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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 March 31, 2019

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	**26-3632015**
(State or Other Jurisdiction of Incorporation or Organization)	**(I.R.S. Employer Identification No.)**
45 Sidney Street Cambridge, Massachusetts	**02139**
(Address of Principal Executive Offices)	**(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 every Interactive Data File required to be submitted 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 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 ☐	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 ☑

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

Title of each class	Trading symbol(s)	Name of each exchange on which registered
Common stock, par value $0.001 per share	BPMC	Nasdaq Global Select Market

Number of shares of the registrant's common stock, $0.001 par value, outstanding on May 6, 2019: 48,853,933

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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 subsidiaries.

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 ongoing clinical trials and any planned clinical trials for avapritinib, BLU-667, BLU-554 and BLU-782, 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. and our collaboration with CStone Pharmaceuticals, as well as our ability to maintain these collaborations and establish other strategic collaborations;
- the development of companion diagnostic tests for our drug candidates;
- 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)

	March 31, 2019	December 31, 2018
Assets		
Current assets:		
Cash and cash equivalents	$ 79,391	$ 68,064
Investments, available-for-sale	336,465	425,948
Prepaid expenses and other current assets	10,660	5,775
Total current assets	426,516	499,787
Property and equipment, net	30,615	29,627
Operating lease right-of-use assets, net	76,528	—
Restricted cash	5,159	5,154
Other assets	5,845	5,556
Total assets	$ 544,663	$ 540,124
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	4,421	3,298
Accrued expenses	50,826	51,711
Current portion of operating lease liabilities	5,278	—
Current portion of deferred revenue	4,238	3,600
Current portion of lease incentive obligation	—	1,714
Total current liabilities	64,763	60,323
Deferred rent, net of current portion	—	5,130
Operating lease liabilities, net of current portion	94,322	—
Deferred revenue, net of current portion	41,198	42,567
Lease incentive obligation, net of current portion	—	12,903
Other long-term liabilities	167	192
Total liabilities	200,450	121,115
Commitments (Note 12)		
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; 44,171,465 and 44,037,026 shares issued and outstanding at March 31, 2019 and December 31, 2018, respectively	44	44
Additional paid-in capital	1,029,046	1,016,690
Accumulated other comprehensive income (loss)	75	(180)
Accumulated deficit	(684,952)	(597,545)
Total stockholders' equity	344,213	419,009
Total liabilities and stockholders' equity	$ 544,663	$ 540,124

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

	Three Months Ended March 31,	
	2019	**2018**
Collaboration revenue	$ 730	$ 954
Operating expenses:		
Research and development	74,250	49,954
General and administrative	16,553	9,911
Total operating expenses	90,803	59,865
Other income (expense):		
Other income (expense), net	2,669	2,394
Interest expense	(3)	(32)
Total other income	2,666	2,362
Net loss	$ (87,407)	$ (56,549)
Other comprehensive loss:		
Changes in foreign currency translation adjustments	(15)	—
Changes in unrealized gain (losses) related to available-for-sale investments	270	(323)
Comprehensive loss	$ (87,152)	$ (56,872)
Net loss per share — basic and diluted	$ (1.98)	$ (1.29)
Weighted-average number of common shares used in net loss per share — basic and diluted	44,097	43,700

Blueprint Medicines Corporation
Condensed Consolidated Statements of Stockholders' Equity
(in thousands)
(Unaudited)

	Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Loss	Accumulated Deficit	Stockholders' Equity
	Shares	Amount				
Balance at December 31, 2018	44,037,026	44	1,016,690	(180)	(597,545)	419,009
Issuance of common stock under stock plan	134,439	—	2,061	—	—	2,061
Stock-based compensation expense	—	—	10,295	—	—	10,295
Cumulative translation adjustment	—	—	—	(15)	—	(15)
Unrealized gain (loss) on available-for-sale securities	—	—	—	270	—	270
Net loss	—	—	—	—	(87,407)	(87,407)
Balance at March 31, 2019	44,171,465	$ 44	$ 1,029,046	$ 75	$ (684,952)	$ 344,213
Balance at December 31, 2017	43,577,526	$ 43	$ 979,785	$ (269)	$ (355,589)	$ 623,970
Issuance of common stock under stock plan	243,721	1	3,552	—	—	3,553
Stock-based compensation expense	—	—	5,549	—	—	5,549
Adoption of new accounting standard					(5,314)	(5,314)
Unrealized gain (loss) on available-for-sale securities	—	—	—	(322)	—	(322)
Other	—	—	(14)	—	—	(14)
Net loss	—	—	—	—	(56,549)	(56,549)
Balance at March 31, 2018	43,821,247	$ 44	$ 988,872	$ (591)	$ (417,452)	$ 570,873

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

	Three Months Ended March 31,	
	2019	**2018**
Cash flows from operating activities		
Net loss	$ (87,407)	$ (56,549)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	2,219	780
Stock-based compensation	10,295	5,549
Accretion of premiums and discounts on investments	(1,332)	(692)
Other	—	4
Changes in assets and liabilities:		
Prepaid expenses and other current assets	(1,923)	3,473
Other assets	(114)	(27)
Accounts payable	982	(482)
Accrued expenses	(1,208)	(525)
Deferred revenue	(731)	(954)
Deferred rent	—	(140)
Operating lease liabilities	(969)	—
Net cash used in operating activities	(80,188)	(49,563)
Cash flows from investing activities		
Purchases of property and equipment	(1,770)	(6,312)
Purchases of investments	(112,916)	(338,816)
Maturities of investments	204,000	126,000
Net cash provided by (used in) investing activities	89,314	(219,128)
Cash flows from financing activities		
Principal payments on loan payable	—	(417)
Proceeds from issuance of common stock	2,039	3,643
Payment of offering costs	—	(164)
Other financing activities	(28)	—
Net cash provided by financing activities	2,011	3,062
Net increase (decrease) in cash, cash equivalents, and restricted cash	11,137	(265,629)
Cash, cash equivalents and restricted cash at beginning of period	73,429	405,072
Effect of exchange rate changes on cash, cash equivalents and restricted cash	(16)	—
Cash, cash equivalents and restricted cash at end of period	$ 84,550	$ 139,443
Supplemental cash flow information		
Public offering costs incurred but unpaid at period end	$ —	$ 166
Property and equipment purchases unpaid at period end	$ 1,478	$ 3,126
Cash paid for interest	$ 2	$ 18

The following table provides a reconciliation of cash, cash equivalents, and restricted cash reported within the condensed consolidated balance sheets that sum to the total of the same such amounts shown in the condensed consolidated statements of cash flows.

