

**UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION**  
Washington, DC 20549

**FORM 10-Q**

(Mark One)

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

**For the quarterly period-ended June 30, 2017**

OR

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

**Commission file number 001-37359**

**BLUEPRINT MEDICINES CORPORATION**

(Exact Name of Registrant as Specified in Its Charter)

**Delaware**  
(State or Other Jurisdiction of  
Incorporation or Organization)

**38 Sidney Street, Suite 200**  
**Cambridge, Massachusetts**  
(Address of Principal Executive Offices)

**26-3632015**  
(I.R.S. Employer  
Identification No.)

**02139**  
(Zip Code)

**(617) 374-7580**

(Registrant's Telephone Number, Including Area Code)

(Former Name, Former Address and Former Fiscal Year, if Changed Since Last Report)

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 whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, smaller reporting company, or an emerging growth company. See definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer

☐

Accelerated filer

☒

Non-accelerated filer

☐ (Do not check if a smaller reporting company)

Smaller reporting company

☐

Emerging growth company

☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☒

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

Number of shares of the registrant's common stock, \$0.001 par value, outstanding on July 31, 2017: 39,122,349

**TABLE OF CONTENTS**

	<b>Page</b>
<b><u>PART I – FINANCIAL INFORMATION</u></b>	
<a href="#"><u>Item 1. Financial Statements (unaudited)</u></a>	5
<a href="#"><u>Condensed Consolidated Balance Sheets as of June 30, 2017 and December 31, 2016</u></a>	5
<a href="#"><u>Condensed Consolidated Statements of Operations and Comprehensive Loss for the three and six months ended June 30, 2017 and 2016</u></a>	6
<a href="#"><u>Condensed Consolidated Statements of Cash Flows for the six months ended June 30, 2017 and 2016</u></a>	7
<a href="#"><u>Notes to Condensed Consolidated Financial Statements</u></a>	8
<a href="#"><u>Item 2. Management’s Discussion and Analysis of Financial Condition and Results of Operations</u></a>	21
<a href="#"><u>Item 3. Quantitative and Qualitative Disclosures About Market Risk</u></a>	32
<a href="#"><u>Item 4. Controls and Procedures</u></a>	32
<b><u>PART II – OTHER INFORMATION</u></b>	
<a href="#"><u>Item 1. Legal Proceedings</u></a>	33
<a href="#"><u>Item 1A. Risk Factors</u></a>	33
<a href="#"><u>Item 2. Unregistered Sales of Equity Securities and Use of Proceeds</u></a>	71
<a href="#"><u>Item 6. Exhibits</u></a>	71
<a href="#"><u>Signatures</u></a>	72

*Unless otherwise stated, all references to “us,” “our,” “Blueprint,” “Blueprint Medicines,” “we,” the “Company” and similar designations in this Quarterly Report on Form 10-Q refer to Blueprint Medicines Corporation and its consolidated subsidiary, Blueprint Medicines Security Corporation.*

#### **FORWARD-LOOKING STATEMENTS**

This Quarterly Report on Form 10-Q contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this Quarterly Report on Form 10-Q 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 Quarterly Report on Form 10-Q 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 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 Quarterly Report on Form 10-Q 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 Quarterly Report on Form 10-Q, 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 Quarterly Report on Form 10-Q and the documents that we have filed as exhibits to this Quarterly Report on Form 10-Q 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 Quarterly Report on Form 10-Q 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 – FINANCIAL INFORMATION

## Item 1. Financial Statements

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

	June 30, 2017	December 31, 2016
Assets		
Current assets:		
Cash and cash equivalents	\$ 91,346	\$ 52,069
Investments, available-for-sale	329,668	162,090
Unbilled accounts receivable	3,075	3,577
Prepaid expenses and other current assets	7,239	2,689
Total current assets	431,328	220,425
Investments, available-for-sale	—	54,059
Property and equipment, net	7,774	6,188
Other assets	852	856
Restricted cash	4,767	1,267
Total assets	\$ 444,721	\$ 282,795
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	2,581	2,211
Accrued expenses	17,396	11,746
Current portion of deferred revenue	9,296	11,426
Current portion of lease incentive obligation	1,714	578
Current portion of deferred rent	26	—
Current portion of term loan payable	1,979	2,551
Total current liabilities	32,992	28,512
Deferred rent, net of current portion	1,659	932
Deferred revenue, net of current portion	32,109	35,809
Lease incentive obligation, net of current portion	3,005	2,792
Term loan payable, net of current portion	692	1,518
Other long term liabilities	175	154
Commitments (Note 10)		
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; 39,080,152 and 33,125,479 shares issued at June 30, 2017 and December 31, 2016, respectively, and 39,080,152 and 33,123,354 shares outstanding at June 30, 2017 and December 31, 2016, respectively	39	33
Additional paid-in capital	643,223	420,533
Accumulated other comprehensive loss	(314)	(18)
Accumulated deficit	(268,859)	(207,470)
Total stockholders' equity	374,089	213,078
Total liabilities and stockholders' equity	\$ 444,721	\$ 282,795

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

	Three Months Ended June 30,		Six Months Ended June 30,	
	2017	2016	2017	2016
Collaboration revenue	\$ 5,890	\$ 7,065	\$ 11,730	\$ 13,921
Operating expenses:				
Research and development	33,271	21,273	61,758	38,908
General and administrative	6,833	4,688	12,516	9,334
Total operating expenses	40,104	25,961	74,274	48,242
Other income (expense):				
Other income (expense), net	861	131	1,286	192
Interest expense	(59)	(129)	(131)	(269)
Total other income (expense)	802	2	1,155	(77)
Net loss	\$ (33,412)	\$ (18,894)	\$ (61,389)	\$ (34,398)
Other comprehensive loss:				
Unrealized (loss) gain on investments	(200)	24	(296)	55
Comprehensive loss	\$ (33,612)	\$ (18,870)	\$ (61,685)	\$ (34,343)
Net loss per share applicable to common stockholders — basic and diluted	\$ (0.86)	\$ (0.70)	\$ (1.71)	\$ (1.27)
Weighted-average number of common shares used in net loss per share applicable to common stockholders — basic and diluted	38,775	27,170	35,998	27,129

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

	Six Months Ended June 30,	
	2017	2016
<b>Operating activities</b>		
Net loss	\$ (61,389)	\$ (34,398)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	791	782
Noncash interest expense	19	42
Stock-based compensation	5,219	2,589
Accretion of premiums and discounts on investments	76	110
Changes in assets and liabilities:		
Unbilled accounts receivable	502	63
Prepaid expenses and other current assets	(2,608)	1,943
Other assets	4	(17)
Accounts payable	297	427
Accrued expenses	3,953	2,202
Deferred revenue	(5,830)	39,412
Deferred rent	369	(237)
Net cash (used in) provided by operating activities	(58,597)	12,918
<b>Investing activities</b>		
Purchases of property and equipment	(457)	(1,814)
Restricted cash	(3,500)	119
Purchases of investments	(209,892)	(69,222)
Maturities of investments	96,000	6,000
Net cash (used in) investing activities	(117,849)	(64,917)
<b>Financing activities</b>		
Principal payments on loan payable	(1,417)	(1,667)
Payment of offering costs	(716)	—
Proceeds from public offering of common stock, net of commissions and underwriting discounts	216,200	—
Proceeds from issuance of common stock, net of repurchases	1,656	345
Net cash provided by (used in) financing activities	215,723	(1,322)
Net increase (decrease) in cash and cash equivalents	39,277	(53,321)
Cash and cash equivalents at beginning of period	52,069	162,707
Cash and cash equivalents at end of period	<u>\$ 91,346</u>	<u>\$ 109,386</u>
<b>Supplemental cash flow information</b>		
Public offering costs incurred but unpaid at period end	<u>\$ 306</u>	<u>\$ —</u>
Property and equipment purchases unpaid at period end	<u>\$ 1,920</u>	<u>\$ 116</u>
Cash paid for interest	<u>\$ 91</u>	<u>\$ 180</u>

**Blueprint Medicines Corporation**  
**Notes to Condensed Consolidated Financial Statements**  
**(Unaudited)**

**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 a follow-on 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 \$134.5 million, after deducting underwriting discounts and commissions and offering expenses payable by the Company.

On April 4, 2017, the Company closed a follow-on public offering of 5,750,000 shares of its common stock at a price to the public of \$40.00 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 April 2017 follow-on public offering). The Company received net proceeds of \$215.6 million, after deducting underwriting discounts and commissions and offering expenses payable by the Company.

As of June 30, 2017, the Company had cash, cash equivalents and investments of \$421.0 million. Based on the Company's current plans, the Company believes its existing cash, cash equivalents and investments, excluding any potential option fees and milestone payments under its existing collaboration with F. Hoffmann-La Roche Ltd and Hoffmann-La Roche Inc. (collectively, Roche), will be sufficient to enable the Company to fund its operating expenses and capital expenditure requirements into the second half of 2019.

**2. Summary of Significant Accounting Policies and Recent Accounting Pronouncements**

***Basis of Presentation***

The unaudited interim condensed 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), Accounting Standards Update (ASU) of the Financial Accounting Standards Board (FASB) and the rules and regulations of the Securities and Exchange Commission (SEC). Certain information and footnote disclosures normally included in financial statements prepared in accordance with GAAP have been condensed or omitted from this report, as is permitted by such rules and regulations. Accordingly, these financial statements should be read in conjunction with the financial statements as of and for the year ended December 31, 2016 and notes thereto included in the Company's Annual Report on Form 10-K for the year ended December 31, 2016, filed with the SEC on March 9, 2017.



The unaudited interim condensed consolidated financial statements have been prepared on the same basis as the audited financial statements and 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 the opinion of the Company's management, the accompanying unaudited interim condensed consolidated financial statements contain all adjustments which are necessary to present fairly the Company's financial position as of June 30, 2017 and the results of its operations for the three and six months ended June 30, 2017 and 2016 and cash flows for the six months ended June 30, 2017 and 2016. Such adjustments are of a normal and recurring nature. The results for the three and six months ended June 30, 2017 are not necessarily indicative of the results for the year ending December 31, 2017, or for any future period.

