milestones, we will pay QIAGEN an aggregate amount of up to approximately $6.1 million over the term of the development program for the companion diagnostic test for BLU-285 plus pass-through costs. These amounts are subject to adjustment if the parties determine that changes in the scope of the development program are required. See "Item 1. Business—Collaborations and Partnerships—Qiagen" of this Annual Report on Form 10-K for additional information on the Qiagen agreement.

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 SEC rules.

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

As of December 31, 2016 and 2015, respectively, we had cash, cash equivalents and investments of $268.2 million and $162.7 million, consisting primarily of money market funds and investments in U.S. treasury obligations.

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 are in short-term marketable securities. Due to the short-term duration of our investment portfolio and the low risk profile of our investments, we believe an immediate 10% change in interest rates would not have a material effect on the fair market value of our investment portfolio. We have the ability to hold our investments until maturity, and therefore, we would not expect our operating results or cash flows to be affected to any significant degree by the effect of a change in market interest rates on our investment portfolio.

We are also exposed to market risk related to changes in foreign currency exchange rates. From time to time, 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 31, 2016 and December 31, 2015, 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, 2016 and 2015.

Item 8. Financial Statements and Supplementary Data.

The financial statements required to be filed pursuant to this Item 8 are appended to this Annual Report on Form 10-K. An index of those financial statements is found in Item 15 of this Annual Report on Form 10-K.

Item 9. Change in and Disagreements with Accountants on Accounting and Financial Disclosure.

None.

Item 9A. Controls and Procedures

Management's Evaluation of our Disclosure Controls and Procedures

We maintain "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended, or the Exchange Act, that are designed to ensure that information required to be disclosed in the reports that we file or submit under the Exchange Act is (1) recorded, processed, summarized and reported, within the time periods specified in the Securities and Exchange Commission's rules and forms and (2) accumulated and communicated to our management, including our principal executive and principal financial officer, as appropriate to allow timely decisions regarding required disclosure. Our management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and our management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Our disclosure controls and procedures are designed to provide reasonable assurance of achieving their control objectives.

Our management, with the participation of our Chief Executive Officer and Vice President of Finance (our principal executive officer and principal financial officer, respectively), evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2016. Based upon such evaluation, our Chief Executive Officer and Vice President of Finance have concluded that, as of December 31, 2016, our disclosure controls and procedures were effective at the reasonable assurance level.

Management's Annual Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting. Internal control over financial reporting is defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act as a process designed by, or under the supervision of, a company's principal executive officer and principal financial officer, or persons performing similar functions, and effected by a company's board of directors, management, and other personnel, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles and includes those policies and procedures that:

- pertain to the maintenance of records that in reasonable detail accurately and fairly reflect the transactions and dispositions of a company's assets;

- provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that a company's receipts and expenditures are being made only in accordance with authorizations of the company's management and directors; and

- provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of our assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Under the supervision of and with the participation of our principal executive officer and principal financial officer, our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2016 based on the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) in Internal Control—Integrated Framework (2013 framework). Based on this assessment, management concluded that our internal control over financial reporting was effective as of December 31, 2016.

Changes in Internal Control over Financial Reporting

No change in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) occurred during the three months ended December 31, 2016 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information

None.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

The information required by this Item 10 will be included in our definitive proxy statement to be filed with the SEC with respect to our 2017 Annual Meeting of Stockholders and is incorporated herein by reference.

Item 11. Executive Compensation.

The information required by this Item 11 will be included in our definitive proxy statement to be filed with the SEC with respect to our 2017 Annual Meeting of Stockholders and is incorporated herein by reference.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters.

The information required by this Item 12 will be included in our definitive proxy statement to be filed with the SEC with respect to our 2017 Annual Meeting of Stockholders and is incorporated herein by reference.

Item 13. Certain Relationships and Related Transactions, and Director Independence.

The information required by this Item 13 will be included in our definitive proxy statement to be filed with the SEC with respect to our 2017 Annual Meeting of Stockholders and is incorporated herein by reference.

Item 14. Principal Accounting Fees and Services.

The information required by this Item 14 will be included in our definitive proxy statement to be filed with the SEC with respect to our 2017 Annual Meeting of Stockholders and is incorporated herein by reference.

PART IV

Item 15. Exhibits and Financial Statement Schedules.

(1) Financial Statements

The following documents are included on pages F-1 through F-27 attached hereto and are filed as part of this Annual Report on Form 10-K.

(2) Financial Statement Schedules

Schedules have been omitted since they are either not required or not applicable or the information is otherwise included herein.

(3) Exhibits

The exhibits filed or furnished as part of this Annual Report on Form 10-K are listed in the Exhibit Index immediately preceding such Exhibits, which Exhibit Index is incorporated herein by reference.

Item 16. Form 10-K Summary.

Not applicable.

SIGNATURES

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

BLUEPRINT MEDICINES CORPORATION

Date: March 9, 2017

By: /s/ Jeffrey W. Albers
Jeffrey W. Albers
President and Chief Executive Officer

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

Signature	Title	Date
/s/ Jeffrey W. Albers Jeffrey W. Albers	President, Chief Executive Officer and Director *(Principal Executive Officer)*	March 9, 2017
/s/ Michael Landsittel Michael Landsittel	Vice President of Finance *(Principal Financial and Accounting Officer)*	March 9, 2017
/s/ Daniel S. Lynch Daniel S. Lynch	Chairman of the Board	March 9, 2017
/s/ Nicholas Lydon Nicholas Lydon, Ph.D.	Director	March 9, 2017
/s/ Alexis Borisy Alexis Borisy	Director	March 9, 2017
/s/ Mark Goldberg Mark Goldberg, M.D.	Director	March 9, 2017
/s/ Charles A. Rowland, Jr. Charles A. Rowland, Jr.	Director	March 9, 2017
/s/ George Demetri George Demetri, M.D.	Director	March 9, 2017
/s/ Lonnel Coats Lonnel Coats	Director	March 9, 2017
/s/ Lynn Seely Lynn Seely, M.D.	Director	March 9, 2017

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Blueprint Medicines Corporation

Index to Consolidated Financial Statements

Report of Independent Registered Public Accounting Firm

The Board of Directors and Stockholders of
Blueprint Medicines Corporation

We have audited the accompanying consolidated balance sheets of Blueprint Medicines Corporation as of December 31, 2016 and 2015 and the related consolidated statements of operations and comprehensive loss, convertible preferred stock and stockholders' equity (deficit), and cash flows for each of the three years in the period ended December 31, 2016. 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 consolidated financial position of Blueprint Medicines Corporation at December 31, 2016 and 2015, and the consolidated results of its operations and its cash flows for each of the three years in the period ended December 31, 2016, in conformity with U.S. generally accepted accounting principles.

/s/ Ernst & Young LLP

Boston, Massachusetts
March 9, 2017

Blueprint Medicines Corporation
Consolidated Balance Sheets
(in thousands, except share and per share data)

	December 31, 2016	December 31, 2015
Assets		
Current assets:		
Cash and cash equivalents	$ 52,069	$ 162,707
Investments, available-for-sale	162,090	—
Restricted cash	—	119
Unbilled accounts receivable	3,577	3,414
Prepaid expenses and other current assets	2,689	4,176
Total current assets	220,425	170,416
Investments, available-for-sale	54,059	—
Property and equipment, net	6,188	6,661
Other assets	856	555
Restricted cash	1,267	1,266
Total assets	$ 282,795	$ 178,898
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	2,211	2,455
Accrued expenses	11,746	6,443
Current portion of deferred revenue	11,426	5,898
Current portion of lease incentive obligation	578	578
Current portion of term loan payable	2,551	3,266
Total current liabilities	28,512	18,640
Deferred rent, net of current portion	932	842
Deferred revenue, net of current portion	35,809	7,742
Lease incentive obligation, net of current portion	2,792	3,370
Term loan payable, net of current portion	1,518	4,072
Other long term liabilities	154	253
Commitments (Note 11)		
Stockholders' equity:		
Preferred stock, $0.001 par value; 5,000,000 shares authorized; no shares issued and outstanding	—	—
Common stock, $0.001 par value; 120,000,000 shares authorized; 33,125,479 and 27,196,053 shares issued at December 31, 2016 and December 31, 2015, respectively, and 33,123,354 and 27,065,558 shares outstanding at December 31, 2016 and December 31, 2015, respectively	33	27
Additional paid-in capital	420,533	278,927
Accumulated other comprehensive loss	(18)	—
Accumulated deficit	(207,470)	(134,975)
Total stockholders' equity	213,078	143,979
Total liabilities and stockholders' equity	$ 282,795	$ 178,898

Blueprint Medicines Corporation
Consolidated Statements of Operations and Comprehensive Loss
(in thousands, except per share data)

	Year Ended December 31,		
	2016	2015	2014
Collaboration revenue	$ 27,772	$ 11,400	$ —
Operating expenses:			
Research and development	81,131	48,588	31,844
General and administrative	19,218	14,456	7,890
Total operating expenses	100,349	63,044	39,734
Other income (expense):			
Other income (expense), net	551	(429)	(98)
Interest expense	(469)	(696)	(453)
Total other income (expense)	82	(1,125)	(551)
Net loss	$ (72,495)	$ (52,769)	$ (40,285)
Other comprehensive loss:			
Unrealized loss on investments	(18)	—	—
Comprehensive loss	$ (72,513)	$ (52,769)	$ (40,285)
Reconciliation of net loss applicable to common stockholders:			
Net loss	$ (72,495)	$ (52,769)	$ (40,285)
Convertible preferred stock dividends	—	(3,153)	(5,765)
Net loss applicable to common stockholders	$ (72,495)	$ (55,922)	$ (46,050)
Net loss per share applicable to common stockholders — basic and diluted	$ (2.64)	$ (3.07)	$ (32.41)
Weighted-average number of common shares used in net loss per share applicable to common stockholders — basic and diluted	27,492	18,236	1,421