	March 31, 2019	**March 31, 2018**
Cash and cash equivalents	$ 79,391	$ 134,886
Restricted cash	5,159	4,557
Total cash, cash equivalents, and restricted cash shown in condensed consolidated statements of cash flows	84,550	139,443

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 precision therapy company focused on genomically defined cancers, rare diseases and cancer immunotherapy. The Company's approach is to leverage its novel target discovery engine to systematically and reproducibly identify kinases that are drivers of diseases and to craft highly selective and potent drug candidates that may provide significant and durable clinical responses for 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 April 2, 2019, the Company closed an underwritten public offering of 4,662,162 shares of its common stock at a price to the public of $74.00 per share, including 608,108 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 2019 follow-on public offering). The Company received estimated net proceeds of $327.2 million, after deducting underwriting discounts and commissions and estimated offering expenses payable by the Company.

As of March 31, 2019, the Company had cash, cash equivalents and investments of $415.9 million. Based on the Company's current plans, the Company expects that its existing cash, cash equivalents and investments, including the $327.2 million in estimated net proceeds from its April 2019 follow-on public offering but excluding any potential option fees and milestone payments under its existing collaborations with Roche and CStone, will be sufficient to enable it to fund its operating expenses and capital expenditure requirements into the middle of 2021.

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, 2018 and notes thereto included in the Company's Annual Report on Form 10-K for the year ended December 31, 2018, filed with the SEC on February 26, 2019 (the 2018 Annual Report on Form 10-K).

The unaudited interim condensed consolidated financial statements have been prepared on the same basis as the audited financial statements, and updated, as necessary, in this report. In the opinion of the Company's management, the accompanying unaudited interim condensed consolidated financial statements contain all adjustments that are necessary to present fairly the Company's financial position as of March 31, 2019, the results of its operations for the three months ended March 31, 2019 and 2018, stockholder's equity for the three months ended March 31, 2019 and 2018 and cash flows for the three months ended March 31, 2019 and 2018. Such adjustments are of a normal and recurring nature. The results for the three months ended March 31, 2019 are not necessarily indicative of the results for the year ending December 31, 2019, or for any future period.

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

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: revenue recognition, operating lease right-of-use assets, operating lease liabilities, stock-based compensation expense, accrued expenses, and income taxes.

Significant Accounting Policies

The significant accounting policies used in preparation of these condensed consolidated financial statements for the three months ended March 31, 2019 are consistent with those discussed in Note 2 to the consolidated financial statements in the 2018 Annual Report on Form 10-K, except as noted below with respect to the Company's accounting policies related to lease obligations and as noted within this Note 2 under the section titled "—New Accounting Pronouncements."

New Accounting Pronouncements

From time to time, new accounting pronouncements are issued by the FASB or other standard setting bodies that the Company adopts as of the specified effective date. Unless otherwise discussed below, the Company does not believe that the adoption of recently issued standards have or may have a material impact on its consolidated financial statements and disclosures.

Leases

In February 2016, the FASB issued Accounting Standards Update *ASU No. 2016-02, Leases (Topic 842)* or ASC 842, a new standard issued to increase transparency and comparability among organizations related to their leasing activities. This standard established a right-of-use model that requires all lessees to recognize right-of-use assets and lease liabilities on their balance sheet that arise from leases as well as provide disclosures with respect to certain qualitative and quantitative information related to a company's leasing arrangements to meet the objective of allowing users of financial statements to assess the amount, timing and uncertainty of cash flows arising from leases.

The FASB subsequently issued the following amendments to ASU 2016-02 that have the same effective date and transition date: *ASU No. 2018-01, Leases (Topic 842): Land Easement Practical Expedient for Transition to Topic 842, ASU No. 2018-10, Codification Improvements to Topic 842, Leases, ASU No. 2018-11, Leases (Topic 842): Targeted Improvements, ASU No. 2018-20, Narrow-Scope Improvement for Lessors, and ASU No. 2019-01, Leases (Topic 842): Codification Improvements.* The Company adopted these amendments with ASU 2016-02 (collectively, the new leasing standards, or ASC 842) effective January 1, 2019.

As permitted by the new leasing standards, the Company elected to adopt ASC 842 using the modified retrospective transition approach, with no restatement of prior periods or cumulative adjustment to retained earnings, and therefore, the consolidated balance sheet prior to January 1, 2019 continues to be reported under ASC Topic 840, Leases, or ASC 840, which did not require the recognition of operating lease liabilities on the balance sheet, and is not comparative.

Upon adoption, the Company elected the package of transition practical expedients, which allowed it to carry forward prior conclusions related to whether any expired or existing contracts are or contain leases, the lease classification for any expired or existing leases and initial direct costs for existing leases. The leases that were classified

as operating leases under ASC 840 were classified as operating leases under ASC 842, and the accounting for finance leases (capital leases) was substantially unchanged. The Company elected to apply the practical expedient not to separate lease and non-lease components for new and modified leases commencing after adoption. The Company also made an accounting policy election to not recognize leases with an initial term of 12 months or less within the condensed consolidated balance sheets and to recognize those lease payments on a straight-line basis in the condensed consolidated statements of income over the lease term.

Impact of Adoption of ASC 842

Upon adoption of the new leasing standards, the Company recognized an adjustment of $54.2 million and $74.1 million to operating lease right-of-use assets and the related lease liabilities, respectively. The operating lease liabilities are based on the present value of the remaining minimum lease payments discounted using the Company's secured incremental borrowing rate at the effective date of January 1, 2019. The adoption of the new leasing standards did not have an impact on the Company's condensed consolidated statements of income.