On December 13, 2016 and April 4, 2017, the Company closed underwritten public offerings of 5,750,000 shares in each offering. The significant increase in shares outstanding 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; revenue recognition; 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.

There have been no significant changes to the Company's critical accounting policies discussed in its Annual Report on Form 10-K for the year ended December 31, 2016 related to available-for-sale investments, revenue recognition, accrued research and development expenses and stock-based compensation.

#### ***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 believes there may be a potential impact in the way it recognizes revenue under its agreement with Roche as well as the recognition of milestone revenue prior to achievement. The Company is in the process of determining the impact of the new guidance on its financial statements.

In March 2016, the FASB issued ASU No. 2016-09, *Compensation – Stock Compensation* (ASU No. 2016-09), 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 was effective for the Company on January 1, 2017. The Company applied ASU 2016-09 using a modified retrospective approach and adopted the option to recognize gross stock compensation expense with actual forfeitures recognized as they occur. Given that the application of the estimated forfeiture rate prior to January 1, 2017 resulted in an insignificant reduction in stock-based compensation expense, the cumulative-effect adjustment to retained earnings recognized as of January 1, 2017 was not material to the consolidated financial statements. The adoption of ASU 2016-09 also requires all income tax adjustments to be recognized in the consolidated statements of operations. As the increase in net deferred tax assets is fully offset by a corresponding increase to the deferred tax asset valuation allowance, there was no material impact of the adoption of this standard. The amount of deferred tax assets that had not been previously recognized due to the recognition of excess tax benefits is \$1.1 million.

In February 2016, the FASB issued ASU No. 2016-02, *Leases* (ASU No. 2016-02), which will change the way the Company recognizes its leased assets. ASU No. 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 No. 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.

In August 2016, the FASB issued ASU No. 2016-15, *Statement of Cash Flows (Topic 230)* (ASU No. 2016-15), which simplifies certain elements of cash flow classification. The new guidance is intended to reduce diversity in practice in how certain transactions are classified in the statement of cash flows. ASU No. 2016-15 is effective for annual periods beginning after December 15, 2017. The Company is currently evaluating the impact the adoption of ASU No. 2016-15 will have on its consolidated financial statements.

In November 2016, the FASB issued ASU No. 2016-18, *Restricted Cash* (ASU No. 2016-18). The amendments in ASU No. 2016-18 require an entity to reconcile and explain the period-over-period change in total cash, cash equivalents and restricted cash within its statements of cash flows. ASU No. 2016-18 is effective for fiscal years (including interim reporting periods within those years) beginning after December 15, 2017. Early adoption is permitted. A reporting entity must apply the amendments in ASU No. 2016-18 using a full retrospective approach. The Company believes that the adoption of this guidance will not have a significant impact on its 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 condensed 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 June 30, 2017 and December 31, 2016 (in thousands):

	Average Maturity	Amortized Cost	Unrealized Gain	Unrealized Losses	Fair Value
<b>June 30, 2017</b>					
Cash equivalents:					
Money market funds		\$ 57,397	\$ —	\$ —	\$ 57,397
Government agency securities		33,949	—	—	33,949
Investments, available-for-sale:					
U.S. treasury obligations	303 Days	317,988	—	(314)	317,674
Government agency securities	91 Days	11,994	—	—	11,994
<b>Total</b>		<b>\$ 421,328</b>	<b>\$ —</b>	<b>\$ (314)</b>	<b>\$ 421,014</b>
<b>December 31, 2016</b>					
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
<b>Total</b>		<b>\$ 268,236</b>	<b>\$ 14</b>	<b>\$ (32)</b>	<b>\$ 268,218</b>

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 three and six months ended June 30, 2017 and June 30, 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 June 30, 2017, the Company held 50 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 June 30, 2017 was \$318.4 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 June 30, 2017.

#### 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 June 30, 2017 are classified below based on the fair value hierarchy described above:

Description	June 30, 2017	Active Markets (Level 1)	Observable Inputs (Level 2)	Unobservable Inputs (Level 3)
<b>Financial Assets</b>				
Cash equivalents:				
Money market funds	\$ 57,397	\$ 57,397	\$ —	\$ —
Government agency securities	33,949	33,949		
Investments, available-for-sale:				
U.S Treasury obligations	317,674	317,674	—	—
Government agency securities	11,994	11,994		
<b>Total</b>	<b>\$ 421,014</b>	<b>\$ 421,014</b>	<b>\$ —</b>	<b>\$ —</b>

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)
<b>Financial Assets</b>				
Cash equivalents:				
Money market funds	\$ 52,069	\$ 52,069	\$ —	\$ —
Investments, available-for-sale:				
U.S Treasury obligations	216,149	216,149	—	—
<b>Total</b>	<b>\$ 268,218</b>	<b>\$ 268,218</b>	<b>\$ —</b>	<b>\$ —</b>

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.

## 5. Restricted Cash

As of June 30, 2017 and December 31, 2016, \$4.8 million and \$1.3 million of restricted cash was included in long-term assets on the Company's balance sheet, respectively. As of June 30, 2017, \$1.3 million of the restricted cash is related to a security deposit for the lease agreement for the Company's current corporate headquarters located at 38 Sidney Street in Cambridge, Massachusetts. On April 28, 2017, the Company entered into a lease agreement (the Lease Agreement) with UP 45/75 Sidney Street, LLC (Landlord) for approximately 99,833 rentable square feet of office and laboratory space located at 45 Sidney Street in Cambridge, Massachusetts which the Company gained control over on June 1, 2017. The initial term of the Lease Agreement will be for a 146 month period, which the Company currently anticipates will commence on October 1, 2017. The Lease Agreement requires the Company to maintain a security deposit with the Landlord in the amount of \$3.5 million, which is included in restricted cash of June 30, 2017. The security deposit is subject to reduction by up to \$1.0 million during the term of the Lease Agreement, subject to the satisfaction of specified terms and conditions.

## 6. 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 both the three months ended June 30, 2017 and 2016, the Company recognized revenue under the Roche agreement of \$1.4 million, which represents a portion of the \$45.0 million upfront payment. During the six months ended June 30, 2017 and 2016, the Company recognized revenue under the Roche agreement of \$2.8 million and \$1.6 million, respectively, 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 one or more drug candidates targeting the ALK2 kinase for the treatment of fibrodysplasia ossificans progressiva. On July 26, 2017, the Company received written notice from Alexion of its election to terminate for convenience the Alexion agreement. In accordance with the Alexion agreement, the termination will become effective on October 24, 2017, which is 90 days following the date of receipt of the notice by the Company. See Note 11 "Subsequent Event."

Under the terms of the Alexion agreement, the Company was responsible for research and pre-clinical development activities related to any drug candidates, and Alexion was responsible for all clinical development, manufacturing and commercialization activities related to any drug candidates. In addition, Alexion was 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 was 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. Prior to receipt by the Company of the notice of termination, the Company had received an aggregate amount of \$3.8 million in pre-clinical milestone payments. The Company will not be entitled to receive payment for additional milestones, if any, achieved after the receipt of the notice of termination of the collaboration. Prior to termination, Alexion was required to 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. Prior to termination, the royalty term for each licensed product in each country was 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.

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 that was anticipated to be completed was the Company's research and development activities and participation on the JSC and JPT, which were expected to be delivered over the same performance period. The Company was utilizing a proportional performance model to recognize revenue under the Alexion agreement. As a result of the termination of the Alexion agreement, the Company anticipates recognizing the remaining deferred revenue balance related to the revenue recognized under the collaboration utilizing the proportional performance model over the remaining period of involvement.

The Company evaluated whether the milestones that it was eligible to receive in connection with the Alexion agreement were substantive or non-substantive milestones. The Company concluded that the first pre-clinical milestone payment received from Alexion was non-substantive due to the certainty at the date the Alexion agreement was entered into that the milestone event would 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. As a result of the termination of the Alexion agreement, the Company anticipates recognizing the remaining deferred revenue balance related to the revenue recognized under the collaboration utilizing the proportional performance model over the remaining period of involvement.

The remaining non-refundable pre-clinical milestones that the Company was eligible to achieve as a result of the Company's efforts prior to the notice of termination by Alexion were considered substantive and would have been recognized as revenue upon the achievement of the milestone, assuming all other revenue recognition criteria were met. The Company has recognized and received an aggregate of \$2.0 million in substantive milestones through June 30, 2017. Milestones that were expected to be achieved after the period of substantial involvement were not considered substantive because the Company would not contribute effort to the achievement of such milestones. These milestones would have been recognized as revenue upon achievement of the milestone, assuming all other revenue recognition criteria were met, as there would have been no undelivered elements remaining and no continuing performance obligations.

During the three and six months ended June 30, 2017, the Company recognized revenue under the Alexion agreement of \$4.5 million and \$8.9 million, respectively, which represents \$3.1 million and \$5.9 million, respectively, of reimbursable research and development costs, as well as a portion of the \$15.0 million upfront payment and the \$1.75 million non-substantive milestone payment previously received. During the three and six months ended June 30, 2016, the Company recognized revenue under the Alexion agreement of \$5.7 million and \$12.3 million, respectively, which represents \$3.4 million and \$7.6 million, respectively, of reimbursable research and development costs, the \$0.75 million milestone payment recognized in the six months ended June 30, 2016, which was recognized upon achievement, as well as the net portion of the \$15.0 million upfront payment and the \$1.75 million non-substantive milestone payment previously received. During the six months ended June 30, 2017, the Company received \$6.4 million related to reimbursable research and development costs under the Alexion agreement. As of June 30, 2017, the Company has recorded unbilled accounts receivable of \$3.1 million related to reimbursable research and development costs under the Alexion agreement for activities performed during the second quarter of 2017.

## 7. 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.

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 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.

Future minimum payments, which include principal and interest due under each of the 2013 Term Loan and the 2014 Term Loan, are \$1.2 million, in the aggregate, for the remainder of 2017 and \$1.6 million, in the aggregate, in 2018.

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).

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 the three and six months ended June 30, 2017 and 2016, respectively.