Blueprint Medicines Corporation
Consolidated Statements of Convertible Preferred Stock and Stockholders' Equity (Deficit)
(in thousands, except 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 Other Comprehensive Loss	Accumulated Deficit	Stockholders' (Deficit) Equity
	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount				
Balance at December 31, 2013	40,000,000	$ 39,958	—	$ —	—	—	1,221,330	$ 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 cost 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	(40,000,000)	(39,958)	(20,916,663)	(24,985)	(24,154,589)	(49,868)	15,467,479	15	114,792	—	—	114,807
Initial public offering, net of issuance costs	—	—	—	—	—	—	9,367,708	9	154,743	—	—	154,752
Reclassification of warrant	—	—	—	—	—	—	—	—	810	—	—	810
Issuance of common stock upon warrant exercise	—	—	—	—	—	—	32,438	—	—	—	—	—
Issuance of common stock under stock plan	—	—	—	—	—	—	571,195	1	580	—	—	581
Stock based compensation expense	—	—	—	—	—	—	—	—	5,180	—	—	5,180
Net loss	—	—	—	—	—	—	—	—	—	—	(52,769)	(52,769)
Balance at December 31, 2015	—	$ —	—	$ —	—	$ —	27,065,558	$ 27	$ 278,927	$ —	$ (134,975)	$ 143,979
Follow on offering, net of issuance costs	—	—	—	—	—	—	5,750,000	6	134,543	—	—	134,549
Issuance of common stock under stock plan	—	—	—	—	—	—	284,471	0	546	—	—	546
Purchase of common stock under ESPP	—	—	—	—	—	—	23,325	0	377	—	—	377
Stock-based compensation expense	—	—	—	—	—	—	—	—	6,140	—	—	6,140
Unrealized loss on available-for-sale securities, net of tax	—	—	—	—	—	—	—	—	—	(18)	—	(18)
Net loss	—	—	—	—	—	—	—	—	—	—	(72,495)	(72,495)
Balance at December 31, 2016	—	$ —	—	$ —	—	$ —	33,123,354	$ 33	$ 420,533	$ (18)	$ (207,470)	$ 213,078

Blueprint Medicines Corporation
Consolidated Statements of Cash Flows
(in thousands)

	Year Ended December 31,		
	2016	2015	2014
Operating activities			
Net loss	$ (72,495)	$ (52,769)	$ (40,285)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	1,582	948	622
Noncash interest expense	73	109	85
Change in fair value of warrant liability	—	445	100
Stock-based compensation	6,140	5,180	2,326
Accretion of premiums and discounts on investments	301	—	—
Changes in assets and liabilities:			
Unbilled accounts receivable	(163)	(3,414)	—
Prepaid expenses and other current assets	1,470	(1,482)	(469)
Other assets	(304)	(552)	—
Accounts payable	4	1,391	(512)
Accrued expenses	5,773	1,956	2,873
Deferred revenue	33,594	13,641	—
Deferred rent	(488)	2,871	(140)
Net cash used in operating activities	(24,513)	(31,676)	(35,400)
Investing activities			
Purchases of property and equipment	(2,354)	(4,883)	(700)
Restricted cash	119	(1,196)	—
Purchases of investments	(264,467)	—	—
Maturities of investments	48,000	—	—
Net cash used in investing activities	(218,702)	(6,079)	(700)
Financing activities			
Proceeds from term loan	—	—	7,000
Principal payments on loan payable	(3,333)	(1,806)	(750)
Proceeds from public offering of common stock, net of commissions and underwriting discounts	135,125	156,815	—
Payment of offering costs	(143)	(2,046)	—
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	—	—	(18)
Proceeds from issuance of common stock, net of repurchases	928	259	268
Net cash provided by financing activities	132,577	153,222	81,353
Net (decrease) increase in cash and cash equivalents	(110,638)	115,467	45,253
Cash and cash equivalents at beginning of period	162,707	47,240	1,987
Cash and cash equivalents at end of period	$ 52,069	$ 162,707	$ 47,240
Supplemental cash flow information			
Cash paid for interest	$ 316	$ 452	$ 215
Public offering costs incurred but unpaid at period end	$ 433	$ —	$ —
Property and equipment purchases incurred but unpaid at period end	$ —	$ 1,244	$ —
Conversion of convertible preferred stock into common stock	$ —	$ 114,808	$ —
Reclassification of warrant liability to additional paid-in-capital	$ —	$ 810	$ —
Issuance of warrants in connection with term loan	$ —	$ —	$ 145

1. Nature of Business

Blueprint Medicines Corporation (the Company), a Delaware corporation incorporated 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 diseases in genomically defined patient populations and to craft drug candidates that may provide significant and durable clinical response to patients without adequate treatment options.

The Company is devoting substantially all of its efforts to research and development, initial market development, and raising capital. The Company is subject to a number of risks similar to those of other early stage companies, including dependence on key individuals; establishing safety and efficacy in clinical trials for its drug candidates; the need to develop commercially viable drug candidates; 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 drug candidates. 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.

On May 5, 2015, the Company completed an initial public offering (IPO) of its common stock, which resulted in the sale of 9,367,708 shares of its common stock at a price to the public of $18.00 per share, including 1,221,874 shares of common stock sold by the Company pursuant to the exercise in full by the underwriters of their option to purchase additional shares in connection with the offering. The Company received net proceeds of $154.8 million, after deducting underwriting discounts and commissions and offering expenses paid by the Company.

On December 13, 2016, the Company closed its underwritten public offering of 5,750,000 shares of its common stock at a price to the public of $25.00 per share, including 750,000 shares of common stock sold by the Company pursuant to the exercise in full by the underwriters of their option to purchase additional shares in connection with the offering. The Company received net proceeds of approximately $134.5 million, after deducting underwriting discounts and commissions and estimated offering expenses payable by the Company.

As of December 31, 2016, the Company had cash, cash equivalents and investments of $268.2 million. Based on the Company's current plans, the Company expects that its existing cash, cash equivalents and investments, excluding any potential option fees and milestone payments under its existing collaborations, will be sufficient to enable it to fund its operating expenses and capital expenditure requirements into at least late 2018.

2. Summary of Significant Accounting Policies and Recent Accounting Pronouncements

Basis of Presentation

The audited consolidated financial statements of the Company included herein have been prepared in accordance with accounting principles generally accepted in the United States (GAAP) as found in the Accounting Standards Codification (ASC) and Accounting Standards Update (ASU) of the Financial Accounting Standards Board (FASB) and the rules and regulations of the SEC.

The accompanying consolidated financial statements include the accounts of the Company and its wholly owned subsidiary, Blueprint Medicines Security Corporation, which is a Massachusetts subsidiary created to buy, sell and hold securities. All intercompany transactions and balances have been eliminated.

In connection with preparing for its IPO, 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. Upon the closing of the IPO in May 2015, all of the Company's outstanding convertible preferred stock automatically converted into 15,467,479 shares of common stock, and warrants exercisable for convertible preferred stock automatically converted into warrants exercisable for 42,423 shares of common stock. On December 13, 2016, the Company closed its underwritten public offering of 5,750,000 shares. The significant increase in

shares outstanding in the years ended December 31, 2016 and 2015 is expected to impact the year-over-year comparability of the Company's net loss per share calculations.

Use of Estimates

The preparation of financial statements in conformity with 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 prior to the IPO; revenue recognition; the valuation of liability-classified warrants prior to the IPO; accrued expenses; and income taxes.

Significant Accounting Policies

The Company's critical accounting policies are those policies that require the most significant judgments and estimates in the preparation of our financial statements. Management has determined that the Company's most critical accounting policies are those relating to revenue recognition, accrued research and development expenses, available-for-sale investments and stock-based compensation.

Available-for-Sale Investments

The Company classifies marketable securities with a remaining maturity when purchased of greater than three months as available-for-sale. Marketable securities with a remaining maturity date greater than one year are classified as non-current. Available-for-sale securities are maintained by an investment manager and may consist of U.S. Treasury securities and U.S. government agency securities. Available-for-sale securities are carried at fair value with the unrealized gains and losses included in other comprehensive income (loss) as a component of stockholders' equity until realized. Any premium or discount arising at purchase is amortized and/or accreted to interest income and/or expense over the life of the instrument. Realized gains and losses are determined using the specific identification method and are included in other income (expense). If any adjustment to fair value reflects a decline in value of the investment, the Company considers all available evidence to evaluate the extent to which the decline is "other-than-temporary" and, if so, will mark the investment to market through a charge to the Company's statement of operations and comprehensive loss.

Revenue Recognition

The Company recognizes revenue from license and collaboration agreements in accordance with FASB ASC Topic 605, *Revenue Recognition* (ASC 605). Accordingly, revenue is recognized when all of the following criteria are met:

- persuasive evidence of an arrangement exists;
- delivery has occurred or services have been rendered;
- the seller's price to the buyer is fixed or determinable; and
- collectability is reasonably assured.