The impact of the adoption of ASC 842 on the condensed consolidated balance sheet was as follows:

	Impact of ASC 842 Adoption on Consolidated Balance Sheet as of January 1, 2019		
(in thousands)	Balances without adoption of ASC 842	ASC 842 Adjustment	Balances with adoption of ASC 842
Operating lease right-of-use assets, net	$ —	$ 54,245	$ 54,245
Total assets	540,124	54,245	594,369
Accrued expenses	51,711	(125)	51,586
Current portion of operating lease liabilities	—	4,730	4,730
Current portion of lease incentive obligation	1,714	(1,714)	—
Total current liabilities	60,323	2,891	63,214
Deferred rent, net of current portion	5,130	(5,130)	—
Operating lease liabilities, net of current portion	—	69,387	69,387
Lease incentive obligation, net of current portion	12,903	(12,903)	—
Total liabilities	121,115	54,245	175,360

Leases Accounting Policy

For contracts entered into on or after the effective date, at the inception of a contract, the Company assesses whether the contract is, or contains, a lease. The assessment is based on: (1) whether the contract involves the use of a distinct identified asset, (2) whether the Company obtains the right to substantially all the economic benefit from the use of the asset throughout the period, and (3) whether the Company has the right to direct the use of the asset. At inception of a lease, the Company allocates the consideration in the contract to each lease component based on its relative stand-alone price to determine the lease payments.

Leases are classified as either finance leases or operating leases. A lease is classified as a finance lease if any one of the following criteria are met: the lease transfers ownership of the asset by the end of the lease term, the lease contains an option to purchase the asset that is reasonably certain to be exercised, the lease term is for a major part of the remaining useful life of the asset or the present value of the lease payments equals or exceeds substantially all of the fair value of the asset. A lease is classified as an operating lease if it does not meet any of these criteria.

For all leases at the lease commencement date, a right-of-use asset and a lease liability are recognized. The right-of-use asset represents the right to use the leased asset for the lease term. The lease liability represents the present value of the lease payments under the lease.

The right-of-use asset is initially measured at cost, which primarily comprises the initial amount of the lease liability, plus any initial direct costs incurred if any, less any lease incentives received. All right-of-use assets are reviewed for impairment. The lease liability is initially measured at the present value of the lease payments, discounted using the interest rate implicit in the lease or, if that rate cannot be readily determined, the secured incremental borrowing rate for the same term as the underlying lease. For real estate leases, the Company uses its secured incremental borrowing rate. For finance leases, the Company uses the rate implicit in the lease or its secured incremental borrowing rate if the implicit lease rate cannot be determined.

Lease payments included in the measurement of the lease liability comprise the following: the fixed noncancelable lease payments, payments for optional renewal periods where it is reasonably certain the renewal period will be exercised, and payments for early termination options unless it is reasonably certain the lease will not be terminated early.

Lease expense for operating leases consists of the lease payments plus any initial direct costs, primarily brokerage commissions, and is recognized on a straight-line basis over the lease term. Included in lease expense are any variable lease payments incurred in the period that are not included in the initial lease liability and lease payments incurred in the period for any leases with an initial term of 12 months or less. Lease expense for finance leases consists of the amortization of the right-of-use asset on a straight-line basis over the lease term and interest expense determined on an amortized cost basis. The lease payments are allocated between a reduction of the lease liability and interest expense.

Credit Losses

In June 2016, the FASB issued *ASU No. 2016-13, Financial Instruments - Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments*. This standard requires that credit losses be reported using an expected losses model rather than the incurred losses model that is currently used, and establishes additional disclosures related to credit risks. For available-for-sale debt securities with unrealized losses, this standard now requires allowances to be recorded instead of reducing the amortized cost of the investment. This standard will be effective for the Company on January 1, 2020. The Company is currently evaluating the potential impact that this standard may have on its consolidated financial position and results of operations.

Debt Securities

In March 2017, the FASB issued *ASU No. 2017-08, Receivables - Nonrefundable Fees and Other Costs (Subtopic 310-20): Premium Amortization on Purchased Callable Debt Securities.* This standard amends the amortization period for certain purchased callable debt securities held at a premium by shortening the amortization period to the earliest call date. This standard became effective for the Company on January 1, 2019, and was adopted using a modified retrospective transition approach. The adoption of this standard did not result in a significant adjustment to the Company's marketable debt securities.

Fair Value Measurements

In August 2018, the FASB issued *ASU No. 2018-13, Fair Value Measurement (Topic 820): Disclosure Framework Changes to the Disclosure Requirements for Fair Value Measurement*. This standard modifies certain disclosure requirements on fair value measurements. This standard will be effective for the Company on January 1, 2020. The Company does not expect that the adoption of this standard will have a material impact on the disclosures.

Collaborative Arrangements

In November 2018, the *FASB issued ASU No. 2018-18, Collaborative Arrangements (Topic 808): Clarifying the Interaction between Topic 808 and Topic 606.* This standard makes targeted improvements for collaborative arrangements as follows:

- Clarifies that certain transactions between collaborative arrangement participants should be accounted for as revenue under *ASC 606, Revenue from Contracts with Customers*, when the collaborative arrangement participant is a customer in the context of a unit of account. In those situations, all the

guidance in ASC 606 should be applied, including recognition, measurement, presentation and disclosure requirements;

- Adds unit-of-account guidance to *ASC 808, Collaborative Arrangements*, to align with the guidance in ASC 606 (that is, a distinct good or service) when an entity is assessing whether the collaborative arrangement or a part of the arrangement is within the scope of ASC 606; and

- Requires that in a transaction with a collaborative arrangement participant that is not directly related to sales to third parties, presenting that transaction together with revenue recognized under ASC 606 is precluded if the collaborative arrangement participant is not a customer.

This standard will be effective for the Company on January 1, 2020; however, early adoption is permitted. A retrospective transition approach is required for either all contracts or only for contracts that are not completed at the date of initial application of ASC 606, with a cumulative adjustment to opening retained earnings. The Company is currently evaluating the potential impact that this standard may have on its consolidated financial position and results of operations.

Internal-Use Software

In August 2018, the FASB issued *ASU No. 2018-15, Intangibles-Goodwill and Other-Internal-Use Software (Subtopic 350-40): Customer's Accounting for Implementation Costs Incurred in a Cloud Computing Arrangement That Is a Service Contract*, which clarifies the accounting for implementation costs in cloud computing arrangements. This standard will be effective for the Company on January 1, 2020, however, early adoption is permitted. The Company currently is evaluating the impact the adoption may have on its consolidated financial position and results of operations.

Reclassifications

Certain items in the prior year's consolidated financial statements have been reclassified to conform to the current presentation.