## 8. 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, 2017, the number of shares reserved for issuance under the 2015 Plan was increased by 1,325,019 shares. 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 June 30, 2017, there were 1,905,829 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, 2016	2,125	\$ 1.25
Vested	(2,125)	1.25
Repurchased	—	—
Unvested at June 30, 2017	—	—

The total fair value of restricted stock that vested during the three months ended June 30, 2017 and 2016 was less than \$0.1 million and \$0.7 million, respectively. The total fair value of restricted stock that vested during the six months ended June 30, 2017 and 2016 was \$0.1 million and \$1.4 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(1) (in thousands)
Outstanding at December 31, 2016	2,622,741	\$ 11.67	8.30	\$ 44,025
Granted	992,572	37.55		
Exercised	(196,970)	8.54		
Canceled	(21,863)	17.36		
Outstanding at June 30, 2017	3,396,480	\$ 19.38	8.45	\$ 106,292
Exercisable at June 30, 2017	1,183,056	\$ 9.73	7.73	\$ 48,431
Vested and expected to vest at June 30, 2017	3,396,480	\$ 19.38	8.45	\$ 106,292

(1) Intrinsic value represents the amount by which the fair market value as of June 30, 2017 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:

	Three Months Ended		Six Months Ended	
	June 30, 2017	June 30, 2016	June 30, 2017	June 30, 2016
Risk-free interest rate	1.93 %	1.36	2.07 %	1.55 %
Expected dividend yield	— %	—	— %	— %
Expected term (years)	5.9	5.7	6.0	6.0
Expected stock price volatility	74.64 %	75.38	75.23 %	76.52 %

The weighted-average grant date fair value of options granted in the three months ended June 30, 2017 and 2016 was \$27.78 and \$12.22, respectively. The total intrinsic value of options exercised in the three months ended June 30, 2017 and 2016 was \$2.7 million and \$0.6 million, respectively. The weighted-average grant date fair value of options granted in the six months ended June 30, 2017 and 2016 was \$24.91 and \$10.61 respectively. The total intrinsic value of options exercised in the six months ended June 30, 2017 and 2016 was \$6.1 million and \$1.0 million, respectively.

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

	Three Months Ended		Six Months Ended	
	June 30, 2017	June 30, 2016	June 30, 2017	June 30, 2016
Research and development	\$ 1,498	\$ 757	\$ 2,622	\$ 1,283
General and administrative	1,481	730	2,597	1,306
Total stock-based compensation expense	\$ 2,979	\$ 1,487	\$ 5,219	\$ 2,589

At June 30, 2017, the Company had \$35.0 million of total unrecognized compensation cost related to non-vested stock awards, which is expected to be recognized over a weighted-average period of 2.65 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 year 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, 2017, the number of shares reserved for issuance under the 2015 ESPP was increased by 331,254 shares. The Company issued 7,703 shares and 11,426 shares under the ESPP during the six months ended June 30, 2017 and 2016, respectively.

### 9. 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. 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 diluted net loss per share applicable to common stockholders calculation, 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.

	Six Months Ended June 30,	
	2017	2016
Stock options	3,396,480	2,462,926
Unvested restricted stock	—	49,575
<b>Total</b>	<b>3,396,480</b>	<b>2,512,501</b>

The weighted average number of common shares used in net loss per share applicable to common stockholders on a basic and diluted basis were 38,774,591 and 27,170,423 for the three months ended June 30, 2017 and 2016, respectively. The weighted average number of common shares used in net loss per share applicable to common stockholders on a basic and diluted basis were 35,997,572 and 27,129,171 for the six months ended June 30, 2017 and 2016, respectively.

## 10. Commitments

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 condensed consolidated balance sheet at June 30, 2017, 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 on the Company's balance sheet.

On April 28, 2017, the Company entered into a lease agreement for approximately 99,833 rentable square feet of office and laboratory space located at 45 Sidney Street in Cambridge, Massachusetts, which the Company gained control over on June 1, 2017. The initial term of the lease agreement will be for a 146 month period, which the Company currently anticipates will commence on October 1, 2017. The lease agreement also provides the Company with an option to extend the lease for two consecutive five-year periods. During the initial term of the lease agreement, the Company has agreed to pay an initial annual base rent of approximately \$7.7 million, which rises periodically until it reaches approximately \$10.6 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 condensed and consolidated balance sheet at June 30, 2017 accordingly. The landlord has also agreed to provide the Company with a tenant improvement allowance of approximately \$14.2 million for improvements to be made to the premises. 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 of \$1.6 million is included in the lease incentive obligation on the balance sheet as of June 30, 2017. The lease agreements required the Company to pay a security deposit of \$3.5 million, which is recorded in restricted cash on the Company's balance sheet.

For the three months ended June 30, 2017 and 2016, rent expense was \$1.1 million and \$0.5 million, respectively. For the six months ended June 30, 2017 and 2016, rent expense was \$1.6 million and \$0.9 million, respectively.

## 11. Subsequent Event

On July 26, 2017, the Company received written notice from Alexion of its election to terminate for convenience the Alexion agreement. In accordance with the Alexion agreement, the termination will become effective on October 24, 2017, which is 90 days following the date of receipt of the notice by the Company.

Under the terms of the Alexion agreement, the Company and Alexion agreed to collaborate to research, develop and commercialize one or more drug candidates targeting the ALK2 kinase for the treatment of fibrodysplasia ossificans progressiva (“FOP”). FOP is a rare genetic disease caused by mutations in the ALK2 gene, ACVR1. Pursuant to the Alexion agreement, the Company was responsible for research and preclinical development activities related to any drug candidates, and Alexion was responsible for all clinical development, manufacturing and commercialization activities related to any drug candidates. In addition, Alexion was 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 the Company’s employees’ time and their associated overhead expenses.

Effective upon the termination, the Company’s exclusivity obligations under the Alexion agreement will terminate, including without limitation, the Company’s exclusivity obligations with respect to (i) the treatment of FOP, heterotopic ossification or diffuse intrinsic pontine glioma, (ii) ALK2, including both wild type and mutated forms, and (iii) certain molecules related to the foregoing. In addition, the research term and all licenses granted to Alexion will terminate, and certain licenses granted by Alexion to the Company will survive and become perpetual, irrevocable and non-terminable. Alexion will remain responsible for the Company’s non-FTE expenses that were incurred or irrevocably committed up to the date of receipt of the notice of termination by the Company, provided that the Company is obligated to use diligent efforts to mitigate such costs to the extent practicable, and for the Company’s FTE expenses for the three month period following the date of receipt of the notice of termination by the Company for personnel that, despite having used diligent efforts, the Company is not able to reallocate from research plan activities to alternative projects. Prior to receipt by the Company of the notice of termination, the Company had received an aggregate amount of \$18.8 million in upfront and milestone payments. The Company will not be entitled to receive payment for milestones, if any, achieved after the receipt of the notice of termination of the collaboration.

The Company plans to evaluate opportunities to advance the research program that was the subject of the collaboration with Alexion. Under the terms of the Alexion agreement, the Company has the option to elect to negotiate a transition agreement with Alexion, which under the terms of the Alexion agreement, may cover, among other things, the reversion to the Company of all rights to any compounds that were the subject of the collaboration, the payment by the Company of any fees associated with such reversion, the grant by Alexion of licenses to certain patents, know-how and marks controlled by Alexion and the allocation between the parties of certain wind-down and transfer costs and expenses.

As a result of the termination of the Alexion agreement, the Company anticipates recognizing the remaining deferred revenue balance of \$3.7 million related to the upfront payment and non-substantive milestone payment previously received under the Alexion collaboration for which revenue was recognized utilizing the proportional performance model over the remaining period of involvement.

## Item 2. 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 unaudited consolidated financial statements and related notes appearing elsewhere in this Quarterly Report on Form 10-Q and the audited consolidated financial statements and related notes thereto and management's discussion and analysis of financial condition and results of operations included in our Annual Report on Form 10-K for the year ended December 31, 2016, filed with the Securities and Exchange Commission, or the SEC, on March 9, 2017. Some of the information contained in this discussion and analysis or set forth elsewhere in this Quarterly Report on Form 10-Q, 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 Quarterly Report on Form 10-Q, 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 PDGFR $\alpha$ , 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. We reported updated data from our Phase 1 clinical trial for GIST at the 2017 ASCO Annual Meeting in Chicago, IL on June 5, 2017, and we plan to report updated data from our Phase 1 clinical trial for advanced SM in the second half of 2017. 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. We plan to report updated data from our Phase 1 clinical trial for advanced HCC at the ESMO 2017 Congress in Madrid, Spain on September 10, 2017. 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 March 2017, we dosed the first patient in our Phase 1 clinical trial for BLU-667 in patients with NSCLC, MTC and other advanced solid tumors, and enrollment is ongoing.

In September 2015, the U.S. Food and Drug Administration, or 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 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 PDGFR $\alpha$  D842V mutation regardless of prior therapy. In addition, in June 2017, the FDA granted breakthrough therapy designation to BLU-285 for the treatment of patients with unresectable or metastatic GIST harboring the PDGFR $\alpha$  D842V mutation, and in July 2017, the European Medicines Agency granted orphan drug designation to BLU-285 for the treatment of GIST. 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 plan to 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 platform to enter into discovery collaborations, including a cancer immunotherapy collaboration with F. Hoffmann-La Roche Ltd and Hoffmann-La Roche Inc., which we refer to collectively as Roche. We also previously entered into a discovery collaboration with Alexion Pharma Holding, or Alexion, targeting the kinase ALK2 for the treatment of fibrodysplasia ossificans progressiva, a rare genetic disease caused by mutations in the ALK2 gene, ACVR1. On July 26, 2017, we received written notice from Alexion of its election to terminate the collaboration for convenience following a strategic review by Alexion of its research and development portfolio. The termination will become effective on October 24, 2017, and we plan to evaluate opportunities to advance the research program that was the subject of the Alexion collaboration.