Amounts received prior to satisfying the revenue recognition criteria are recognized as deferred revenue in the Company's balance sheets. Amounts expected to be recognized as revenue within the 12 months following the balance sheet date are classified as deferred revenue, current portion. Amounts not expected to be recognized as revenue within the 12 months following the balance sheet date are classified as deferred revenue, net of current portion.

The Company's revenue is currently generated through its collaboration agreements with Alexion Pharma Holding (Alexion) and F. Hoffmann-La Roche Ltd and Hoffmann-La Roche Inc. (collectively, Roche) . The terms of these agreements contain multiple elements, or deliverables, including an exclusive license granted by the Company to Alexion and Roche to research, develop, manufacture and commercialize the licensed products and the compounds in the field in the territory, as well as research and development activities to be performed by the Company on behalf of Alexion and Roche related to the licensed product candidates. In addition, the terms of these agreements include payments to the Company of one or more of the following: a nonrefundable, upfront payment; contingent milestone payments related to specified pre-clinical milestones, development milestones and sales-based commercial milestones; fees for research and development services rendered; and royalties on commercial sales of licensed product candidates, if any. To date, the Company has received the upfront payments, payments for the achievement of certain pre-clinical milestones under the Alexion agreement and payments for certain research and development services. The Company is eligible to earn additional milestone payments under both agreements. The Company has not earned royalty revenue as a result of product sales. See Note 13 for additional information on this agreement.

When evaluating multiple element arrangements, the Company considers whether the deliverables under the arrangement represent separate units of accounting. This evaluation requires subjective determinations and requires management to make judgments about the individual deliverables and whether such deliverables are separable from the other aspects of the contractual relationship. In determining the units of accounting, management evaluates certain criteria, including whether the deliverables have standalone value, based on the consideration of the relevant facts and circumstances for each arrangement. The consideration received is allocated among the separate units of accounting using the relative selling price method, and the applicable revenue recognition criteria are applied to each of the separate units. Deliverables are considered separate units of accounting provided that: (i) the delivered item(s) has value to the customer on a stand-alone basis and (ii) if the arrangement includes a general right of return relative to the delivered item(s), delivery or performance of the undelivered item(s) is considered probable and substantially in the control of the Company. In assessing whether an item has stand-alone value, the Company considers factors such as the research, manufacturing and commercialization capabilities of the collaboration partner and the availability of the associated expertise in the general marketplace. In addition, the Company considers whether the collaboration partner can use the deliverable(s) for their intended purpose without the receipt of the remaining element(s), whether the value of the deliverable is dependent on the undelivered item(s) and whether there are other vendors that can provide the undelivered element(s). The Company's collaboration agreements with Alexion and Roche do not contain a general right of return relative to the delivered item(s).

Arrangement consideration that is fixed or determinable is allocated among the separate units of accounting using the relative selling price method. Then, the applicable revenue recognition criteria in ASC 605-25 are applied to each of the separate units of accounting in determining the appropriate period and pattern of recognition. The Company determines the selling price of a unit of accounting following the hierarchy of evidence prescribed by ASC 605-25. Accordingly, the Company determines the estimated selling price for units of accounting within each arrangement using vendor-specific objective evidence (VSOE) of selling price, if available, third-party evidence (TPE) of selling price if VSOE is not available, or best estimate of selling price (BESP) if neither VSOE nor TPE is available. The Company typically uses BESP to estimate the selling price, since it generally does not have VSOE or TPE of selling price for its units of accounting. Determining the BESP for a unit of accounting requires significant judgment. In developing the BESP for a unit of accounting, the Company considers applicable market conditions and relevant entity-specific factors, including factors that were contemplated in negotiating the agreement with the customer and estimated costs. The Company validates the BESP for units of accounting by evaluating whether changes in the key assumptions used to determine the BESP will have a significant effect on the allocation of arrangement consideration between multiple units of accounting.

In the event that an element of a multiple element arrangement does not represent a separate unit of accounting, the Company recognizes revenue from the combined element over the period over which it expects to fulfill its performance obligations or as undelivered items are delivered, as appropriate, if all of the other revenue recognition criteria in ASC 605-25 are met. If the pattern of performance in which the service is provided to the customer can be determined and objectively measurable performance measures exist, then the Company recognizes revenue under the arrangement using the proportional performance method. If there is no discernible pattern of performance and/or objectively measurable performance measures do not exist, then the Company recognizes revenue under the arrangement on a straight-line basis over the period the Company is expected to complete its performance obligations. Revenue recognized is limited to the lesser of the cumulative amount of payments received or the cumulative amount of revenue earned, as determined using the straight-line method or proportional performance method, as applicable, as of the period ending date.

The Company's multiple-element revenue arrangements may include the following:

Exclusive Licenses

The deliverables under the Company's collaboration agreements may include exclusive licenses to research, develop, manufacture and commercialize licensed products. To account for this element of an arrangement, management evaluates whether an exclusive license has stand-alone value from the undelivered elements based on the consideration of the relevant facts and circumstances of the arrangement, including the research and development capabilities of the collaboration partner. The Company may recognize the arrangement consideration allocated to licenses upon delivery of the license if facts and circumstances indicate that the license has stand-alone value from the undelivered elements, which generally include research and development services. The Company defers arrangement consideration allocated to licenses if facts and circumstances indicate that the delivered license does not have stand-alone value from the undelivered elements.

When management believes a license does not have stand-alone value from the other deliverables to be provided in the arrangement, the Company recognizes revenue attributed to the license on a proportional basis over the Company's contractual or estimated performance period, which is typically the term of the Company's research and development obligations. If management cannot reasonably estimate when the Company's performance obligation ends, then revenue is deferred until management can reasonably estimate when the performance obligation ends. The periods over which revenue should be recognized are subject to estimates by management and may change over the course of the research and development and licensing agreement. Such a change could have a material impact on the amount of revenue the Company records in future periods.

Research and Development Services

The deliverables under the Company's collaboration agreements may include research and development services to be performed by the Company on behalf of the partner. Payments or reimbursements resulting from the Company's research and development efforts are recognized as the services are performed and presented on a gross basis because the Company is the principal for such efforts, so long as there is persuasive evidence of an arrangement, the fee is fixed or determinable, and collection of the related amount is reasonably assured.

Milestone Revenue

The Company's collaboration agreements may include contingent milestone payments related to specified pre-clinical milestones, development milestones and sales-based commercial milestones.

At the inception of an arrangement that includes milestone payments, the Company evaluates whether each milestone is substantive and at risk to both parties on the basis of the contingent nature of the milestone. This evaluation includes an assessment of whether:

- the consideration is commensurate with either the Company's performance to achieve the milestone or the enhancement of the value of the delivered item(s) as a result of a specific outcome resulting from the Company's performance to achieve the milestone;
- the consideration relates solely to past performance; and
- the consideration is reasonable relative to all of the deliverables and payment terms within the arrangement.

The Company evaluates factors such as the scientific, clinical, regulatory, commercial and other risks that must be overcome to achieve the respective milestone and the level of effort and investment required to achieve the respective milestone in making this assessment. There is considerable judgment involved in determining whether a milestone satisfies all of the criteria required to conclude that a milestone is substantive. Milestones that are not considered substantive are accounted for as license payments and recognized over the remaining period of performance from the date of achievement of the milestone. Milestones that are considered substantive will be recognized in their entirety upon successful accomplishment of the milestone with a cumulative catch up adjustments, assuming all other revenue recognition criteria are met.

Royalty Revenue.

The Company will recognize royalty revenue in the period of sale of the related product(s), based on the underlying contract terms, provided that the reported sales are reliably measurable and the Company has no remaining performance obligations, assuming all other revenue recognition criteria are met.

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. Other comprehensive income (loss) consisted of unrealized gains and losses on investments for the year ended December 31, 2016. For the years ended December 31, 2015 and 2014, comprehensive loss was equal to net loss.

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 discovery 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. In circumstances where amounts have been paid in excess of costs incurred, the Company records a prepaid expense.

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, 2016.

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 time the warrants no longer conditionally or unconditionally obligate the Company to transfer assets or liabilities, which occurred upon the IPO, at which time the warrant liability was reclassified to stockholders' equity.

Stock-Based Compensation Expense

The Company expenses the fair value of employee stock awards net of estimated 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. Prior to April 30, 2015, the Company was a privately-held company and lacked company-specific historical and implied volatility information. 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 a period equal to the expected term of the option grant. Beginning in the fourth quarter of 2015, the Company began to include its own volatility into the average calculation. The Company intends to consistently apply this process using the same representative companies until a sufficient amount of historical information regarding the volatility of its 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;

- prior to becoming a public company, fair value estimates of the underlying common shares, which were determined using the option-pricing method (OPM) or a hybrid of the probability-weighted expected return method and the OPM and were approved by the Company's board of directors. Upon becoming a public company, the fair value of the underlying common shares equals the closing price of the Company's stock on The NASDAQ Global Select Market on the date of grant; 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 and accounts receivable.

The Company maintains its cash, cash equivalents and investments in a custodian account at a high quality financial institution, and consequently, the Company believes that such funds are subject to minimal credit risk.

Accounts receivable represents amounts due from the Company's collaboration partner. The Company monitors economic conditions to identify facts or circumstances that may indicate that its accounts receivable is at risk of collection.

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.