3. Cash Equivalents and Investments

Cash equivalents and investments, available-for-sale, consisted of the following at March 31, 2019 and December 31, 2018 (in thousands):

March 31, 2019	**Amortized Cost**	**Unrealized Gain**	**Unrealized Losses**	**Fair Value**
Cash equivalents:				
Money market funds	$ 79,391	$ —	$ —	$ 79,391
Investments, available-for-sale:				
U.S. treasury obligations	336,359	129	(23)	336,465
Total	$ 415,750	$ 129	$ (23)	$ 415,856

December 31, 2018	**Amortized Cost**	**Unrealized Gain**	**Unrealized Losses**	**Fair Value**
Cash equivalents:				
Money market funds	$ 68,064	$ —	$ —	$ 68,064
Investments, available-for-sale:				
U.S. treasury obligations	426,112	—	(164)	425,948
Total	$ 494,176	$ —	$ (164)	$ 494,012

At March 31, 2019 and December 31, 2018, the Company held 15 and 54 debt securities, respectively, that were in an unrealized loss position. The aggregate fair value of debt securities in an unrealized loss position at March 31, 2019 and December 31, 2018 was $94.5 million and $397.5 million, respectively. There were no individual securities

that were in a significant unrealized loss position as of March 31, 2019 and December 31, 2018. As of March 31, 2019, there were three securities in a total aggregate fair value of $14.0 million were in an unrealized loss position for more than twelve months. The Company has the intent and ability to hold such securities until recovery, and there was no material change in the credit risk of these investments. As a result, the Company determined it did not hold any investments with an other-than-temporary impairment as of March 31, 2019.

No available-for-sale securities held as of March 31, 2019 or December 31, 2018 had remaining maturities greater than one year.

4. Fair Value of Financial Instruments

The following table summarizes our cash equivalents and marketable securities measured at fair value on a recurring basis as of March 31, 2019 (in thousands):

Description	March 31, 2019	Active Markets (Level 1)	Observable Inputs (Level 2)	Unobservable Inputs (Level 3)
Financial Assets				
Cash equivalents:				
Money market funds	$ 79,391	$ 79,391	$ —	$ —
Investments, available-for-sale:				
U.S Treasury obligations	336,465	336,465	—	—
Total	$ 415,856	$ 415,856	$ —	$ —

The following table summarizes our cash equivalents and marketable securities measured at fair value on a recurring basis as of December 31, 2018 (in thousands):

Description	December 31, 2018	Active Markets (Level 1)	Observable Inputs (Level 2)	Unobservable Inputs (Level 3)
Financial Assets				
Cash equivalents:				
Money market funds	$ 68,064	$ 68,064	$ —	$ —
Investments, available-for-sale:				
U.S Treasury obligations	425,948	425,948	—	—
Total	$ 494,012	$ 494,012	$ —	$ —

5. Restricted Cash

At March 31, 2019 and December 31, 2018, $5.2 million and $5.4 million, respectively, of the Company's cash is restricted by a bank related to security deposits for the lease agreements for the Company's current and former corporate headquarters.

For additional information on these security deposits, see Note 11, *Leases.*

6. Property and Equipment, Net

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

	Estimated Useful Life (Years)	March 31, 2019	December 31, 2018
Lab equipment	5	$ 6,742	$ 6,232
Furniture and fixtures	4	2,455	2,369
Computer equipment	3	1,554	1,805
Leasehold improvements	Term of lease	26,660	26,640
Software	3	408	280
Construction-in-progress		2,542	956
		40,361	38,282
Less: accumulated depreciation and amortization		(9,746)	(8,655)
Total		$ 30,615	$ 29,627

Property, plant and equipment are recorded at historical cost, net of accumulated depreciation. For the three months ended March 31, 2019, depreciation expense totaled $1.2 million, compared to $0.8 million in the prior year comparative period.

7. Accrued Expenses

Accrued expenses consist of the following (in thousands):

	March 31, 2019	December 31, 2018
External research and development	$ 36,641	$ 36,213
Employee compensation	4,545	8,071
Accrued professional fees	5,758	4,423
Property and equipment costs	1,338	912
Other	2,544	2,092
Total	$ 50,826	$ 51,711

8. Collaborations

CStone Pharmaceuticals

On June 1, 2018, the Company entered into a Collaboration and License Agreement (the CStone agreement) with CStone pursuant to which the Company granted CStone exclusive rights to develop and commercialize the Company's drug candidates BLU-554, avapritinib and BLU-667, including back-up forms and certain other forms thereof, in Mainland China, Hong Kong, Macau and Taiwan (each, a CStone region and collectively, the CStone territory), either as a monotherapy or as part of a combination therapy. The Company will retain exclusive rights to the licensed products outside the CStone territory.

The Company received an upfront cash payment of $40.0 million, and subject to the terms of the CStone agreement, will be eligible to receive up to approximately $346.0 million in milestone payments, including $118.5 million related to development and regulatory milestones and $227.5 million related to sales-based milestones. In addition, CStone will be obligated to pay the Company tiered percentage royalties on a licensed product-by-licensed product basis ranging from the mid-teens to low twenties on annual net sales of each licensed product in the CStone territory, subject to adjustment in specified circumstances. CStone will be responsible for costs related to the development of the licensed products in the CStone territory, other than specified costs related to the development of BLU-554 as a combination therapy in the CStone territory that will be shared by the Company and CStone.

Pursuant to the terms of the CStone agreement, CStone will be responsible for conducting all development and commercialization activities in the CStone territory related to the licensed products, and the Company and CStone plan to conduct a proof-of-concept clinical trial in China evaluating BLU-554 in combination with CS1001, a clinical stage anti-programmed death ligand-1 immunotherapy being developed by CStone, as a first-line therapy for the treatment of patients with hepatocellular carcinoma.

The CStone agreement will continue on a licensed product-by-licensed product and CStone region-by-CStone region basis until the later of (i) 12 years after the first commercial sale of a licensed product in a CStone region in the CStone territory and (ii) the date of expiration of the last valid patent claim related to the Company's patent rights or any joint collaboration patent rights for the licensed product that covers the composition of matter, method of use or method of manufacturing such licensed product in such region. Subject to the terms of the CStone agreement, CStone may terminate the CStone agreement in its entirety or with respect to one or more licensed products for convenience by providing written notice to the Company after June 1, 2019, and CStone may terminate the CStone agreement with respect to a licensed product for convenience at any time by providing written notice to the Company following the occurrence of specified events. In addition, the Company may terminate the CStone agreement under specified circumstances if CStone or certain other parties challenges the Company's patent rights or any joint collaboration patent rights or if CStone or its affiliates do not conduct any material development or commercialization activities with respect to one or more licensed products for a specified period of time, subject to specified exceptions. Either party may terminate the CStone agreement for the other party's uncured material breach or insolvency. In certain termination circumstances, the parties are entitled to retain specified licenses to be able to continue to exploit the licensed products, and in the event of termination by CStone for the Company's uncured material breach, the Company will be obligated to pay CStone a low single digit percentage royalty on a licensed product-by-licensed product basis on annual net sales of such licensed product in the CStone territory, subject to a cap and other specified exceptions.