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 June 30, 2017, we have received an aggregate of \$731.3 million from such transactions, including \$542.4 million in aggregate gross proceeds from the sale of common stock in our May 2015 initial public offering, or IPO, and December 2016 and April 2017 follow-on public offerings, \$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 a result of Alexion's decision to discontinue our collaboration, we will not be entitled to receive payment for any additional milestones, if any, achieved after the receipt of the notice of termination of the collaboration.

Since inception, we have incurred significant operating losses. Our net losses were \$61.4 million for the six months ended June 30, 2017 and \$72.5 million, \$52.8 million and \$40.3 million for the years ended December 31, 2016, 2015 and 2014, respectively. As of June 30, 2017, we had an accumulated deficit of \$268.9 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 our lead drug candidates, BLU-285, BLU-554 and BLU-667;
- commence additional potential clinical development activities for our lead drug candidates, such as registration clinical trials or indication expansion clinical trials (which may include expansion into earlier lines of therapy or additional diseases);
- continue to produce drug substance and drug product material for use in pre-clinical studies, clinical trials, and for use as commercial supply;
- continue to discover, validate and develop additional drug candidates;
- conduct research and development activities under our collaboration with 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;
- expand our pre-commercial development activities and operations, including additional costs related to new office and laboratory space under the lease agreement that we entered into in April 2017; and
- incur additional costs associated with operating as a public company.

In addition, our expenses related to our program targeting ALK2 for the treatment of FOP will increase if we elect to advance that program.

## **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 our research, development and commercialization agreement that we entered into with Alexion in March 2015, which we refer to as the Alexion Agreement, and our collaboration and license agreement that we entered into with Roche in March 2016, which we refer to as the 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 collaboration agreement with Roche. We will not be entitled to receive payment for additional milestones, if any, achieved under the collaboration agreement with Alexion after July 26, 2017, which was the date we received notice of Alexion's election to terminate the collaboration. Subject to the terms of the Alexion agreement, we will be entitled to receive payments from Alexion for certain research and development services through October 24, 2017, which is the effective date of the termination of the collaboration. 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 Investigational New Drug, or IND, application-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 of 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 three and six months ended June 30, 2017 and 2016. Other development and pre-development candidate expenses and unallocated expenses and internal research and development expenses have been classified separately.

	Three Months Ended June 30,		Six Months Ended June 30,	
	2017	2016	2017	2016
	(in thousands)		(in thousands)	
BLU-285 external expenses	\$ 10,342	\$ 2,775	\$ 16,884	\$ 4,416
BLU-554 external expenses	2,862	3,627	7,762	5,103
BLU-667 external expenses	2,541	2,488	4,559	4,353
Other external research and development expenses	10,729	7,813	19,783	16,139
Internal research and development expenses	6,797	4,570	12,770	8,897
Total research and development expenses	\$ 33,271	\$ 21,273	\$ 61,758	\$ 38,908

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 existing clinical trials and initiate additional 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, drug product and drug substance manufacturing expenses and development activities for companion diagnostic tests, including our companion diagnostic tests with Ventana and Qiagen. 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 existing collaboration agreement with Roche and if we elect to advance our program targeting ALK2 for the treatment of FOP that was the subject of our collaboration with Alexion.

#### *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, compliance, human resources and commercial planning 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 are currently an “emerging growth company,” as defined in the Jumpstart Our Business Startups Act of 2012. However, as of June 30, 2017, the market value of our common stock that was held by non-affiliates exceeded \$700 million, and as a result, we will no longer qualify for such status commencing January 1, 2018. We have incurred and will continue to incur additional costs associated with operating as a public company, including as a result of becoming a large accelerated filer.

#### *Other Income (Expense), net*

Other income (expense), net consists primarily of income earned on cash equivalents and investments.

#### *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 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.

There have been no significant changes to our critical accounting policies discussed in our Annual Report on Form 10-K for the year ended December 31, 2016 related to available-for-sale investments, revenue recognition, accrued research and development expenses and stock-based compensation.

## Results of Operations

### Comparison of Three Months Ended June 30, 2017 and 2016

The following table summarizes our results of operations for the three months ended June 30, 2017 and 2016, together with the changes in those items in dollars and as a percentage:

	Three Months Ended June 30,		Dollar Change	% Change
	2017	2016 (in thousands)		
Collaboration revenue	\$ 5,890	\$ 7,065	\$ (1,175)	(17)%
Operating expenses:				
Research and development	33,271	21,273	11,998	56
General and administrative	6,833	4,688	2,145	46
Total operating expenses	40,104	25,961	14,143	54
Other income (expense):				
Other income (expense), net	861	131	730	557
Interest expense	(59)	(129)	70	54
Total other income (expense)	802	2	800	40,000
Net loss	<u>\$ (33,412)</u>	<u>\$ (18,894)</u>	<u>\$ (14,518)</u>	<u>(77)%</u>

#### Collaboration Revenue

Collaboration revenue decreased by \$1.2 million from \$7.1 million for the three months ended June 30, 2016 to \$5.9 million for the three months ended June 30, 2017. Collaboration revenue for the three months ended June 30, 2017 was related to the Alexion and Roche agreements. We recorded collaboration revenue of \$4.5 million and \$5.7 million under the Alexion agreement for the three months ended June 30, 2017 and 2016, respectively. The decrease in collaboration revenue under the Alexion agreement was primarily related to a decrease in reimbursable research and development activities and a decrease in the recognition of portions of the \$15.0 million upfront payment and \$1.8 million in milestone payments received from Alexion that are recognized utilizing the proportional performance model. As a result of the termination of the Alexion agreement, we anticipate recognizing the remaining deferred revenue balance of \$3.7 million related to the revenue recognized utilizing the proportional performance model over the remaining period of involvement. We also will not be entitled to receive payment for additional milestones, if any, achieved under the collaboration agreement with Alexion after July 26, 2017, which was the date we received notice of Alexion's election to terminate the collaboration. In addition, subject to the terms of the Alexion agreement, we will be entitled to receive payments from Alexion for certain research and development services through October 24, 2017, which is the effective date of the termination of the collaboration. As a result, we anticipate collaboration revenue related to reimbursable research and development expenses will decrease significantly in future periods. We entered into the Roche agreement in March 2016 and recorded \$1.4 million in collaboration revenue under the Roche agreement for the three months ended June 30, 2017 and June 30, 2016.

#### Research and Development Expense

Research and development expense increased by \$12.0 million from \$21.3 million for the three months ended June 30, 2016 to \$33.3 million for the three months ended June 30, 2017. The increase in research and development expense was primarily related to the following:

- approximately \$5.1 million in increased expenses associated with clinical manufacturing activities

- approximately \$3.0 million in increased personnel expense primarily due to a 39% increase in headcount and an increase in stock-based compensation expense, which were driven by growth in the clinical and non-clinical organizations; and
- approximately \$2.6 million in increased expenses for external clinical activities as we advanced our lead drug candidates, BLU-285, BLU-554 and BLU-667, in Phase 1 clinical trials.

#### *General and Administrative Expense*

General and administrative expense increased by \$2.1 million from \$4.7 million for the three months ended June 30, 2016 to \$6.8 million for the three months ended June 30, 2017. The increase in general and administrative expense was primarily related to approximately \$1.4 million in increased personnel expenses due to an increase of 32% in general and administrative headcount to support our overall growth as a publicly traded company and an increase in stock-based compensation expense.

#### *Other Income (Expense), Net*

Other income (expense), net, increased by \$0.7 million from \$0.1 million of income for the three months ended June 30, 2016 to \$0.8 million of income for the three months ended June 30, 2017. The increase in other income (expense), net, was primarily related to an increase in investment income due to higher average investment balances during the three months ended June 30, 2017.

#### *Interest Expense*

Interest expense decreased by less than \$0.1 million from \$0.1 million for the three months ended June 30, 2016 to less than \$0.1 million for the three months ended June 30, 2017. The decrease was primarily related to a decrease in the average outstanding principle balance under the loan and security agreement with Silicon Valley Bank for the three months ended June 30, 2017. We expect that interest expense will continue to decrease in subsequent periods as the principal amount under the loan decreases.

#### **Comparison of Six Months Ended June 30, 2017 and 2016**

	Six Months Ended June 30,		Dollar Change	% Change
	2017	2016		
	(in thousands)			
Collaboration revenue	\$ 11,730	\$ 13,921	\$ (2,191)	(16)%
Operating expenses:				
Research and development	61,758	38,908	22,850	59
General and administrative	12,516	9,334	3,182	34
Total operating expenses	74,274	48,242	26,032	54
Other income (expense):				
Other income (expense), net	1,286	192	1,094	570
Interest expense	(131)	(269)	138	51
Total other income (expense)	1,155	(77)	1,232	1,600
Net loss	\$ (61,389)	\$ (34,398)	\$ (26,991)	(78)%

#### *Collaboration Revenue*

Collaboration revenue decreased by \$2.2 million from \$13.9 million for the six months ended June 30, 2016 to \$11.7 million for the six months ended June 30, 2017. Collaboration revenue for the six months ended June 30, 2017 was related to the Alexion and Roche agreements. We recorded collaboration revenue of \$8.9 million and \$12.3 million under the Alexion agreement for the six months ended June 30, 2017 and June 30, 2016, respectively. The decrease in collaboration revenue under the Alexion agreement was primarily related to a decrease in reimbursable research and development costs and a decrease in recognition of portions of the \$15.0 million upfront payment and \$1.8 million in milestone payments received from Alexion that are recognized utilizing the proportional performance model. Also

contributing to the decrease was the impact of the recognition of a milestone payment upon achievement included in the six months ended June 30, 2016. As a result of the termination of the Alexion agreement, we anticipate recognizing the remaining deferred revenue balance of \$3.7 million related to revenue recognized utilizing the proportional performance model over the remaining period of involvement. We also will not be entitled to receive payment for additional milestones, if any, achieved under the collaboration agreement with Alexion after July 26, 2017, which was the date we received notice of Alexion's election to terminate the collaboration. In addition, subject to the terms of the Alexion agreement, we will be entitled to receive payments from Alexion for certain research and development services through October 24, 2017, which is the effective date of the termination of the collaboration. As a result, we anticipate collaboration revenue related to reimbursable research and development expenses will decrease significantly in future periods. We entered into the Roche agreement in March 2016 and recorded \$2.8 million and \$1.6 million in collaboration revenue under the Roche agreement for the six months ended June 30, 2017 and June 30, 2016, respectively.