Recent Accounting Pronouncements

In May 2014, the FASB issued ASU No. 2014-09, *Revenue from Contracts with Customers* (ASU 2014-09), which supersedes the revenue recognition requirements in ASC 605-25, *Multiple-Element Arrangements* and most industry-specific guidance. The new standard requires that an entity recognize revenue to depict the transfer of promised goods or services to customers in an amount that reflects the consideration to which the company expects to be entitled in exchange for those goods or services. The update also requires additional disclosure about the nature, amount, timing and uncertainty of revenue and cash flows arising from customer contracts, including significant judgments and changes in judgments and assets recognized from costs incurred to obtain or fulfill a contract. This new guidance will be effective for annual reporting periods (including interim reporting periods within those years) beginning January 1, 2018. Early adoption in 2017 is permitted. Companies have the option of applying this new guidance retrospectively to each prior reporting period presented (the full retrospective method) or retrospectively with the cumulative effect of initially applying this update recognized at the date of initial application (the modified retrospective method). The Company currently anticipates adoption of the new standard effective January 1, 2018 under the modified retrospective method. The Company is in the process of determining the impact of the new guidance on its financial statements.

In August 2014, the FASB issued ASU No. 2014-15, *Presentation of Financial Statements—Going Concern (Subtopic 205-40): Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern.* This new standard is intended to define management's responsibility to evaluate whether there is substantial doubt about an entity's ability to continue as a going concern within one year of the date of issuance of the entity's financial statements and to provide related footnote disclosures. The standard is effective for interim and annual periods ending after December 15, 2016. The standard did not have a material impact on the Company's consolidated financial statements or footnote disclosures as of the December 31, 2016 adoption date, but may require additional disclosures in future periods.

In March 2016, the FASB issued ASU No. 2016-09, *Compensation – Stock Compensation*, which amends ASC Topic 718, *Compensation – Stock Compensation*. The new standard identifies areas for simplification involving several aspects of accounting for share-based payment transactions, including the income tax consequences, classification of awards as either equity or liabilities, an option to recognize gross stock compensation expense with actual forfeitures recognized as they occur, as well as certain classifications on the statement of cash flows. The new standard will be effective for the Company on January 1, 2017. The adoption of this standard is expected to impact the income tax footnote disclosures and is not expected to have a material impact on the Company's consolidated financial statements.

In November, 2015, the FASB issued ASU No. 2015-17, *Income Taxes—Balance Sheet Classification of Deferred Taxes(*Topic 740). The new standard requires that deferred tax assets and liabilities be classified as noncurrent in a classified statement of financial position. The adoption of this standard in the last quarter of 2016 did not have a

material impact on the Company's financial position or results of operations as its net deferred tax assets have been fully offset by a valuation allowance.

In February 2016, the FASB issued ASU No. 2016-02, *Leases*. ASU 2016-02 will change the way the Company recognizes its leased assets. ASU 2016-02 will require organizations that lease assets—referred to as "lessees"—to recognize on the balance sheet the assets and liabilities representing the rights and obligations created by those leases. ASU 2016-02 will also require disclosures to help investors and other financial statement users better understand the amount, timing, and uncertainty of cash flows arising from leases. The standard is effective for annual reporting periods (including interim reporting periods within those years) beginning after December 15, 2018. Early adoption is permitted. The Company is currently evaluating the methods of adoption allowed by the new standard and the effect that adoption of the standard is expected to have on the Company's consolidated financial statements and related disclosures.

3. Cash Equivalents and Investments

Cash equivalents are highly liquid investments that are readily convertible into cash with original maturities of three months or less when purchased. Investments consist of securities with original maturities greater than 90 days when purchased. The Company classifies these investments as available-for-sale and records them at fair value in the accompanying consolidated balance sheets. Unrealized gains or losses are included in accumulated other comprehensive income (loss). Premiums or discounts from par value are amortized to investment income over the life of the underlying investment.

Cash equivalents and investments, available-for-sale, consisted of the following at December 31, 2016 and December 31, 2015 (in thousands):

December 31, 2016	**Average Maturity**	**Amortized Cost**	**Unrealized Gain**	**Unrealized Losses**	**Fair Value**
Cash equivalents:					
Money market funds		$ 52,069	$ —	$ —	$ 52,069
Investments, available-for-sale:					
U.S. treasury obligations	298 Days	216,167	14	(32)	216,149
Total		$ 268,236	$ 14	$ (32)	$ 268,218

December 31, 2015	**Average Maturity**	**Amortized Cost**	**Unrealized Gain**	**Unrealized Losses**	**Fair Value**
Cash equivalents:					
Money market funds		$ 162,707	$ —	$ —	$ 162,707
Total		$ 162,707	$ —	$ —	$ 162,707

Although available to be sold to meet operating needs or otherwise, securities are generally held through maturity. The cost of securities sold is determined based on the specific identification method for purposes of recording realized gains and losses. During the year ended December 31, 2016, there were no realized gains or losses on sales of investments, and no investments were adjusted for other than temporary declines in fair value.

At December 31, 2016, the Company held 33 securities that were in an unrealized loss position. The aggregate fair value of securities held by the Company in an unrealized loss position for less than twelve months as of December 31, 2016 was $147.1 million and there were no securities held by the Company in an unrealized loss position for more than twelve months. The Company has the intent and ability to hold such securities until recovery. The Company determined that there was no material change in the credit risk of the above investments. As a result, the Company determined it did not hold any investments with an other-than temporary impairment as of December 31, 2016.

4. 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, 2016, are classified below based on the fair value hierarchy described above:

Description	December 31, 2016	Active Markets (Level 1)	Observable Inputs (Level 2)	Unobservable Inputs (Level 3)
Financial Assets				
Cash equivalents:				
Money market funds	$ 52,069	$ 52,069	$ —	$ —
Investments, available-for-sale:				
U.S Treasury obligations	216,149	216,149	—	—
Total	$ 268,218	$ 268,218	$ —	$ —

Financial instruments measured at fair value as of December 31, 2015, are classified below based on the fair value hierarchy described above:

Description	December 31, 2015	Active Markets (Level 1)	Observable Inputs (Level 2)	Unobservable Inputs (Level 3)
Financial Assets				
Cash equivalents:				
Money market funds	$ 162,707	$ 162,707	$ —	$ —

At December 31, 2016 and December 31, 2015, 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 10). On May 5, 2015, upon completion of the IPO, the warrants to purchase preferred stock converted into warrants to purchase common stock and the Company reclassified the fair value of the warrants as of May 5, 2015 to additional paid-in capital. The following table presents activity in the preferred stock warrant liability during the years ended December 31, 2015 and 2014 (in thousands):

	Year Ended December 31,	
	2015	2014
Beginning balance	$ 365	$ 119
Issuance of warrant at fair value	—	146
Change in fair value	445	100
Reclassification of fair value to additional paid-in capital	(810)	—
Ending balance	$ —	$ 365

5. Restricted Cash

At December 31, 2016 and 2015, $1.3 million and $1.4 million, respectively, of the Company's cash is restricted by a bank. As of December 31, 2016 and 2015, $1.3 million of the restricted cash was included in long-term assets on the Company's balance sheet related to a security deposit for the lease agreement for the Company's corporate headquarters. The balance as of December 31, 2015 also included $0.1 million of restricted cash 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 former corporate headquarters, which ended in October 2015.

6. Property and Equipment, Net

Property and equipment and related accumulated depreciation are as follows (in thousands):

	Estimated Useful Life (Years)	December 31, 2016	December 31, 2015
Lab equipment	5	$ 3,059	$ 2,712
Furniture and fixtures	4	784	632
Computer equipment	3	768	615
Leasehold improvements	Term of lease	4,673	4,612
Software	3	172	167
		9,456	8,738
Less: accumulated depreciation and amortization		(3,268)	(2,077)
Total property and equipment, net		$ 6,188	$ 6,661

Depreciation expense for the years ended December 31, 2016, 2015 and 2014 was $1.6 million, $0.9 million and $0.6 million, respectively.

7. Accrued Expenses

Accrued expenses consist of the following (in thousands):

	December 31, 2016	December 31, 2015
External research and development	$ 5,696	$ 1,471
Employee compensation	4,118	2,731
Professional fees and other	1,697	1,207
Interest	212	34
Property and equipment costs	23	994
Severance	—	6
	$ 11,746	$ 6,443

8. Collaborations

Roche

In March 2016, the Company entered into a collaboration and license agreement (as amended, Roche agreement) with Roche for the discovery, development and commercialization of up to five small molecule therapeutics targeting kinases believed to be important in cancer immunotherapy, as single products or possibly in combination with other therapeutics. The parties initiated activities for three of the collaboration programs in 2016, and the parties have agreed to work together to use the Company's novel target discovery engine and proprietary compound library to select targets for up to two additional collaboration programs.

Under the Roche agreement, Roche is granted up to five option rights to obtain an exclusive license to exploit products derived from the collaboration programs in the field of cancer immunotherapy. Such option rights are triggered upon the achievement of Phase 1 proof-of-concept. For up to three of the five collaboration programs, if Roche exercises

its option, Roche will receive worldwide, exclusive commercialization rights for the licensed products. For up to two of the five collaboration programs, if Roche exercises its option, the Company will retain commercialization rights in the United States for the licensed products, and Roche will receive commercialization rights outside of the United States for the licensed products. The Company will also retain worldwide rights to any products for which Roche elects not to exercise its applicable option.

Prior to Roche's exercise of an option, the Company will have the lead responsibility for drug discovery and pre-clinical development of all collaboration programs. In addition, the Company will have the lead responsibility for the conduct of all Phase 1 clinical trials other than those Phase 1 clinical trials for any product in combination with Roche's portfolio of therapeutics, for which Roche will have the right to lead the conduct of such Phase 1 clinical trials. Pursuant to the Roche agreement, the parties will share the costs of Phase 1 development for each collaboration program. In addition, Roche will be responsible for post-Phase 1 development costs for each licensed product for which it retains global commercialization rights, and the Company and Roche will share post-Phase 1 development costs for each licensed product for which the Company retains commercialization rights in the United States.