The Company evaluated the CStone agreement to determine whether it is a collaborative arrangement for purposes of ASC 808. The Company determined that there were two material components of the CStone agreement: (i) the CStone territory-specific license and related activities in the CStone territory, and (ii) the parties' participation in global development of the licensed products. The Company concluded that the CStone territory-specific license and related activities in the CStone territory are not within the scope of ASC 808 because the Company is not exposed to significant risks and rewards. The Company concluded that CStone is a customer with regard to the component that includes the CStone territory-specific license and related activities in CStone territory, which include manufacturing. For the parties' participation in global development of the licensed products, the Company concluded that the research and development activities and cost-sharing payments related to such activities are within the scope of ASC 808 as both parties are active participants exposed to the risk of the activities under the CStone agreement. The Company concluded that CStone is not a customer with regard to the global development component in the context of the CStone agreement. Therefore, payments received by the Company for global development activities under the CStone agreement, including manufacturing, will be accounted for as a reduction of related expenses. Accordingly, the Company recorded a reduction of expenses of $0.8 million for the three months ended March 31, 2019.

The Company evaluated the CStone territory-specific license and related activities in the CStone territory under ASC 606 as these transactions are considered transactions with a customer. The Company identified the following material promises under the arrangement: (1) the three exclusive licenses granted in the CStone territory to develop, manufacture and commercialize the three licensed products; (2) the initial know-how transfer for each licensed product; (3) manufacturing activities related to development and commercial supply of the licensed products; (4) participation in the joint steering committee (JSC) and joint project teams (JPT); (5) regulatory responsibilities; and (6) manufacturing technology and continuing know-how transfers. The Company determined that each licensed product is distinct from the other licensed products. In addition, the Company determined that the exclusive licenses and initial know-how transfers for each licensed product were not distinct from each other, as each exclusive license has limited value without the corresponding initial know-how transfer. For purposes of ASC 606, the Company determined that that participation on the JSC and JPTs, the regulatory responsibilities and the manufacturing technology and continuing know-how transfers are qualitatively and quantitatively immaterial in the context of the CStone agreement and therefore are excluded from performance obligations. As such, the Company determined that these six material promises, described above, should be combined into one performance obligation for each of the three candidates.

The Company evaluated the provision of manufacturing activities related to development and commercial supply of the licensed products as an option for purposes of ASC 606 to determine whether these manufacturing

activities provide CStone with any material rights. The Company concluded that the manufacturing activities were not issued at a significant and incremental discount, and therefore do not provide CStone with any material rights. As such, the manufacturing activities are excluded as performance obligations at the outset of the arrangement.

Based on these assessments, the Company identified three distinct performance obligations at the outset of the CStone agreement, which consists of the following for each licensed product: (1) the exclusive license and (2) the initial know-how transfer.

Under the CStone agreement, in order to evaluate the transaction price for purposes of ASC 606, the Company determined that the upfront amount of $40.0 million constituted the entirety of the consideration to be included in the transaction price as of the outset of the arrangement, which was allocated to the three performance obligations. The potential milestone payments that the Company is eligible to receive were excluded from the transaction price, as all milestone amounts were fully constrained based on the probability of achievement. The Company will reevaluate the transaction price at the end of each reporting period and as uncertain events are resolved or other changes in circumstances occur, and if necessary, the Company will adjust its estimate of the transaction price. There was no adjustment in the transaction price as of March 31, 2019. Because the performance obligations have been satisfied, any addition to the transaction price would be immediately recognized as revenue.

The Company satisfied the performance obligations upon delivery of the licenses, initial know-how transfers and product trademark and recognized the upfront payment of $40.0 million as revenue during the second quarter of 2018, and there was no revenue deferred as a contract liability associated with the CStone agreement as of December 31, 2018 and March 31, 2019.

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 are currently conducting activities for up to five programs under the collaboration, including up to two collaboration programs leveraging the Company's novel target discovery engine and proprietary compound library to select potential targets.

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.

The Company received an upfront cash payment of $45.0 million in March 2016 upon execution of the Roche agreement, and subject to the terms of the Roche agreement, the Company 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 June 2018, the Company achieved and received a $10.0 million research milestone payment.

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 assessed this arrangement in accordance with ASC 606 upon the adoption of the new standard on January 1, 2018, and concluded that the contract counterparty, Roche, is a customer prior to the exercise, if any, of an option by Roche. The Company identified the following material promises under the arrangement: (1) a non-transferable, sub-licensable and non-exclusive license to use the Company's intellectual property and collaboration compounds to conduct research activities; (2) research and development activities through Phase 1 clinical trials under the research plan; (3) five option rights for licenses to develop, manufacture, and commercialize the collaboration targets; (4) participation on a joint research committee (JRC) and joint development committee (JDC); and (5) regulatory responsibilities under Phase 1 clinical trials. The Company determined that the license and research and development activities were not distinct from another, as the license has limited value without the performance of the research and development activities. Participation on the JRC and JDC to oversee the research and development activities was determined to be quantitatively and qualitatively immaterial and therefore is excluded from performance obligations. The regulatory responsibilities related to filings and obtaining approvals related to the products that may result from each program do not represent separate performance obligations based on their dependence on the research and development efforts. As such, the Company determined that these promises should be combined into a single performance obligation.

The Company evaluated the option rights for licenses to develop, manufacture, and commercialize the collaboration targets to determine whether it provides Roche with any material rights. The Company concluded that the options were not issued at a significant and incremental discount, and therefore do not provide material rights. As such, they are excluded as performance obligations at the outset of the arrangement.

Based on these assessments, the Company identified one performance obligation at the outset of the Roche agreement, which consists of: (1) the non-exclusive license; (2) the research and development activities through Phase 1; and (3) regulatory responsibilities under Phase 1 clinical trials.