#### *Research and Development Expense*

Research and development expense increased by \$22.9 million from \$38.9 million for the six months ended June 30, 2016 to \$61.8 million for the six months ended June 30, 2017. The increase in research and development expense was primarily related to the following:

- approximately \$9.4 million in increased expenses associated with clinical manufacturing activities
- approximately \$7.6 million in increased expenses for external clinical activities as we advanced our lead drug candidates, BLU-285, BLU-554 and BLU-667, in Phase 1 clinical trials; and
- approximately \$4.8 million in increased personnel expense primarily due to a 34% increase in headcount and an increase in stock-based compensation expense, which were driven by growth in the clinical and non-clinical organizations.

#### *General and Administrative Expense*

General and administrative expense increased by \$3.2 million from \$9.3 million for the six months ended June 30, 2016 to \$12.5 million for the six months ended June 30, 2017. The increase in general and administrative expense was primarily related to the following:

- approximately \$2.3 million in increased personnel expenses due to an increase of 29% in general and administrative headcount to support our overall growth as a publicly traded company and an increase in stock-based compensation expense; and
- approximately \$0.7 million in increased professional fees including market research and public relations costs.

#### *Other Income (Expense), Net*

Other income (expense), net, increased by \$1.1 million from \$0.2 million of income for the six months ended June 30, 2016 to \$1.3 million of income for the six months ended June 30, 2017. The increase in other income (expense), net, was primarily related to an increase in investment income during the six months ended June 30, 2017.

#### *Interest Expense*

Interest expense decreased by \$0.1 million from \$0.2 million for the six months ended June 30, 2016 to \$0.1 million for the six months ended June 30, 2017. The decrease was primarily related to a decrease in the average outstanding principle balance under the loan and security agreement with Silicon Valley Bank for the six months ended June 30, 2017. We expect that interest expense will continue to decrease in subsequent periods as the principal amount under the loan decreases.

## 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 June 30, 2017, we have received an aggregate of \$731.3 million from such transactions, including \$542.4 million in aggregate gross proceeds from the sale of common stock in our IPO and December 2016 and April 2017 follow on public offerings, \$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 a result of Alexion's decision to discontinue our collaboration, we will not be entitled to receive payment for any additional milestones, if any, achieved after the receipt of the notice of termination of the collaboration.

As of June 30, 2017, we had cash, cash equivalents and investments of \$421.0 million.

### Cash Flows

The following table provides information regarding our cash flows for the three months ended June 30, 2017 and 2016:

(in thousands)	Six Months Ended June 30,	
	2017	2016
Net cash (used in) provided by operating activities	\$ (58,597)	\$ 12,918
Net cash used in investing activities	(117,849)	(64,917)
Net cash provided by (used in) financing activities	215,723	(1,322)
Net increase (decrease) in cash and cash equivalents	\$ 39,277	\$ (53,321)

*Net Cash (Used in) Provided by Operating Activities.* Net cash used in operating activities was \$58.6 million during the six months ended June 30, 2017 compared to net cash provided by operating activities of \$12.9 million during the six months ended June 30, 2016. The change in net cash used in operating activities was primarily due to changes in deferred revenue related to the timing of the upfront payment from Roche. In the six months ended June 30, 2016, we received a \$45.0 million upfront payment from Roche, and in the six months ended June 30, 2017 we did not receive any upfront payments. Further, the change in net cash used by operating activities was related to an increase in net loss of \$27.0 million for the six months ended June 30, 2017 as compared to the six months ended June 30, 2016.

*Net Cash Used in Investing Activities.* Net cash used in investing activities was \$117.8 million during the six months ended June 30, 2017 compared to net cash used in investing activities of \$64.9 million during the six months ended June 30, 2016. Net cash used in investing activities for the six months ended June 30, 2017 consisted primarily of purchases of investments offset by 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 also consisted of a \$3.5 million security deposit related to the lease agreement entered into on April 28, 2017. Net cash used in investing activities for three months ended March 31, 2016 consisted primarily of purchases of investments offset by maturities in investments and purchases of property and equipment.

*Net Cash Provided by (Used in) Financing Activities.* Net cash provided by financing activities was \$215.7 million during the six months ended June 30, 2017 compared to net cash used in financing activities of \$1.3 million during the six months ended June 30, 2016. Net cash provided by financing activities for the six months ended June 30, 2017 was primarily due to \$216.2 million in gross proceeds from our April 2017 follow-on underwritten public offering, after deducting underwriting discounts and commissions. Net cash used in financing activities for the six months ended June 30, 2016 was primarily due to principal payments under the loan and security agreement with Silicon Valley Bank.

### 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. Through June 30, 2017, we have made principal payments of \$7.3 million on the \$10.0 million of advances. 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 June 30, 2017, we had \$2.7 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 have classified the outstanding principal in current and long term liabilities based on scheduled principal payments.

See Note 7, "Term Loan," in the accompanying notes to our unaudited 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 June 30, 2017, we had cash, cash equivalents and investments of \$421.0 million. Based on our current plans, we believe our existing cash, cash equivalents and investments, excluding any potential option fees and milestone payments under our existing collaboration with Roche, will be sufficient to enable us to fund our operating expenses and capital expenditure requirements into the second half of 2019. 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 securing and 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 collaboration with Roche;
- the success of our current or future collaborations for companion diagnostic tests, 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 additional collaborations on favorable terms, if at all;
- the achievement of milestones or occurrence of other developments that trigger payments under our collaboration agreement with Roche or any collaboration agreements that we may enter into in the future;
- 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; 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 collaboration agreement with 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**

On April 28, 2017, we entered into a lease agreement with UP 45/75 Sidney Street, LLC, as the landlord, pursuant to which we will lease approximately 99,833 rentable square feet of office and laboratory space located at 45 Sidney Street, Cambridge, Massachusetts 02139, which we refer to as the new premises, and will relocate our corporate headquarters to the new premises. We gained control over the space on June 1, 2017 and currently anticipate relocating our corporate headquarters in the first quarter of 2018. We currently anticipate that the date on which we will become responsible for paying rent under the lease agreement, or the commencement date, will be October 1, 2017. The initial term of the lease agreement will be for a 146 month period beginning on the commencement date, unless terminated sooner. The lease agreement also provides us with an option to extend the lease agreement for two consecutive five-year periods at the then fair market annual rent, as defined in the lease agreement, as well as a right of first offer with respect to leasing additional space adjacent to the new premises. During the initial term of the lease agreement, our monthly base rent for the new premises will start at approximately \$641,000 beginning on the commencement date through the 14 month anniversary of the commencement date. Our monthly base rent will increase by 3.0% on the 14 month anniversary of the commencement date and will increase by an additional 3.0% on an annual basis for the remainder of the initial term up to a maximum monthly base rent of approximately \$887,000. Pursuant to the lease agreement, we will also be obligated to pay certain taxes and operating costs associated with the new premises during the term of the lease agreement. The landlord has also agreed to provide us with a tenant improvement allowance of approximately \$14.2 million for improvements to be made to the new premises. We will be obligated to maintain a security deposit with the landlord in the amount of \$3.5 million, which is subject to reduction by up to \$1.0 million during the term of the lease agreement, subject to the satisfaction of specified terms and conditions.

As of June 30, 2017, there have been no other material changes to our contractual obligations and commitments from those described under “Management’s Discussion and Analysis of Financial Condition and Results of Operations” included in the Annual Report on Form 10-K for the year ended December 31, 2016.

## 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 3. Quantitative and Qualitative Disclosures About Market Risk

As of June 30, 2017, we had cash, cash equivalents and investments of \$421.0 million, consisting primarily of money market funds and investments in U.S. treasury obligations and U.S government agency securities.

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 June 30, 2017 and December 31, 2016, we had minimal 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 three months or six ended June 30, 2017 and 2016.

### Item 4. 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 June 30, 2017. Based upon such evaluation, our Chief Executive Officer and Vice President of Finance have concluded that, as of June 30, 2017, our disclosure controls and procedures were effective at the reasonable assurance level.

#### *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 June 30, 2017 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.



## PART II – OTHER INFORMATION

### Item 1. Legal Proceedings

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

#### Item 1A. Risk Factors

*The following risk factors and other information included in this Quarterly Report on Form 10-Q 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 3 of this Quarterly Report on Form 10-Q 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, BLU-285 in an ongoing Phase 1 clinical trial for advanced systemic mastocytosis, or SM, BLU-554 in an ongoing Phase 1 clinical trial in patients with advanced hepatocellular carcinoma, or HCC, and BLU-667 in an ongoing Phase 1 clinical trial in patients with non-small cell lung cancer, or NSCLC, medullary thyroid cancer, or MTC, and other advanced solid tumors.

In September 2015, the U.S. Food and Drug Administration, or 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 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 PDGFR $\alpha$  D842V mutation regardless of prior therapy. In addition, in June 2017, the FDA granted breakthrough therapy designation to BLU-285 for the treatment of patients with unresectable or metastatic GIST harboring the PDGFR $\alpha$  D842V mutation, and in July 2017, the European Medicines Agency granted orphan drug designation to BLU-285 for the treatment of GIST. 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 June 30, 2017, we have received an aggregate of \$731.3 million from such transactions, including \$542.4 million in aggregate gross proceeds from the sale of common stock in our May 2015 initial public offering, or IPO, and December 2016 and April 2017 follow-on public offerings, \$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. As a result of Alexion's decision to discontinue our collaboration, we will not be entitled to receive payment for any additional milestones, if any, achieved after July 26, 2017, which is the date we received notice from Alexion of its termination of the collaboration.