Subject to the terms of the Roche agreement, the Company received an upfront cash payment of $45.0 million and will be eligible to receive up to approximately $965.0 million in contingent option fees and milestone payments related to specified research, pre-clinical, clinical, regulatory and sales-based milestones. Of the total contingent payments, up to approximately $215.0 million are for option fees and milestone payments for research, pre-clinical and clinical development events prior to licensing across all five potential collaboration programs, including contingent milestone payments for initiation of each of the collaboration programs for which the parties will work together to select targets (pre-option exercise milestones). In addition, for any licensed product for which Roche retains worldwide commercialization rights, the Company will be eligible to receive tiered royalties ranging from low double-digits to high-teens on future net sales of the licensed product. For any licensed product for which the Company retains commercialization rights in the United States, the Company and Roche will be eligible to receive tiered royalties ranging from mid-single-digits to low double-digits on future net sales in the other party's respective territories in which it commercializes the licensed product. The upfront cash payment and any payments for milestones, option fees and royalties are non-refundable, non-creditable and not subject to set-off.

The Roche agreement will continue until the date when no royalty or other payment obligations are or will become due, unless earlier terminated in accordance with the terms of the Roche agreement. Prior to its exercise of its first option, Roche may terminate the Roche agreement at will, in whole or on a collaboration target-by-collaboration target basis, upon 120 days' prior written notice to the Company. Following its exercise of an option, Roche may terminate the Roche agreement at will, in whole, on a collaboration target-by-collaboration target basis, on a collaboration program-by-collaboration program basis or, if a licensed product has been commercially sold, on a country-by-country basis, (i) upon 120 days' prior written notice if a licensed product has not been commercially sold or (ii) upon 180 days' prior written notice if a licensed product has been commercially sold. Either party may terminate the Roche agreement for the other party's uncured material breach or insolvency and in certain other circumstances agreed to by the parties. In certain termination circumstances, the Company is entitled to retain specified licenses to be able to continue to exploit the licensed products.

The Company determined that there were five deliverables under the Roche agreement: (i) a non-transferable, sub-licensable and non-exclusive license to use the Company's intellectual property and collaboration compounds to conduct research activities;(ii) conducting research and development activities through Phase 1 clinical trials under the research plan; (iii) providing pre-clinical and clinical supply of collaboration compounds; (iv) participation on a joint research committee (JRC) and joint development committee (JDC); and (v) regulatory responsibilities under Phase 1 clinical trials.

The Company determined that the license did not have value to Roche on a stand-alone basis due to the specialized nature of the research activities to be provided by the Company that are not available in the marketplace and the fact that the license is to perform research and development only. Therefore, the license has limited value without the performance of the research and development activities and is not separable. The pre-clinical and clinical supply activities are integral to the performance of the research and development activities and can only be used for the performance of such activities, and the regulatory responsibilities are dependent on the research and development activities. The Company determined that the best estimate for the selling price of the JRC and JDC participation was inconsequential. Accordingly, the Company combined the license, pre-clinical and clinical supply, JRC and JDC participation and regulatory responsibilities deliverables with the research and development activities, the last item to be

delivered in the arrangement, as one unit of accounting. The Company is recognizing the total allocable arrangement consideration consisting of the upfront payment of $45.0 million as revenue on a straight-line basis over the Company's best estimate of the period it expects to perform research and development activities. The Company expects the services to be delivered ratably.

The Company evaluated whether the option fees that may be received in connection with the Roche agreement are substantive. The Company concluded that the option fees were substantive due to the uncertainty around whether the goals of the collaboration will be achieved, and therefore the options are not a deliverable in the current arrangement. If Roche elects to exercise the options, the exercises and related contingent deliverables would be accounted for as a separate arrangement.

The Company evaluated whether the milestones that may be received in connection with the Roche agreement are substantive milestones. Pre-option exercise milestones, of up to $215.0 million, that are expected to be achieved as a result of the Company's efforts during the performance of the research and development activities are considered substantive and are recognized as revenue upon the achievement of the milestone, assuming all other revenue recognition criteria are met. The development event milestones are not considered substantive because the Company does not contribute effort to the achievement of such milestones as they are expected to be achieved after the performance of the research and development activities. Consideration received with respect to these milestones will be added to the total arrangement consideration that has been allocated to the identified units of accounting. As a result, that amount is recognized as revenue ratably over the period starting from the effective date of the agreement to the date that the Company will complete all of its obligations, with a cumulative catch-up from the effective date through the date of achievement of the milestone. If the consideration is received after the completion of all of the Company's obligations, the amount will be recognized as revenue immediately.

During the year ended December 31, 2016, the Company recognized revenue under the Roche agreement of $4.5 million, which represents a portion of the $45.0 million upfront payment.

Alexion

In March 2015, the Company entered into a research, development and commercialization agreement (Alexion 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 the Alexion agreement, the Company is responsible for research and pre-clinical development activities related to drug candidates and Alexion is 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 a negotiated yearly rate per full-time equivalent for its employees' time and their 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 $250.0 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 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. There are no refund provisions in the Alexion agreement.

Alexion has the right to terminate the Alexion agreement if the Company undergoes a change of control or becomes an affiliate of a biotechnology or pharmaceutical company, and may terminate the Alexion agreement at will upon 90 days prior written notice. The Company 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.

The Company determined that there were three deliverables under the Alexion agreement: (i) an exclusive license to research, develop, manufacture and commercialize the licensed products and the compounds in the field in the

territory, (ii) conducting research and development activities under the research plan and (iii) participation on a joint steering committee (JSC) and joint project team (JPT).

The Company determined that the license did not have value to Alexion on a stand-alone basis due to the specialized nature of the research services to be provided by the Company that are not available in the marketplace. Therefore, the deliverables are not separable and, accordingly, the license, undelivered research and development activities and JSC and JPT participation are a single unit of accounting. When multiple deliverables are accounted for as a single unit of accounting, the Company bases its revenue recognition model on the final deliverable. Under the Alexion agreement, the last deliverable to be completed is its research and development activities and participation on the JSC and JPT, which are expected to be delivered over the same performance period. The Company is utilizing a proportional performance model to recognize revenue under the Alexion agreement.

The Company evaluated whether the milestones that may be received in connection with the Alexion agreement are substantive or non-substantive milestones. The Company concluded that the first pre-clinical milestone payment in the Alexion agreement is non-substantive due to the certainty at the date the arrangement was entered into that the event will be achieved. In the second quarter of 2015, the Company achieved the first pre-clinical milestone under the Alexion agreement and received a $1.8 million payment from Alexion. The Company is recognizing revenues from the related milestone payment over the period of performance.

The remaining non-refundable pre-clinical milestones that are expected to be achieved as a result of the Company's efforts during the period of substantial involvement are considered substantive and are recognized as revenue upon the achievement of the milestone, assuming all other revenue recognition criteria are met. The Company has recognized and received an aggregate of $2.0 million in substantive milestones through December 31, 2016. Milestones that are expected to be achieved after the period of substantial involvement are not considered substantive because the Company does not contribute effort to the achievement of such milestones. These milestones are recognized as revenue upon achievement of the milestone, assuming all other revenue recognition criteria are met, as there are no undelivered elements remaining and no continuing performance obligations.

During the year ended December 31, 2016, the Company recognized revenue under the Alexion agreement of $23.3 million, which represents $14.6 million of reimbursable research and development costs, $1.8 million in milestone payments that were recognized upon achievement, as well as a portion of the $15.0 million upfront payment and the $1.8 million non-substantive milestone payment previously received. During the year ended December 31, 2016, the Company received $14.2 million related to reimbursable research and development costs under the Alexion agreement. As of December 31, 2016, the Company has recorded unbilled accounts receivable of $3.6 million related to reimbursable research and development costs under the Alexion agreement for activities performed during the fourth quarter of 2016.

9. Term Loan

In May 2013, the Company entered into a loan and security agreement with Silicon Valley Bank (the 2013 Term Loan), which provided for up to $5.0 million in funding, to be made available in three tranches. 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 2013 Term Loan 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 2013 Term Loan 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 2013 Term Loan and was 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 2013 Term Loan to allow the Company to borrow an additional $5.0 million (the 2014 Term Loan). The Company accounted for the amendment as a modification to the existing 2013 Term Loan. The Company immediately drew the additional $5.0 million under the 2014 Term Loan and was 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% of the total loan advances at the end of the term of each of the 2013 Term Loan and the 2014 Term Loan. The fee is being accreted to interest expense over the term of the 2013 Term Loan and the 2014 Term 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. There are no financial covenants associated with the loan and security agreement.

The 2013 Term Loan and 2014 Term Loan are 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 covenants, including restrictions on dividends and default provisions. The 2013 Term Loan and 2014 Term Loan contain 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 2013 Term Loan and the 2014 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 each of the 2013 Term Loan and the 2014 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, 2016, are as follows (in thousands):

2017	2,583
2018	1,528
Total	$ 4,111

10. Warrants

In connection with the 2013 Term Loan, 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 (the Series A Warrant). In connection with the 2014 Term Loan, the Company issued an additional 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 (the Series B Warrant). Both warrants were exercisable immediately and have a ten-year life.

The Company initially valued the Series A Warrant and the Series B Warrant 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 common stock valuations on those dates.