Under the Roche agreement, in order to evaluate the appropriate transaction price, the Company determined that as of January 1, 2018, the upfront amount of $45.0 million constituted the entirety of the consideration to be included in the transaction price as of the outset of the arrangement, which was allocated to the single performance obligation. The option exercise payments that may be received are excluded from the transaction price until each customer option is exercised as it was determined that the options are not material rights. The potential milestone payments that the Company is eligible to receive prior to the exercise of the options were initially excluded from the transaction price, as all milestone amounts were fully constrained based on the probability of achievement. The Company will reevaluate the transaction price at the end of each reporting period and as uncertain events are resolved or other changes in circumstances occur, and, if necessary, adjust its estimate of the transaction price.

In June 2018, the Company achieved and received a $10.0 million research milestone payment related to the Roche agreement, and it became probable that a significant reversal of cumulative revenue would not occur for the $10.0 million research milestone achieved. At such time, the associated consideration was added to the estimated transaction price and allocated to the existing performance obligation.

The Company recognizes revenue associated with the performance obligation as the research and development services are provided using an input method, according to the costs incurred as related to the research and development activities on each program and the costs expected to be incurred in the future to satisfy the performance obligation. The transfer of control occurs over this time period and, in management's judgment, is the best measure of progress towards satisfying the performance obligation. The amounts received that have not yet been recognized as revenue are deferred as a contract liability on the Company's consolidated balance sheet, and will be recognized over the remaining research and development period until the performance obligation is satisfied.

During the three months ended March 31, 2019, there has been no significant changes in the costs expected to be incurred in the future to satisfy the performance obligation, and the Company recognized revenue of $0.7 million under the Roche collaboration, of which $1.0 million was recognized as a result of the change in the contract liability balances as of December 31, 2018. As of March 31, 2019, the Company had revenue deferred as a contract liability related to the Roche agreement of $45.4 million, of which $4.2 million was included in current liabilities, and the research and development services related to the performance obligation are expected to be performed over a remaining period of approximately six years.

9. Stock-based compensation

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, 2019, the number of shares reserved for issuance under the 2015 Plan was increased by 1,761,481 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 March 31, 2019, there were 2,244,841 shares available for future grant under the 2015 Plan.

Stock options

The following table summarizes the stock option activity for the three months ended March 31, 2019:

	Shares	Weighted-Average Exercise Price
Outstanding at December 31, 2018	4,557,800	$ 44.64
Granted	1,061,306	85.05
Exercised	(134,439)	15.34
Canceled	(23,785)	63.18
Outstanding at March 31, 2019	5,460,882	$ 53.13
Exercisable at March 31, 2019	2,199,374	$ 27.46

At March 31, 2019, the total unrecognized compensation expense related to unvested stock option awards was $135.3 million, which is expected to be recognized over a weighted-average period of approximately 3.0 years.

Restricted stock units

The following table summarizes the restricted stock units activity for the three months ended March 31, 2019:

	Shares	Weighted-Average Grant Date Fair Value
Unvested shares at December 31, 2018	36,868	$ 66.28
Granted	256,124	85.40
Vested	—	—
Forfeited	(1,000)	86.60
Unvested shares at March 31, 2019	291,992	$ 82.98

At March 31, 2019, the total unrecognized compensation expense related to unvested restricted stock units was $23.4 million, which is expected to be recognize over a weighted-average period of approximately 3.9 years.

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, 2019, the number of shares reserved for issuance under the 2015 ESPP was increased by 440,370 shares. No shares were issued under the 2015 ESPP during the three months ended March 31, 2019 and 2018.

Stock-based compensation expense

The Company recognized stock-based compensation expense totaling $10.3 million and $5.5 million for the three months ended March 31, 2019 and 2018, respectively. Stock-based compensation expense by award type included within the unaudited condensed consolidated statements of operations and comprehensive loss was as follows (in thousands):

	Three Months Ended March 31,	
	2019	2018
Stock options	$ 9,579	$ 5,491
Restricted stock units	624	—
Employee stock purchase plan	92	58
Total stock-based compensation expense	$ 10,295	$ 5,549

Stock-based compensation expense by classification within the unaudited condensed consolidated statements of operations and comprehensive loss is as follows (in thousands):

	Three Months Ended March 31,	
	2019	2018
Research and development	$ 5,790	$ 3,011
General and administrative	4,505	2,538
Total stock-based compensation expense	$ 10,295	$ 5,549

10. Net Loss per Share

Basic net loss per share is calculated by dividing net loss by the weighted average shares outstanding during the period, without consideration for common stock equivalents. Diluted net loss per share is calculated by adjusting weighted average shares outstanding for the dilutive effect of common stock equivalents outstanding for the period. For purposes of the dilutive net loss per share calculation, stock options, unvested restricted stock units and ESPP shares are considered to be common stock equivalents but are excluded from the calculation of diluted net loss per share, as their effect would be anti-dilutive; therefore, basic and diluted net loss per share 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 for the periods indicated because including them would have had an anti-dilutive effect.

	Three Months Ended March 31,	
	2019	2018
Stock options	5,460,882	4,119,870
Restricted stock units	291,992	—
ESPP shares	10,275	5,722
Total	5,763,149	4,125,592

The weighted average number of common shares used in net loss per share on a basic and diluted basis were 44,096,806 and 43,700,226 for the three months ended March 31, 2019 and 2018, respectively.

11. Leases

38 Sidney Street

On February 12, 2015, the Company entered into a lease for approximately 38,500 rentable square feet of office and laboratory space at 38 Sidney Street in Cambridge, Massachusetts, which the Company gained control over on June 15, 2015, and occupancy commenced in October 2015. The initial term of the lease agreement will expire on October 31, 2022, unless terminated sooner. 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 initial 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 lease provided the Company with an allowance for leasehold improvements of $4.3 million. Prior to adoption of ASC 842, the Company recorded rent expense on a straight-line basis through the end of the lease term and the associated deferred rent on the consolidated balance sheet. The Company also recorded the leasehold improvement incentives as a reduction to rent expense ratably over the lease term, and the balance from the leasehold improvement incentives was included in lease incentive obligations on the consolidated balance sheet as of December 31, 2018. The lease agreement required the Company to pay a security deposit of $1.3 million, of which $0.2 million was released in February 2018 and February 2019, respectively. The remaining $0.9 million is recorded in restricted cash on the Company's condensed consolidated balance sheet as of March 31, 2019.