Since inception, we have incurred significant operating losses. Our net losses were \$61.4 million for the six months ended June 30, 2017 and \$72.5 million, \$52.8 million and \$40.3 million for the years ended December 31, 2016, 2015 and 2014, respectively. As of June 30, 2017, we had an accumulated deficit of \$268.9 million. 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 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 June 30, 2017, we had cash, cash equivalents and investments of \$421.0 million. Based on our current plans, we believe our existing cash, cash equivalents and investments, excluding any potential option fees and milestone payments under our existing collaboration with Roche, will be sufficient to enable us to fund our operating expenses and capital expenditure requirements into the second half of 2019. 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 securing and 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 collaboration with Roche;
- the success of our current or future collaborations for companion diagnostic tests, 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 additional collaborations on favorable terms, if at all;
- the achievement of milestones or occurrence of other developments that trigger payments under our collaboration agreement with Roche or any collaboration agreements that we may enter into in the future;
- 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; 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 collaboration with Roche, 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, for some of our drug candidates, in order to select patients most likely to respond to treatment and rapidly confirm mechanistic and clinical proof-of-concept, we may seek to develop 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 aberrantly 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 PDGFR $\alpha$  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, BLU-554 and BLU-667;
- successful completion of pre-clinical studies for our other drug candidates;
- approval of Investigational New Drug applications for future clinical trials for our other drug candidates;
- successful development of any 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 PDGFR $\alpha$  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 drug candidates. Our pre-clinical studies, current Phase 1 clinical trials and future clinical trials may not be successful.

We are currently evaluating BLU-285 in an ongoing Phase 1 clinical trial for defined subsets of patients with GIST, BLU-285 in an ongoing Phase 1 clinical trial for advanced SM, BLU-554 in an ongoing Phase 1 clinical trial in patients with advanced HCC and BLU-667 in an ongoing Phase 1 clinical trial in patients with NSCLC, MTC and other advanced solid tumors.

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 current or 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 drug 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 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 PDGFR $\alpha$  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 the 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 drug candidates 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 any 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 any 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 PDGFR $\alpha$  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 any 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 current or future drug candidates or related companion diagnostic tests 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, if approval is obtained at all, both in the United States and abroad is expensive, may take many years if additional clinical trials are required 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, including BLU-285 for the treatment of patients with unresectable or metastatic GIST harboring the PDGFRα D842V mutation, 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.***

In June 2017, the FDA granted breakthrough therapy designation to BLU-285 for the treatment of patients with unresectable or metastatic GIST harboring the PDGFRα D842V mutation. We may also seek breakthrough therapy designation for some of our other 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. In addition, in July 2017, the European Medicines Agency granted orphan drug designation to BLU-285 for the treatment of GIST. 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 PDGFR $\alpha$  D842V-driven GIST; (iii) 6,300 second line and third line patients with GIST who have a KIT Exon 17 mutation; (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 patients with HCC 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, it will face competition from Novartis AG's midostaurin, a multi-kinase inhibitor with KIT D816V inhibitory activity that was approved in April 2017 by the FDA for the treatment of advanced SM. In addition, if BLU-285 receives marketing approval for advanced SM, GIST and/or for GIST patients with the PDGFR $\alpha$  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., ARIAD Pharmaceuticals, Inc., a wholly-owned subsidiary of Takeda Pharmaceutical Company Limited, AROG Pharmaceuticals, Inc., Celldex Therapeutics, Inc., Deciphera Pharmaceuticals, LLC and Plexxikon Inc., a wholly-owned subsidiary of Daiichi Sankyo Company, Limited. Further, if BLU-554 receives marketing approval for HCC patients with aberrantly active FGFR4 signaling, as indicated by FGF19 overexpression, it will face competition from sorafenib and regorafenib, the only approved systemic medical therapies for HCC. In addition, BLU-554 may face competition from other drug candidates in development by AstraZeneca plc, Bayer AG, Bristol-Myers Squibb Company, Celgene Corporation, Eisai Inc., H3 Biomedicine Inc., Incyte Corporation, Johnson & Johnson, Novartis AG, Sanofi S.A., Taiho Pharmaceutical Co., Ltd., U3 Pharma GmbH, a wholly-owned subsidiary of Daiichi Sankyo Company, Limited, and Xoma Ltd. If BLU-667 receives marketing approval for patients with RET-driven cancers, 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 any related companion diagnostic tests, 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 PDGFR $\alpha$  D842V mutation. However, we have not yet initiated commercialization of these companion diagnostic tests or development and commercialization of 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 treatment 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.

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. In addition, on May 4, 2017, the U.S. House of Representatives passed the American Health Care Act, and the Senate is currently debating legislation, which would repeal certain aspects of the Affordable Care Act. It is uncertain whether any legislation will be enacted, and if it is, what impact it will have on the availability and cost of healthcare. We plan to continue to evaluate the effect that the Affordable Care Act and its possible repeal and replacement may have on our business.

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 our collaboration agreement with Roche from entering into future agreements on certain terms with potential collaborators. Collaborations are complex and time-consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators.

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

In addition, our collaboration with 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. For example, on July 26, 2017, we received written notice from Alexion of its election to terminate our rare genetic disease collaboration for convenience following a strategic review by Alexion of its research and development portfolio. The termination will become effective on October 24, 2017, and we plan to evaluate opportunities to advance the research program that was the subject of the Alexion collaboration. Any termination or expiration of a current or future collaboration agreement could adversely affect us financially or 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 do not have any long-term supply agreements with our contract manufacturers, and we purchase our required drug supply, including the drug product and drug substance used in our lead drug candidates, on a purchase order basis. In addition, we may be unable to establish or maintain any agreements with third-party manufacturers or to do so on acceptable terms. Even if we are able to establish and maintain 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. We do not currently have arrangements in place for redundant supply for bulk drug substances. 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 could result in significant delays or gaps in availability of such drug candidates or drugs and 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, or API, 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 API, drug product and drug substance used in our lead drug candidates are currently supplied to us from single-source suppliers. Our ability to successfully develop our drug candidates, supply our drug candidates for clinical trials 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 clinical testing and commercialization. Although we have entered into arrangements to establish redundant or second-source supply of some of the API, drug product or drug substance for our lead drug candidates, if any of our suppliers ceases its operations for any reason or is unable or unwilling to supply API, drug product or drug substance in sufficient quantities or on the timelines necessary to meet our needs, it could significantly and adversely affect our business, the supply of our drug candidates and our financial condition.

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, BLU-554 and BLU-667 as composition of matter. We also own applications relating to composition of matter for KIT inhibitors with multiple compound families, composition of matter for FGFR4 inhibitors with multiple compound families and composition of matter for inhibitors of RET, including predicted RET resistant mutants, with multiple compound families, 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.

As of July 31, 2017, we owned three issued U.S. patents, six pending U.S. non-provisional patent applications, one pending U.S. provisional patent application, 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 application 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 July 31, 2017, we owned five issued U.S. patents, three pending U.S. non-provisional patent applications, three pending U.S. provisional patent applications, one issued foreign patent 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 July 31, 2017, we owned four pending U.S. non-provisional patent applications, five pending PCT applications, six pending foreign patent applications filed in Argentina, Lebanon, Uruguay and Taiwan, and one pending U.S. provisional 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 July 31, 2017, we owned ten U.S. patent applications and ten European Union patent applications 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, BLU-667 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 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 July 31, 2017, we had 123 full-time employees, and we expect to continue to increase our number of employees and expand the scope of our operations. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. 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. In April 2017, we entered into a lease agreement new office and laboratory space located at 45 Sidney Street, Cambridge, Massachusetts 02139, and we currently anticipate relocating our corporate headquarters to the new premises in the first quarter of 2018. The physical expansion of our operations may lead to significant costs, including capital expenditures, 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.

***We may be subject to adverse legislative or regulatory tax changes that could negatively impact our financial condition.***

The rules dealing with U.S. federal, state and local income taxation are constantly under review by persons involved in the legislative process and by the IRS and the U.S. Treasury Department. Changes to tax laws (which changes may have retroactive application) could adversely affect our stockholders or us. In recent years, many such changes have been made and changes are likely to continue to occur in the future. We cannot predict whether, when, in what form, or with what effective dates, tax laws, regulations and rulings may be enacted, promulgated or decided, which could result in an increase in our, or our stockholders', tax liability or require changes in the manner in which we operate in order to minimize increases in our tax liability.

**Risks Related to Our Common Stock**

***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 \$56.81 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 July 31, 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.***

Our executive officers, directors and stockholders who own more than 5% of our outstanding common stock, together with their affiliates and related persons, beneficially own shares of common stock representing a significant percentage of our capital stock. As a result, if these stockholders were to choose to act together, they would 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 bylaws 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.

***Commencing January 1, 2018, we will no longer be an “emerging growth company,” and the reduced disclosure requirements applicable to emerging growth companies will no longer apply to us.***

We are currently an “emerging growth company,” as defined in the Jumpstart Our Business Startups Act of 2012. However, as of June 30, 2017, the market value of our common stock that was held by non-affiliates exceeded \$700 million, and as a result, we will no longer qualify for such status commencing January 1, 2018. As a large accelerated filer, we will be subject to certain disclosure requirements that are applicable to other public companies that have not been applicable to us as an emerging growth company. These requirements include:

- compliance with the auditor attestation requirements in the assessment of our internal control over financial reporting;
- compliance 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;
- full disclosure obligations regarding executive compensation; and
- compliance with the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved.

In addition, we will no longer be able to take advantage of transition periods for complying with new or revised accounting standards that are available to emerging growth companies.

***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 and corporate governance practices.***

As a public company, and particularly commencing January 1, 2018 when we will no longer be an emerging growth company, we have incurred and expect to continue to incur significant legal, accounting and other expenses that we did not incur as a private company. In addition, the Sarbanes-Oxley Act of 2002 and rules subsequently implemented by the Securities and Exchange Commission, 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.

Commencing January 1, 2018, we will no longer be an emerging growth company. As a result, we will not be able to take advantage of certain exemptions from various reporting requirements that are applicable to other public companies that are emerging growth companies as has been the case to date.

Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404, we are required to furnish an annual report by our management on our internal control over financial reporting. Commencing January 1, 2018, because we will no longer be an emerging growth company, we will be required to include with this annual report 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.