In accordance with ASC 480, the characteristics of these warrants and the rights and privileges of the underlying preferred stock resulted in the classification of these warrants as a liability, and they were re-measured to the-then current fair value at each balance sheet date through the completion of the IPO. Re-measurement gains or losses were recorded in other income (expense) in the statements of operations and comprehensive loss. Changes in the fair value of the warrants represented a recurring measurement that was classified within Level 3 of the fair value hierarchy wherein fair value is estimated using significant unobservable inputs. The Company recorded $0.4 million of expense associated with the change in fair value of the warrants in the year ended December 31, 2015 equal to the change in fair value of the warrants from December 31, 2014 to May 5, 2015.

Upon completion of the IPO, the Series A Warrant became exercisable for 27,272 shares of the common stock at an exercise price of $5.50 per share, and the Series B Warrant became exercisable for 15,151 shares of the common stock at an exercise price of $6.60 per share. On the date of the conversion of the warrants, the Company revalued the outstanding warrants using the Black-Scholes option pricing model with the following assumptions:

	Series A Warrant	Series B Warrant
	May 5, 2015	May 5, 2015
Fair value of underlying instrument	$ 20.82	$ 20.82
Expected volatility	91.58 %	87.75 %
Expected term (in years)	8.1	9.5
Risk-free interest rate	2.06 %	2.19 %
Expected dividend yield	— %	— %

The fair value of the warrants at May 5, 2015 was $0.8 million and the Company reclassified the balance to additional paid-in capital.

On May 13, 2015, Silicon Valley Bank exercised the Series A Warrant and the Series B Warrant pursuant to the cashless exercise feature of the warrants. In connection with the exercise of the Series A Warrant under the 2013 Term Loan, the Company issued 21,281 shares of common stock to Silicon Valley Bank. Warrants to purchase 5,991 shares of common stock were cancelled as payment for the aggregate exercise price of the Series A Warrant to Silicon Valley Bank. In connection with the exercise of the Series B Warrant under the 2014 Term Loan, the Company issued 11,157 shares of common stock. Warrants to purchase 3,994 shares of common stock were cancelled as payment for the aggregate exercise price of the Series B Warrant.

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 recorded interest expense related to the Series A Warrant and the Series B Warrant of less than $0.1 million in each of the years ended December 31, 2016, 2015 and 2014.

11. Stock Awards

2015 Stock Option and Incentive Plan

In 2015, the Company's board of directors and stockholders approved the 2015 Stock Option and Incentive Plan (the 2015 Plan), which replaced the Company's 2011 Stock Option and Grant Plan, as amended (the 2011 Plan). The 2015 Plan includes incentive stock options, nonstatutory stock options, stock appreciation rights, restricted stock, restricted stock units, unrestricted stock, performance share awards and cash-based awards. The Company initially reserved a total of 1,460,084 shares of common stock for the issuance of awards under the 2015 Plan. The 2015 Plan provides that the number of shares reserved and available for issuance under the 2015 Plan 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 or such lesser amount as specified by the compensation committee of the board of directors. For the calendar year beginning January 1, 2016 and 2017, the number of shares reserved for issuance under the 2015 Plan was increased by 1,087,842 and 1,325,019 shares, respectively. In addition, the total number of shares reserved for issuance is subject to adjustment in the event of a stock split, stock dividend or other change in our capitalization. At December 31, 2016, there were 1,551,519 shares available for future grant under the 2015 Plan.

Awards

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.

A summary of the Company's unvested restricted stock and related information follows:

	Shares	Weighted-Average Grant Date Fair Value
Unvested at December 31, 2015	130,495	$ 0.60
Vested	(126,741)	0.59
Repurchased	(1,629)	0.55
Unvested at December 31, 2016	2,125	1.25

The total fair value of restricted stock that vested during the years ended December 31, 2016, 2015 and 2014 was $2.7 million, $4.9 million and $1.5 million, respectively.

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(2) (in thousands)
Outstanding at December 31, 2015	1,802,802	$ 5.88	8.76	$ 37,008
Granted	1,077,013	19.75		
Exercised	(150,230)	3.60		
Canceled	(106,844)	6.88		
Outstanding at December 31, 2016	2,622,741	$ 11.67	8.30	$ 44,025
Exercisable at December 31, 2016	883,660	$ 6.93	7.64	$ 18,662
Vested and expected to vest at December 31, 2016(1)	2,570,522	$ 11.56	8.29	$ 43,382

(1) Represents the number of vested options as of December 31, 2016, plus the number of unvested options expected to vest as of December 31, 2016 based on a forfeiture rate of 2.5%.

(2) Intrinsic value represents the amount by which the fair market value as of December 31, 2016 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, 2016	December 31, 2015	December 31, 2014
Risk-free interest rate	1.55 %	1.66 %	1.92 %
Expected dividend yield	— %	— %	— %
Expected term (years)	6.0	6.0	6.1
Expected stock price volatility	75.94 %	85.43 %	92.99 %

The weighted-average grant date fair value of options granted in the years ended December 31, 2016, 2015 and 2014 was $13.06, $8.55 and $3.46, respectively. The total intrinsic value of options exercised in the years ended December 31, 2016, 2015 and 2014 was $3.1 million, $6.8 million and $0.1 million, respectively.

Total stock-based compensation expense recognized for all stock-based compensation awards in the statements of operations and comprehensive loss is as follows (in thousands):

	Year Ended December 31,		
	2016	2015	2014
Research and development	$ 2,674	$ 2,148	$ 1,052
General and administrative	3,466	3,032	1,274
Total stock-based compensation expense	$ 6,140	$ 5,180	$ 2,326

At December 31, 2016, there was $15.0 million of total unrecognized compensation cost related to non-vested stock awards, which is expected to be recognized over a weighted-average period of 2.39 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.

2015 Employee Stock Purchase Plan

In 2015, the Company's board of directors and stockholders approved the 2015 Employee Stock Purchase Plan (the 2015 ESPP), which became effective upon the closing of the IPO in May 2015. The Company initially reserved a total of 243,347 shares of common stock for issuance under the 2015 ESPP. The 2015 ESPP provides that the number of shares reserved and available for issuance under the 2015 ESPP will be cumulatively increased on January 1 of each calendar years by 1% of the number of shares of common stock issued and outstanding on the immediately preceding December 31 or such lesser amount as specified by the compensation committee of the board of directors. For the calendar year beginning January 1, 2016 and 2017, the number of shares reserved for issuance under the 2015 ESPP was increased by 271,960 and 331,254 shares. The Company issued 23,325 shares under the ESPP during the year ended December 31, 2016.

12. Net Loss per Share

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 as a result of the Company's net loss.

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:

	Year Ended December 31,		
	2016	2015	2014
Convertible preferred stock	—	—	15,467,479
Warrants	—	—	42,423
Stock options	2,622,741	1,802,802	1,501,912
Unvested restricted stock	2,125	130,495	425,279
Total	2,624,866	1,933,297	17,437,093

The weighted average number of common shares used in net loss per share applicable to common stockholders on a basic and diluted basis were 27,491,669, 18,235,614 and 1,420,518 for the years ended December 31, 2016, 2015 and 2014, respectively.

13. 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. 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. 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.

Upon the closing of the IPO in May 2015, all of the Company's outstanding convertible preferred stock automatically converted into 15,467,479 shares of common stock. In addition, upon the completion of the IPO, the

Company's board of directors was 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. The board of directors can designate the rights, preferences and privileges of the shares of each series and any of its qualifications, limitations or restrictions.

As of December 31, 2016, no shares of preferred stock were issued or outstanding.

14. 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, 2016, 2015 and 2014:

	Year Ended December 31,		
	2016	2015	2014
Federal income tax (benefit) at statutory rate	34.00 %	34.00 %	34.00 %
Permanent differences	(2.74)	(3.30)	(1.87)
Federal research and development credits	1.02	1.09	1.3
Federal orphan drug credits	6.63	0.55	—
State income tax, net of federal benefit	4.81	4.72	4.93
Other	(0.78)	0.56	0.7
Change in valuation allowance	(42.94)	(37.62)	(39.06)
Effective income tax rate	— %	— %	— %

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:

	Year Ended December 31,		
	2016	2015	2014
Deferred tax assets:			
Net operating loss carryforwards	$ 69,443	$ 48,291	$ 30,603
Research and development credit carryforwards	3,833	2,829	1,949
Orphan drug credit carryforwards	5,095	289	—
Accrued expenses and other	2,914	1,374	628
Deferred revenue	2,627	—	—
Deferred lease incentive	1,324	1,551	—
Deferred rent	366	331	54
Total gross deferred tax asset	85,602	54,665	33,234
Deferred tax liability	(1,535)	(1,702)	(85)
Debt discount	(14)	(39)	(74)
Valuation allowance	(84,053)	(52,924)	(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 $84.1 million, $52.9 million and $33.1 million has been established at December 31, 2016, 2015 and 2014, respectively. The change in the valuation allowance was $31.1 million, $19.8 million and $15.7 million for the years ended December 31, 2016, 2015 and 2014, respectively. The Company has incurred net operating losses (NOL) since inception. At December 31, 2016, the Company had federal and state NOL carryforwards of $179.8 million and $177.3 million, respectively, which expire beginning in 2030. As of December 31, 2016, the Company had federal and state research and development tax credit carryforwards of $2.8 million and $1.5 million, respectively, which expire beginning in 2025. The Company had net NOLs related to stock compensation in the amount of $2.7 million that is not included in the deferred tax assets. When the excess stock-based compensation related to NOL carryover tax assets are realized, the benefit will be credited directly to equity. As of

December 31, 2016, the Company had federal orphan drug credits of $5.1 million, which expire beginning in 2035 and state investment tax credits of $0.1 million, which expire beginning in 2018.