In the first quarter of 2018, the Company subleased its former corporate headquarters at 38 Sidney Street, Cambridge, Massachusetts through October 31, 2020. Subject to the terms of the sublease agreement and the master lease agreement, including a right of recapture by the Company, the sublessee has the option to extend the sublease through October 31, 2022. The sublease includes a total commitment by the sublessee of $8.2 million over the 32 month term of the sublease agreement. During the 32 month term, the Company will be responsible for total rental payments of $6.9 million and an additional $0.7 million in total payments related to the Company's profit on the sublease income which are payable by the Company to the landlord. As of March 31, 2019, the minimum sublease rental commitment by the sublessee was $5.0 million.

45 Sidney Street

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. The initial term of the lease agreement commenced on October 1, 2017 and will expire on November 30, 2029, unless terminated sooner. The lease agreement also provides the Company 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.

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 increases annually until it reaches approximately $10.6 million in the last year of the initial term. The lease provided the Company with a tenant improvement allowance of approximately $14.2 million for improvements to be made to the premises. Prior to adoption of ASC 842, the Company recorded rent expense on a straight-line basis through the end of the lease term and the associated deferred rent on the consolidated balance sheet. The Company also recorded the leasehold improvement incentives as a reduction to rent expense ratably over the lease term, and the balance from the leasehold improvement incentives was included in lease incentive obligations on the consolidated balance sheet as of December 31, 2018. The lease agreement required the Company to pay a security deposit of $3.5 million, which is recorded in restricted cash on the Company's condensed consolidated balance sheet as of March 31, 2019.

On September 19, 2018, the Company entered into an amendment to the lease agreement for its office and laboratory space located at 45 Sidney Street in Cambridge, Massachusetts to expand the rentable square footage from approximately 99,833 square feet to approximately 139,216 square feet. The initial term of the lease with respect to the expansion premises commenced on March 1, 2019 and will expire on November 30, 2029, unless terminated sooner. Pursuant to the lease amendment, the date on which the Company will become responsible for paying rent with respect to the expansion space will be the earlier of (i) the date upon which the Company first occupies the expansion premises for business purposes or (ii) July 1, 2019. The Company currently anticipates the rent commencement date for the expansion premises will be July 1, 2019.

The Company has agreed to pay an initial annual base rent of approximately $3.2 million for the expansion premises, which increases annually until it reaches approximately $4.2 million in the last year of the initial term for the expansion premises. Pursuant to the lease amendment, the landlord has also agreed to provide the Company with a tenant improvement allowance of approximately $3.2 million for improvements to be made to the expansion premises. The lease amendment required the Company to pay an additional security deposit of $0.8 million to the landlord for the expansion premises, which is recorded in restricted cash on the Company's condensed consolidated balance sheet as of March 31, 2019.

The components of lease expense for the three months ended March 31, 2019 were as follows:

Operating leases:	Three Months Ended March 31, 2019
Lease cost	$ 3,564
Sublease income	(701)
Net lease cost	2,863

For the three months ended March 31, 2018, rent expense under ASC 840, net of sublease income, was $2.2 million.

Supplemental cash flow information related to leases for the three months ended March 31, 2019 was as follows:

	Three Months Ended March 31, 2019
Cash paid for amounts included in the measurement of lease liabilities:	
Operating cash flows from operating leases	$ 2,621
Lease liabilities arising from obtaining right-of-use assets:	
Operating leases	$ 23,300

The weighted average remaining lease term and weighted average discount rate of the operating leases are as follows:

	Operating leases
Weighted Average Remaining Lease Term	10 years
Weighted Average Discount Rate	8.2%

Future minimum lease payments under non-cancellable leases as of March 31, 2019 were as follows (in thousands):

2019 (excluding the 3 months ended March 31,2019)	$ 9,627
2020	14,341
2021	14,764
2022	14,719
2023	12,746
Thereafter	83,471
Total future minimum lease payments (1)	149,668
Less imputed interest	(50,068)
Total	$ 99,600

(1) Minimum lease payments have not been reduced by minimum sublease rentals of $4.6 million due in the future under the Company's non-cancelable sublease for the office and laboratory space located at 38 Sidney Street, Cambridge, Massachusetts. The minimum lease payments above do not include any related common area maintenance charges or real estate taxes.

Under the prior lease guidance minimum rental commitments under non-cancelable leases for each of the next five years and total thereafter as of December 31, 2018, were as follows (in thousands):

2019	$ 12,247
2020	14,341
2021	14,764
2022	14,719
2023	12,746
Thereafter	83,471
Total minimum lease payments (1)	$ 152,288

(1) Minimum lease payments have not been reduced by minimum sublease rentals of $5.3 million due in the future under the Company's non-cancelable sublease for the office and laboratory space located at 38 Sidney Street, Cambridge, Massachusetts. The minimum lease payments above do not include any related common area maintenance charges or real estate taxes.

12. Commitments

The Company has no other commitments other than the minimum lease payments commitment as disclosed in Note 11, *Leases*.

13. Subsequent Events

On April 2, 2019, the Company closed an underwritten public offering of 4,662,162 shares of its common stock at a price to the public of $74.00 per share, including 608,108 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 estimated net proceeds of $327.2 million, after deducting underwriting discounts and commissions and estimated offering expenses payable by the Company.

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 unaudited 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, 2018, filed with the Securities and Exchange Commission, or the SEC, on February 26, 2019. 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 precision therapy company focused on genomically defined cancers, rare diseases and cancer immunotherapy. Our approach is to leverage our novel target discovery engine to systematically and reproducibly identify kinases that are drivers of diseases and to craft highly selective and potent 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. We believe that our uniquely targeted, scalable approach empowers the rapid design and development of new treatments and increases the likelihood of success. Our most advanced drug candidates are avapritinib, BLU-667, BLU-554 and BLU-782.