***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 2. Unregistered Sales of Equity Securities and Use of Proceeds**

### *Use of Proceeds from Initial Public Offering of Common Stock*

On May 5, 2015, we completed an 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 of 1933, as amended, 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 expenses paid by us. As of June 30, 2017, we have used all of the net proceeds from the offering, primarily to fund our Phase 1 clinical trials for BLU-285, BLU-554 and BLU-667, new and ongoing research activities, research and development activities and 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.

## **Item 6. Exhibits**

The exhibits filed as part of this Quarterly Report on Form 10-Q are set forth on the Exhibit Index, which is incorporated herein by reference.

## 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: August 2, 2017

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

Date: August 2, 2017

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



## EXHIBIT INDEX

Exhibit Number	Description of Exhibit
10.1†*	Amendment #1, effective June 12, 2017, to Project Schedule #1, effective March 1, 2016, to the Master Collaboration Agreement, effective March 1, 2016, between Ventana Medical Systems, Inc. and the Registrant
10.2†*	Amendment No. 1, dated July 14, 2017, to Project Schedule #1, dated August 22, 2016, to the Master Collaboration Agreement, dated August 22, 2016, between QIAGEN Manchester Limited and the Registrant
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
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

† 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 Quarterly Report on Form 10-Q 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.

\*\*\* INDICATES MATERIAL THAT HAS BEEN OMITTED AND FOR WHICH CONFIDENTIAL TREATMENT HAS BEEN REQUESTED. ALL SUCH OMITTED MATERIAL HAS BEEN FILED WITH THE SECURITIES AND EXCHANGE COMMISSION PURSUANT TO RULE 24b-2 PROMULGATED UNDER THE SECURITIES EXCHANGE ACT OF 1934, AS AMENDED.

#### Amendment #1 to Project Schedule #1

#### DEVELOP A PREMARKET APPROVAL (PMA) READY AUTOMATED IHC IUO ENROLLMENT ASSAY FOR FGF19

This Amendment #1 (this “Amendment #1”) to Project Schedule #1, effective as of March 1, 2016 (“Project Schedule #1”), is entered into by Blueprint Medicines Corporation, a Delaware corporation with offices located at 38 Sidney Street, Suite 200, Cambridge, MA 02139 USA (“Blueprint”) and Ventana Medical Systems, Inc., a Delaware corporation with offices located at 1910 E. Innovation Park Drive, Tucson, AZ 85755 USA (“Ventana”).

The effective date of this Amendment #1 shall be June 12, 2017 (the “Amendment Effective Date”).

Capitalized terms used and not otherwise defined in this Amendment #1 shall have the meanings ascribed to such terms in the Master Collaboration Agreement between Blueprint and Ventana, effective as of March 1, 2016 (the “Collaboration Agreement”), or Project Schedule #1, as applicable.

#### Recitals

WHEREAS, the Parties previously entered into Project Schedule #1, pursuant to which, among other things, Ventana is developing an Investigational Use Only Assay (“IUO”) for Blueprint’s drug candidate BLU-554 in hepatocellular carcinoma (“HCC”);

WHEREAS, the Parties desire to amend Project Schedule #1 in order to authorize Ventana to undertake the activities set forth in this Amendment #1, in accordance with the timelines and estimated pass through costs set forth in this Amendment #1; and

WHEREAS, Ventana desires to contract with [\*\*\*], to perform certain of the activities as set forth in this Amendment #1;

NOW, THEREFORE, the Parties agree as follows:

#### Objectives

The key objective of this Amendment #1 is to gain clinical evidence related to the clinical activity of BLU-554 and the FGF19 IHC IUO as a companion diagnostic.

#### Samples

The samples will be shipped from clinical sites to [\*\*\*] in accordance with the diagnostic study protocol. [\*\*\*] will analyze the samples using the Ventana FGF19 IHC IUO Assay on the Ventana Benchmark platform in accordance with the protocol provided by Ventana.

#### Activities Description and Pass Through Costs

The Parties hereby agree that Ventana and [\*\*\*] will perform the activities as set forth below, and any activities to be performed by Ventana will be performed by Ventana Clinical Affairs based in Tucson, AZ.

Activity	Pass Through Cost (US\$)	Units	Total
1. One-time fees at site including [***] fees for site training, study setup, database, and collection site set-up fee	***	***	***
2. Individual per test site fees including site and Ventana fees	***	***	***
3. Ongoing Fees: database amendments, data transfers, collection kit handling fees, monitoring and FDA audit	***	***	***
4. Collection Kit Costs	***	***	***
5. Outbound shipment of Kits to collection sites (US via [***])	***	***	***
6. Inbound shipment of Kits from collection sites (US via [***])	***	***	***

Activity	Pass Through Cost (US\$)	Units	Total
7. Outbound shipment of Kits to collection sites (EU and Asia-Pacific via [***])	[***]	[***]	[***]
8. Inbound shipment of Kits from collection sites (EU via [***])	[***]	[***]	[***]
9. Ventana fee associated with inbound/outbound shipment of Kits to/from collection sites			[***] <sup>1</sup>
<b>Total Estimated Pass Through Costs</b>			[***]

\* Represents estimated number of units.

#### Final Study Deliverable (Data/Results Reporting)

Results of sample analyses will be provided to the clinical trial investigator for Blueprint's ongoing Phase 1 clinical study for BLU-554 in patients with HCC (the "Phase 1 clinical study") based on data transfer plans agreed to within the JPT and mutually agreed to by Ventana, [\*\*\*] and the third party CRO conducting certain activities on Blueprint's behalf.

#### Project Timelines

The first patient tested at [\*\*\*] was [\*\*\*], and the last patient tested is expected to be completed approximately [\*\*\*].

#### Assay for Clinical Study

Ventana will be responsible for manufacture of the assay components required for analysis of samples obtained from the Phase 1 clinical study. Based upon a forecast provided to Ventana by Blueprint (which forecast may be updated by Blueprint from time to time upon reasonable advance notice to Ventana), Ventana will ensure that it maintains sufficient inventories of assay reagents as necessary to complete the conduct of the Phase 1 clinical study. Ventana will transfer the FGF19 IUO assay and train staff at [\*\*\*] on the performance of the assay and will monitor the performance of the assay in connection with the diagnostic clinical study.

#### Project Management

In accordance with Project Schedule #1, Ventana will [\*\*\*].

#### Payment Terms

All pass through costs will be invoiced monthly by Ventana after completion of sample analysis. The Parties agree that Ventana will only invoice Blueprint for the actual, not estimated, pass through costs for services and/or activities performed as described herein without any markup (except as set forth in Activity #9 above).

All invoices should contain the following information in order for them to be processed efficiently:

- ☐ Invoice Number
- ☐ Invoice Date
- ☐ Reference to <agreed to reference point>
- ☐ Blueprint Medicines, Purchase Order Number (PO#)
- ☐ Blueprint Medicines, Project Number <may be redundant>
- ☐ Description of Services with Itemization: Stage and milestone identifications
- ☐ Deliverables
- ☐ Total Amount Due
- ☐ Payee Name and Tax ID Number
- ☐ Payment Address

<sup>1</sup> Fee is equal to [\*\*\*] and for purposes of estimated pass through costs is based on [\*\*\*] for inbound/outbound shipment of Kits to/from collection sites.

- ☐ Name of requisitioner
- ☐ Contact person for any invoice questions

Additionally, invoices shall be submitted to Blueprint at the following email address: [\*\*\*]

Blueprint shall pay invoices for any undisputed amounts within [\*\*\*] days of receipt of the invoice.

All invoices will be paid by Blueprint as follows:

Credit DDA Name:	Ventana Medical Systems, Inc.
Tax Payer ID#:	[***]
Address:	[***]
Credit Bank:	[***]
Credit Bank address	[***]
Credit ABA:	[***]
Credit: DDA	[***]
Citi SWIFT Code:	[***]

Additional Pass Through Expenses

Any unforeseen project related expenses incurred by Ventana pursuant to this Amendment will be discussed in good faith by the Parties and agreed to prior to Ventana submitting to Blueprint invoices due for reimbursement.

Roles and Responsibilities:

For purposes of the activities set forth in this Amendment #1, the Parties initial representatives will be:

Name	Title	Phone	Address	Email Address
[***]	Project Leader	[***]	1910 E. Innovation Park Dr., Tucson, AZ 85755	[***]
[***]	Director Pharma Partnering	[***]	1910 E. Innovation Park Dr., Tucson, AZ 85755	[***]
[***]	Associate Director, Business Development	[***]	38 Sidney Street, Suite 200, Cambridge, MA 02139	[***]
[***]	Vice President, Translational Medicine	[***]	38 Sidney Street, Suite 200, Cambridge, MA 02139	[***]

Each Party shall provide notice to the other Party of any change in its representatives, which such notice shall be in writing within the JPT minutes and delivered in accordance with the terms of the Collaboration Agreement.

Miscellaneous

This Amendment contains the entire agreement between the Parties concerning the subject matter hereof and supersedes all prior agreements, written or oral, between the parties relating to the subject matter of this Amendment #1.

Except as expressly modified by this Amendment #1, the Collaboration Agreement, Project Schedule #1 and any other Project Schedule previously entered into by the Parties shall remain in full force and effect in accordance with their respective terms, without any waiver, amendment or modification thereof. Upon the effectiveness of this Amendment #1, all references to “this Project Schedule,” “hereunder,” “hereof,” “herein” or words of like import in Project Schedule #1 shall mean Project Schedule #1, as amended by this Amendment #1.

The headings and subheadings used in this Amendment #1 are used for convenience only and are not to be considered in construing or interpreting this Amendment #1.

The invalidity or unenforceability of any provision of this Agreement shall not affect the validity or enforceability of any other provision which shall remain in full force and effect.

This Amendment #1 shall be construed and interpreted in accordance with the internal laws of the State of Delaware, without giving effect to the principles of conflicts of law thereof.

The Amendment may be signed in two (2) or more counterparts (electronic transmission of scanned signatures included), each of which shall be deemed an original, but all of which shall constitute one and the same instrument. After electronic transmission of scanned signatures, the Parties shall, upon either Party's request, execute and exchange documents with original signatures.