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. In addition, 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 and comprehensive loss. As of December 31, 2016 and 2015, the Company has no accrued interest related to uncertain tax positions. 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.

For all years through December 31, 2016, the Company generated research credits but has not conducted a study to document the qualified activities. This study may result in an adjustment to the Company's research and development credit carryforwards; however, until a study is completed and any adjustment is known, no amounts are being presented as an uncertain tax position. A full valuation allowance has been provided against the Company's research and development credits, and if an adjustment is required, this adjustment would be offset by an adjustment to the valuation allowance. Thus, there would be no impact to the balance sheets or statements of operations and comprehensive loss if an adjustment were required.

15. Commitments

The Company leased its former corporate headquarters under an operating lease that expired on November 1, 2015. 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 to extend the term of the lease.

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, which the Company gained control over on June 15, 2015, and occupancy commenced in October 2015. The lease ends on October 31, 2022. The Company has an option to extend the lease for five additional years. The lease has a total commitment of $17.8 million over the seven year term. The Company has agreed to pay an initial annual base rent of approximately $2.3 million, which rises periodically until it reaches approximately $2.8 million. The Company is recording rent expense on a straight-line basis through the end of the lease term. The Company has recorded deferred rent on the consolidated balance sheet at December 31, 2016, accordingly. The lease provides the Company with an allowance for leasehold improvements of $4.3 million. The Company accounts for leasehold improvement incentives as a reduction to rent expense ratably over the lease term. The balance from the leasehold improvement incentives is included in lease incentive obligations on the balance sheets. The lease agreement required the Company to pay a security deposit of $1.3 million, which is recorded in restricted cash, included in long term assets, on the Company's balance sheet.

The future minimum lease payments at December 31, 2016, are as follows (in thousands):

2017	2,396
2018	2,468
2019	2,542
2020	2,618
2021	2,697
Thereafter	2,303
Total minimum lease payments	$ 15,024

The Company records rent expense under its lease agreements on a straight line basis. For the years ended December 31, 2016, 2015, and 2014, rent expense was $1.8 million, $1.8 million, and $0.8 million, respectively.

16. 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 and incurred expenses of $0.3 million for these services during the year ended December 31, 2014. The Company did not receive any consulting services from Third Rock Ventures during the years ended December 31, 2016 and 2015.

17. Defined Contribution Benefit Plan

The Company maintains a 401(k) plan for employees (the 401(k) Plan). 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 the Company, and the investment earnings thereon, are not taxable to the employees until withdrawn from the 401(k) Plan, and so that contributions by the Company, if any, will be deductible by the Company 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 the Company to make contributions up to the limits allowed by law on behalf of all eligible employees. Effective September 1, 2015, the Company instituted an employer match of 50% of eligible contributions up to 6% of employee contributions. For the years ended December 31, 2016 and 2015, the Company contributed $0.4 million and $0.1 million, respectively, to the 401(k) Plan.

18. Selected Quarterly Financial Data (unaudited)

The following table contains selected quarterly financial information for 2016 and 2015. The Company believes that the following information reflects all normal recurring adjustments necessary for a fair statement of the information for the periods presented. The operating results for any quarter are not necessarily indicative of results for any future period.

	Three Months Ended			
	March 31, 2016	June 30, 2016	September 30, 2016	December 31, 2016
	(in thousands, except per share data)			
Total revenue	$ 6,856	$ 7,065	$ 6,160	$ 7,691
Total operating expenses	22,281	25,961	23,043	29,064
Total other income (expense), net	(79)	2	49	110
Net loss	$ (15,504)	$ (18,894)	$ (16,834)	$ (21,263)
Net loss applicable to common stockholders	$ (15,504)	$ (18,894)	$ (16,834)	$ (21,263)
Net loss per share applicable to common stockholders — basic and diluted	$ (0.57)	$ (0.70)	$ (0.62)	$ (0.75)

	Three Months Ended			
	March 31, 2015	June 30, 2015	September 30, 2015	December 31, 2015
	(in thousands, except per share data)			
Total revenue	652	2,687	3,426	4,635
Total operating expenses	$ 12,002	$ 15,083	$ 15,903	$ 20,056
Total other expense, net	(222)	(584)	(165)	(154)
Net loss	$ (11,572)	$ (12,980)	$ (12,642)	$ (15,575)
Net loss applicable to common stockholders	$ (13,842)	$ (13,863)	$ (12,642)	$ (15,575)
Net loss per share applicable to common stockholders — basic and diluted	$ (8.23)	$ (0.81)	$ (0.47)	$ (0.58)

EXHIBIT INDEX

Exhibit Number	Description of Exhibit	Incorporated by Reference			
		Form	File No.	Exhibit Number	Filing Date
3.1	Fifth Amended and Restated Certificate of Incorporation of the Registrant	10-Q	001-37359	3.1	November 9, 2015
3.2	Amended and Restated Bylaws of the Registrant	10-Q	001-37359	3.2	November 9, 2015
4.1	Specimen Common Stock Certificate	S-1/A	333-202938	4.1	April 20, 2015
4.2	Second Amended and Restated Investors' Rights Agreement, dated as of November 7, 2014, by and among the Registrant and the Investors listed therein	S-1	333-202938	4.4	March 23, 2015
10.1	2011 Stock Option and Grant Plan, as amended, and forms of award agreements thereunder	S-1	333-202938	10.1	March 23, 2015
10.2	2015 Stock Option and Incentive Plan and forms of award agreements thereunder	10-K	001-37359	10.2	March 11, 2016
10.3	2015 Employee Stock Purchase Plan	S-8	333-203749	99.3	April 30, 2015
10.4	Lease Agreement, dated February 11, 2015, by and between the Registrant and 38 Sidney Street Limited Partnership	S-1	333-202938	10.4	March 23, 2015
10.5#	Employment Agreement, dated November 6, 2015, by and between the Registrant and Jeffrey W. Albers	10-Q	001-37359	10.2	November 9, 2015
10.6#	Employment Agreement, dated November 6, 2015, by and between the Registrant and Christoph Lengauer	10-Q	001-37359	10.3	November 9, 2015
10.7#	Employment Agreement, dated November 6, 2015, by and between the Registrant and Anthony L. Boral	10-Q	001-37359	10.4	November 9, 2015
10.8†	Resignation Agreement, dated August 13, 2015, by and between the Registrant and Kyle D. Kuvalanka	10-Q	001-37359	10.1	November 9, 2015
10.9#	Employment Agreement, dated March 10, 2016, by and between the Registrant and Kathryn Haviland	10-K	001-37359	10.9	March 11, 2016
10.10#	Employment Agreement, dated September 6, 2016, by and between the Registrant and Tracey L. McCain	10-Q	001-37359	10.3	November 10, 2016
10.11#	Employment Agreement, dated November 9, 2016, by and between the Registrant and Marion Dorsch	8-K	001-37359	10.1	November 14, 2016
10.12#	First Amendment to Employment Agreement, dated November 9, 2016, by and between the Registrant and Christoph Lengauer	8-K	001-37359	10.2	November 14, 2016
10.13#	Change in Control Agreement, dated March 10, 2016, by and between the Registrant and Michael Landsittel	10-K	001-37359	10.10	March 11, 2016
10.14	Loan and Security Agreement, dated May 24, 2013, by and between the Registrant and Silicon Valley Bank, as amended by First Amendment, dated January 21, 2014, Second Amendment, dated June 27, 2014, Third Amendment, dated November 4, 2014 and Consent and Fourth Amendment, dated December 22, 2015	10-K	001-37359	10.11	March 11, 2016

Exhibit Number	Description of Exhibit	Incorporated by Reference			
		Form	File No.	Exhibit Number	Filing Date
10.15†	Research, Development & Commercialization Agreement, dated March 2, 2015, by and between the Registrant and Alexion Pharma Holding	S-1/A	333-202938	10.10	April 10, 2015
10.16†	Collaboration and License Agreement, effective March 14, 2016, by and among F. Hoffmann-La Roche Ltd, Hoffmann-La Roche Inc. and the Registrant, as amended by Amendment to Collaboration and License Agreement, effective April 15, 2016	10-Q/A	001-37359	10.2	July 22, 2016
10.17†	Second Amendment to Collaboration and License Agreement, effective April 27, 2016, by and among F. Hoffmann-La Roche Ltd, Hoffmann-La Roche Inc. and the Registrant	10-Q	001-37359	10.1	August 9, 2016
10.18	Third Amendment to Collaboration and License Agreement, effective August 4, 2016, by and among F. Hoffmann-La Roche Ltd, Hoffmann-La Roche Inc. and the Registrant	10-Q	001-37359	10.1	November 10, 2016
10.19†	Master Collaboration Agreement, effective March 1, 2016, by and between Ventana Medical Systems, Inc. and the Registrant, including Project Schedule #1, effective March 1, 2016, Project Agreement #2, effective March 11, 2016, and Project Schedule #3, effective April 8, 2016	10-Q/A	001-37359	10.1	July 22, 2016
10.20†	Master Collaboration Agreement, dated August 22, 2016, between the Registrant and QIAGEN Manchester Limited, including Project Schedule #1, dated August 22, 2016	10-Q	001-37359	10.2	November 10, 2016
10.21	Form of Indemnification Agreement entered into between the Registrant and its directors	S-1	333-202938	10.11	March 23, 2015
10.22	Form of Indemnification Agreement entered into between the Registrant and its officers	S-1	333-202938	10.12	March 23, 2015
10.23	Senior Executive Cash Incentive Bonus Plan	10-K	001-37359	10.15	March 11, 2016
21.1	Subsidiaries of the Registrant				*
23.1	Consent of Ernst & Young LLP				*
31.1	Certification of Principal Executive Officer pursuant to Rule 13a-14(a) or Rule 15d-14(a) of the Exchange Act, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002				*
31.2	Certification of Principal Financial Officer pursuant to Rule 13a-14(a) or Rule 15d-14(a) of the Exchange Act, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002				*
32.1	Certifications of Principal Executive Officer and Principal Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002				+
101.INS	XBRL Instance Document				*

Exhibit Number	Description of Exhibit	Incorporated by Reference			
		Form	File No.	Exhibit Number	Filing Date
101.SCH	XBRL Taxonomy Extension Schema Document				*
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document				*
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document				*
101.LAB	XBRL Taxonomy Extension Label Linkbase Document				*
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document				*

# Indicates management contract or compensatory plan or arrangement.

† Confidential treatment requested as to portions of the exhibit. Confidential materials omitted and filed separately with the Securities and Exchange Commission.