*[Signature Page Follows]*

IN WITNESS WHEREOF, the Parties hereto have caused this Amendment #1 to be executed by their duly authorized representatives as of the Amendment Effective Date first written above.

**Ventana Medical Systems, Inc.**

By: /s/ Christoph Majewski  
Name: Christoph Majewski  
Title: VP & LCL, CDx

**Blueprint Medicines Corporation**

By: /s/ Jeffrey Albers  
Name: Jeffrey Albers  
Title: President and Chief Executive Officer

*[Signature Page to Amendment #1 to Project Schedule #1]*

[\*\*\*] INDICATES MATERIAL THAT HAS BEEN OMITTED AND FOR WHICH CONFIDENTIAL TREATMENT HAS BEEN REQUESTED. ALL SUCH OMITTED MATERIAL HAS BEEN FILED WITH THE SECURITIES AND EXCHANGE COMMISSION PURSUANT TO RULE 24b-2 PROMULGATED UNDER THE SECURITIES EXCHANGE ACT OF 1934, AS AMENDED.

#### Amendment No. 1 to Project Schedule #1

This Amendment No. 1 to Project Schedule #1, dated as of July 14, 2017 (this “Amendment”), between Blueprint Medicines Corporation (“Blueprint”) and QIAGEN Manchester Limited (“QIAGEN”) amends that certain Project Schedule #1, dated August 22, 2016 (“Project Schedule #1”) to the Master Collaboration Agreement, dated August 22, 2016, between Blueprint and QIAGEN (together with Project Schedule #1, the “Agreement” or “MCA”). Blueprint and QIAGEN are each referred to herein as a “Party” and, collectively, as the “Parties.” Capitalized terms used and not otherwise defined in this Amendment shall have the meanings set forth in the Agreement.

#### Recitals

WHEREAS, pursuant to the Agreement, the Parties have agreed to certain activities, timelines and payments related to the development and commercialization of an assay as a companion diagnostic test to identify gastrointestinal stromal tumor patients with the PDGFR $\alpha$  D842V mutation for use with Blueprint’s drug candidate BLU-285; and

WHEREAS, as recommended by the Joint Project Team, the Parties desire to amend certain activities, timelines and payments under Project Schedule #1;

NOW, THEREFORE, for good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the parties hereby agree as follows:

1. Part B (CDx development and validation) of Section 12 of Project Schedule #1 is hereby deleted in its entirety and replaced as set forth in Exhibit A attached hereto.
2. The table set forth in Section 13 of Project Schedule #1 under the heading “CDx Development and Validation Milestone Schedule” is hereby deleted in its entirety and replaced as set forth in Exhibit B attached hereto.
3. The table set forth in Section 14 of Project Schedule #1 under the heading “Pass-Through Cost Estimate for CDx Development and Validation” is hereby deleted in its entirety and replaced as set forth in Exhibit C attached hereto.
4. Project Schedule #1, as supplemented and modified by this Amendment, constitutes the entire agreement and understanding of the parties thereto with respect to the subject matter thereof and supersedes all prior agreements and understandings relating to such subject matter.
5. This Amendment shall be effective as of the date first set forth above (the “Amendment Effective Date”). On and after the Amendment Effective Date, each reference in the Project Schedule #1 to “this Schedule,” “hereunder,” “hereof,” “herein” or words of like

import, and each similar reference in the other documents entered into in connection with Project Schedule #1, shall mean and be a reference to Project Schedule #1, as amended hereby. Except as specifically amended above, the Agreement and Project Schedule #1 shall remain in full force and effect and are hereby ratified and confirmed.

6. This Agreement may be executed in two or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument. Counterparts may be delivered via facsimile, electronic mail (including pdf or any electronic signature complying with the U.S. Federal ESIGN Act of 2000) or other transmission method and any counterpart so delivered shall be deemed to have been duly and validly delivered and be valid and effective for all purposes.

7. This Amendment shall be construed and interpreted in accordance with the internal laws of the State of Delaware, without giving effect to the principles of conflicts of law thereof.

*[Remainder of page intentionally left blank.]*



[\*\*\*] INDICATES MATERIAL THAT HAS BEEN OMITTED AND FOR WHICH CONFIDENTIAL TREATMENT HAS BEEN REQUESTED. ALL SUCH OMITTED MATERIAL HAS BEEN FILED WITH THE SECURITIES AND EXCHANGE COMMISSION PURSUANT TO RULE 24b-2 PROMULGATED UNDER THE SECURITIES EXCHANGE ACT OF 1934, AS AMENDED

IN WITNESS WHEREOF, the undersigned have executed this Amendment No. 1 to Project Schedule #1 as of the date first set forth above.

**BLUEPRINT MEDICINES CORPORATION**

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

**QIAGEN MANCHESTER LIMITED**

By: /s/ Douglas Liu  
Name: Douglas Liu  
Title: SVP Global Operations

**Exhibit A**

**Section 12 – Part B (CDx development and validation)**

**Milestone 11:**

Design Control Planning (CDx)

[\*\*\*]

**Milestone 12:**

Completion of Design Inputs: Design Input Lock and Design & Development Plan (CDx)

[\*\*\*]

**Milestone 13:**

Manufacturing Robustness Study

[\*\*\*]

**Milestone 14:**

Manufacturing Transfer and Prototype Batch Production (CDx) required for assay performance studies

[\*\*\*]

**Milestone 15:**

CDx Assay Performance Studies Complete

[\*\*\*]

**Milestone 16:**

Completion of Verification Batches (Pilot Batches)

[\*\*\*]

**Milestone 17:**

System Design Lock

[\*\*\*]

**Milestone 18:**

Design Output and Design Verification Lock (Completion of Verification)

[\*\*\*]

**Milestone 19:**

Assay Software Available

[\*\*\*]

**Milestone 20:**

Completion of Lab Set-up Bridging Study

[\*\*\*]

**Milestone 21:**

[\*\*\*]

**Milestone 22:**

Design Validation Lock

[\*\*\*]

**Milestone 23** [\*\*\*]:

PMA Submissions

[\*\*\*]

**Milestone 24:**

CE Marking

[\*\*\*]

**Milestone 25:**

PMA Approval

[\*\*\*]

[\*\*\*] INDICATES MATERIAL THAT HAS BEEN OMITTED AND FOR WHICH CONFIDENTIAL TREATMENT HAS BEEN REQUESTED. ALL SUCH OMITTED MATERIAL HAS BEEN FILED WITH THE SECURITIES AND EXCHANGE COMMISSION PURSUANT TO RULE 24b-2 PROMULGATED UNDER THE SECURITIES EXCHANGE ACT OF 1934, AS AMENDED

**Milestone 26:**

Product Implementation

[\*\*\*]

**Exhibit B**

Section 13 – CDx Development and Validation Milestone Schedule

Milestone	Description	Estimated Completion Date	Milestone Amount (\$US)
11	Design Control Planning (CDx)	[***]	[***]
12	Completion of Design Inputs; Design Input Lock and Design & Development Plan (CDx)	[***]	[***]
13	Manufacturing Robustness Study	[***]	[***]
14	Manufacturing Transfer and Prototype Batch Production (CDx) required for assay performance studies	[***]	[***]
15	CDx Assay Performance Studies Complete	[***]	[***]
16	Completion of Verification Batches (Pilot Batches)	[***]	[***]
17	System Design Lock	[***]	[***]
18	Design Output and Design Verification Lock (Completion of Verification)	[***]	[***]
19	Assay Software Available	[***]	[***]
20	Completion of Lab Set-up Bridging Study	[***]	[***]
21	Completion of Reproducibility Study	[***]	[***]
22	Design Validation Lock	[***]	[***]
23	PMA Submissions* [***] * Each portion of this milestone will be invoiced separately upon submission of the respective module.	[***]	[***]
24	CE Marking	[***]	[***]
25	PMA Approval	[***]	[***]
26	Product Implementation	[***]	[***]
<b>Total CDx Development and Validation Milestones</b>			[***]

**Exhibit C**

Pass-Through Cost Estimate for CDx Development and Validation

Name	Description	Estimated Cost (\$US)
Reproducibility Studies	Contracting for Reproducibility Studies[***]	[***]
GLP Sequencing	Completion of Clinical Accuracy Study - Outsourced	[***]
GMP Raw materials	Primers & Probes for the development and manufacture of PDGFR $\alpha$ tests. Estimate in HPLC and Mass determination for each oligonucleotide	[***]
Positive control oligos	Long oligonucleotides for the generation of positive controls	[***]
Sample Costs	Procurement of sample will be required to support development. The cost of sample procurement varies depending on the disease tissue of interest.	[***]
Clinical Test Site Monitoring	During the course of the clinical trials monitoring of sites carrying out clinical testing will be conducted. The number of visits will be dependent on recruitment rate and site performance. For clarity, the estimated cost per visit includes any travel and accommodation costs incurred during each such visit.	[***]
Travel & Accommodation	During the course of the program, face-to-face Joint Project Team and Joint Steering Committee meetings will take place. The frequency of these meetings will be mutually agreed between QIAGEN and Blueprint in accordance with the MCA.	[***]
Canada Registration	Product implementation together with IVD registration activities and submission fees for Health Canada (Assumes no additional data generation)	[***]
IP	Analyze third party rights for freedom-to-operate of the assay. Does not include licensing fees. – covered under IUO development	[***]
QIAamp DSP DNA FFPE kits	Kits required for sample preparation	[***]
<b>Total Estimated Pass-Through Costs for CDx Development and Validation</b>		[***]

## CERTIFICATIONS

I, Jeffrey W. Albers, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q 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: August 2, 2017

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

---

## CERTIFICATIONS

I, Michael Landsittel, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q 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: August 2, 2017

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

---



**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 Quarterly Report on Form 10-Q of Blueprint Medicines Corporation (the "Company") for the period ended June 30, 2017 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: August 2, 2017

By: /s/ Jeffrey W. Albers

Jeffrey W. Albers  
President and Chief Executive Officer  
(Principal Executive Officer)

Date: August 2, 2017

By: /s/ Michael Landsittel

Michael Landsittel  
Vice President of Finance  
(Principal Financial and Accounting Officer)

---