* Filed herewith.

+ The certifications furnished in Exhibit 32.1 hereto are deemed to be furnished with this Annual Report on Form 10-K and will not be deemed to be "filed" for purposes of Section 18 of the Exchange Act. Such certifications will not be deemed to be incorporated by reference into any filing under the Securities Act or the Exchange Act, except to the extent that the Registrant specifically incorporates it by reference.

Exhibit 21.1

Subsidiaries of the Registrant

Entity	State of Incorporation or Organization
Blueprint Medicines Security Corporation	Massachusetts

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the following Registration Statements:

(1) Registration Statement (Form S-3 No. 333-211266) of Blueprint Medicines Corporation,

(2) Registration Statement (Form S-8 No. 333-203749) pertaining to the 2011 Stock Option and Grant Plan, 2015 Stock Option and Incentive Plan, and 2015 Employee Stock Purchase Plan of Blueprint Medicines Corporation, and

(3) Registration Statement (Form S-8 No. 333-210125) pertaining to the 2015 Stock Option and Incentive Plan and 2015 Employee Stock Purchase Plan of Blueprint Medicines Corporation;

of our report dated March 9, 2017, with respect to the consolidated financial statements of Blueprint Medicines Corporation included in this Annual Report (Form 10-K) of Blueprint Medicines Corporation for the year ended December 31, 2016.

/s/ Ernst & Young LLP

Boston, Massachusetts
March 9, 2017

Exhibit 31.1

CERTIFICATIONS

I, Jeffrey W. Albers, certify that:

1. I have reviewed this Annual Report on Form 10-K of Blueprint Medicines Corporation;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the registrant and have:

(a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

(b) (Paragraph omitted pursuant to SEC Release Nos. 33-8238/34-47986 and 33-8392/34-49313);

(c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

(d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

(a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

(b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 9, 2017

By:/s/ Jeffrey W. Albers
Jeffrey W. Albers
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATIONS

I, Michael Landsittel, certify that:

1. I have reviewed this Annual Report on Form 10-K of Blueprint Medicines Corporation;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the registrant and have:

(a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

(b) (Paragraph omitted pursuant to SEC Release Nos. 33-8238/34-47986 and 33-8392/34-49313);

(c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

(d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

(a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

(b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 9, 2017

By:/s/ Michael Landsittel
Michael Landsittel
Vice President of Finance
(Principal Financial and Accounting Officer)

Exhibit 32.1

CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report on Form 10-K of Blueprint Medicines Corporation (the "Company") for the year ended December 31, 2016 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), each of the undersigned officers of the Company hereby certifies, pursuant to 18 U.S.C. Section 1350, that to his knowledge:

(1) the Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 9, 2017

By: /s/ Jeffrey W. Albers
Jeffrey W. Albers
President and Chief Executive Officer
(Principal Executive Officer)

Date: March 9, 2017

By: /s/ Michael Landsittel
Michael Landsittel
Vice President of Finance
(Principal Financial and Accounting Officer)

Executive Leadership

Jeff Albers
Chief Executive Officer and President

Anthony L. Boral, M.D., Ph.D.
Chief Medical Officer

Marion Dorsch, Ph.D.
Chief Scientific Officer

Debbie Durso-Bumpus
Senior Vice President, Human Resources

Kate Haviland
Chief Business Officer

Mike Landsittel
Vice President, Finance

Christoph Lengauer, Ph.D.
Executive Vice President

Tracey L. McCain, Esq.
Executive Vice President, Chief Legal Officer

Board of Directors

Daniel Lynch
Chairman, Blueprint Medicines Corporation

Jeff Albers
Chief Executive Officer and President,
Blueprint Medicines Corporation

Alexis Borisy
Partner, Third Rock Ventures

Lonnel Coats
Chief Executive Officer and President,
Lexicon Pharmaceuticals, Inc.

George D. Demetri, M.D.
Professor of Medicine, Harvard Medical School,
and Director of the Center for Sarcoma and Bone
Oncology, Dana-Farber Cancer Institute

Mark Goldberg, M.D.
Associate Professor of Medicine,
Harvard Medical School

Nicholas Lydon, Ph.D.
Co-Founder,
Blueprint Medicines Corporation

Charles A. Rowland, Jr.
Former Chief Executive Officer,
Aurinia Pharmaceuticals Inc.

Lynn Seely, M.D.
Chief Executive Officer and President,
Myovant Sciences, Inc.

Annual Meeting of Stockholders

The 2017 annual meeting of stockholders will be held on Tuesday, June 20, 2017, at 3:00 p.m. EDT at Blueprint Medicines' headquarters, which are located at 38 Sidney Street, Suite 200, Cambridge, MA 02139.

SEC Form 10-K

A copy of Blueprint Medicines' Form 10-K filed with the Securities and Exchange Commission is available free of charge from the company's Investor Relations Department by calling (617) 714-6674, emailing ir@blueprintmedicines.com or sending a written request to:

Investor Relations
Blueprint Medicines Corporation
38 Sidney Street, Suite 200
Cambridge, MA 02139

Stock Listing

NASDAQ: BPMC

Independent Auditors

Ernst & Young LLP

Transfer Agent

The transfer agent is responsible, among other things, for handling stockholder questions regarding lost stock certificates, address changes, including duplicate mailings, and changes in ownership or name in which shares are held. These requests may be directed to the transfer agent at the following address:

Computershare Trust Company, N.A.
250 Royall Street
Canton, MA 02021
www-us.computershare.com/contactus

Cautionary Note Regarding Forward-Looking Statements

This annual report contains forward-looking statements as defined in the Private Securities Litigation Reform Act of 1995, as amended, including, without limitation, statements regarding plans and timelines for the clinical development of BLU-285, BLU-554 and BLU-667, and Blueprint Medicines' ability to implement those clinical development plans; plans and timelines for regulatory submissions, filings or discussions; plans and timelines for current or future discovery programs; plans and timelines for future collaborations, if any, with strategic partners; Blueprint Medicines' future financial performance; expectations regarding potential milestones in 2017; expectations regarding Blueprint Medicines' existing cash, cash equivalents and investments; and Blueprint Medicines' strategy, business plans and focus. The words "may," "will," "could," "would," "should," "expect," "plan," "anticipate," "intend," "believe," "estimate," "predict," "project," "potential," "continue," "target" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Any forward-looking statements in this annual report are based on management's current expectations and beliefs and are subject to a number of risks, uncertainties and important factors that may cause actual events or results to differ materially from those expressed or implied by any forward-looking statements contained in this annual report, including, without limitation, risks and uncertainties related to the delay of any current or future clinical trials or the development of Blueprint Medicines' drug candidates, including BLU-285, BLU-554 and BLU-667; Blueprint Medicines' advancement of multiple early-stage efforts; Blueprint Medicines' ability to successfully demonstrate the efficacy and safety of its drug candidates; the preclinical and clinical results for Blueprint Medicines' drug candidates, which may not support further development of such drug candidates; actions or decisions of regulatory agencies or authorities, which may affect the initiation, timing and progress of current or future clinical trials; Blueprint Medicines' ability to obtain, maintain and enforce patent and other intellectual property protection for any drug candidates it is developing; Blueprint Medicines' ability to develop and commercialize companion diagnostics for its current and future drug candidates, including a companion diagnostic for BLU-554 with Ventana Medical Systems, Inc. and a companion diagnostic for BLU-285 with QIAGEN Manchester Limited; and the success of Blueprint Medicines' rare genetic disease collaboration with Alexion Pharma Holding and its cancer immunotherapy collaboration with F. Hoffmann-La Roche Ltd and Hoffmann-La Roche Inc.

These and other risks and uncertainties are described in greater detail in the section entitled "Risk Factors" in Blueprint Medicines' Annual Report on Form 10-K for the year ended December 31, 2016, as filed with the Securities and Exchange Commission (SEC) on March 9, 2017, and other filings that Blueprint Medicines may make with the SEC in the future. Any forward-looking statements contained in this annual report represent Blueprint Medicines' views only as of April 28, 2017, and should not be relied upon as representing its views as of any subsequent date. Except as required by law, Blueprint Medicines assumes no obligation to update or revise these forward-looking statements for any reason, even if new information becomes available in the future.

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