Our lead drug candidate, avapritinib, is an orally available, potent and highly selective inhibitor that targets KIT and PDGFRA mutations. 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. GIST is a rare disease that is a sarcoma, or tumor of bone or connective tissue, of the gastrointestinal 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 are currently evaluating avapritinib for the treatment of GIST in an ongoing Phase 1 clinical trial in advanced GIST, which we refer to as our NAVIGATOR trial, and an ongoing global, randomized Phase 3 clinical trial comparing avapritinib to regorafenib in third-line GIST, which we refer to as our VOYAGER trial. We have completed enrollment of the NAVIGATOR trial, and we expect to complete enrollment of the VOYAGER trial in the second half of 2019. In November 2018, we reported updated data from the NAVIGATOR trial at the Connective Tissue Oncology Society Annual Meeting, and in January 2019, we reported top-line data from the NAVIGATOR trial. We plan to present additional data from the NAVIGATOR trial on June 1, 2019 at the 2019 American Society of Clinical Oncology, or ASCO, Annual Meeting. We plan to initiate a Phase 3 precision medicine trial in second-line GIST in the second half of 2019, which we refer to as our COMPASS-2L trial. In addition, we plan to submit a new drug application, or NDA, to the U.S. Food and Drug Administration, or FDA, for avapritinib for the treatment of PDGFRA Exon 18 mutant GIST and fourth-line GIST in the second quarter of 2019, and if approved, we plan to submit a supplemental NDA to the FDA for the treatment of third-line GIST in 2020. We plan to submit a marketing authorization application to the European Medicines Agency for avapritinib for the treatment of PDGFRa D842V mutant GIST and fourth-line GIST in the third quarter of 2019.

In addition, we are currently evaluating avapritinib for the treatment of SM in an ongoing Phase 1 clinical trial in advanced SM, which we refer to as our EXPLORER trial, an ongoing registration enabling Phase 2 clinical trial in advanced SM, which we refer to as our PATHFINDER trial, and an ongoing registration enabling Phase 2 clinical trial in indolent and smoldering SM, which we refer to as our PIONEER trial. In December 2018, we reported updated data from the EXPLORER trial at the 60th American Society of Hematology Annual Meeting and Exposition, and we plan to present updated data from the EXPLORER trial in advanced SM at the 24th Congress of the European Hematology Association in mid-June 2019. We expect to complete the dose-finding portion of the PIONEER trial and plan to present initial data from the PIONEER trial in indolent and smoldering SM in the second half of 2019. We expect to complete enrollment of the PATHFINDER trial in the second half of 2019. We plan to submit an NDA to the FDA for avapritinib for the treatment of advanced SM in the first quarter of 2020, subject to continued discussions with the FDA under its

breakthrough therapy program to determine whether the clinical data from the ongoing Phase 1 EXPLORER trial and the initial clinical data from the ongoing Phase 2 PATHFINDER trial will support an NDA submission. The FDA has granted orphan drug designation to avapritinib for the treatment of GIST and the treatment of mastocytosis, and the European Commission has granted orphan medicinal product designation to avapritinib for the treatment of GIST and the treatment of mastocytosis. The FDA has granted fast track designation to avapritinib for (i) the treatment of patients with unresectable or metastatic GIST that progressed following treatment with imatinib and a second TKI and (ii) the treatment of patients with unresectable or metastatic GIST with the PDGFRA D842V mutation regardless of prior therapy. In addition, the FDA has granted breakthrough therapy designation to avapritinib for the treatment of patients with unresectable or metastatic GIST harboring the PDGFRA D842V mutation and to avapritinib for the treatment of advanced SM, including the subtypes of aggressive SM, SM with an associated hematologic neoplasm and mast cell leukemia.

BLU-667 is an orally available, potent and highly selective inhibitor that targets RET, a receptor tyrosine kinase that is abnormally activated by mutations or fusions and RET resistance mutations that we predict will arise from treatment with first generation therapies. RET drives disease in subsets of patients with non-small cell lung cancer, or NSCLC, and cancers of the thyroid, including medullary thyroid carcinoma, or MTC, and papillary thyroid cancer, or PTC, and our research suggests that RET may drive disease in subsets of patients with colon cancer, breast cancer and other cancers. We are currently evaluating BLU-667 in an ongoing Phase 1 clinical trial in patients with RET-altered NSCLC, MTC and other advanced solid tumors, which we refer to as our ARROW trial. In March 2019, we reported updated top-line data from the ongoing ARROW trial in RET-fusion NSCLC and RET-mutant MTC. We plan to present updated RET-fusion NSCLC data on June 3, 2019 at the 2019 ASCO Annual Meeting, and we plan to present updated RET-mutant data on June 1, 2019 at the 2019 ASCO Annual Meeting. In March 2019, we announced the enrollment target was reached and patient screening was closed for the registration-enabling ARROW trial cohort for patients with RET-fusion NSCLC previously treated with platinum-based chemotherapy, and we recently reached the enrollment target for the registration-enabling ARROW trial cohort for patients with RET-mutant MTC previously treated with an approved multi-kinase inhibitor. We plan to submit an NDA to the FDA for BLU-667 for the treatment of patients with RET-fusion NSCLC previously treated with platinum-based chemotherapy in the first quarter of 2020, and we plan to submit an NDA to the FDA for BLU-667 for the treatment of patients with RET-mutant MTC previously treated with an approved multi-kinase inhibitor in the first half of 2020. In addition, in September 2018, we presented two clinical cases demonstrating proof-of-concept for BLU-667 in combination with osimertinib (Tagrisso®) in treatment-resistant, EGFR-mutant NSCLC at the International Association for the Study of Lung Cancer 19th World Conference on Lung Cancer and published online in *Cancer Discovery*. In the second half of 2019, we plan to initiate a Phase 3 clinical trial evaluating BLU-667 in first-line RET-fusion NSCLC and plan to initiate a Phase 2 clinical trial evaluating BLU-667 in combination with osimertinib in treatment-resistant, EGFR-mutant NSCLC harboring an acquired RET fusion. The FDA has granted orphan drug designation to BLU-667 for the treatment of RET-rearranged NSCLC, JAK1/2-positive NSCLC or TRKC-positive NSCLC, and the FDA has granted breakthrough therapy designation to BLU-667 for the treatment of patients with RET-fusion positive NSCLC that has progressed following platinum-based chemotherapy and to BLU-667 for the treatment of patients with RET mutation-positive MTC that requires systemic treatment and for which there are no acceptable alternative treatments.

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. In addition, under our collaboration with CStone Pharmaceuticals, or CStone, the China National Medicinal Products Administration approved an initial new drug application for our ongoing Phase 1 trial of BLU-554 in advanced HCC in the first quarter of 2019, and we dosed the first patient in China in May 2019. We and CStone also plan to initiate a proof-of-concept clinical trial in the second half of 2019 in the CStone territory evaluating BLU-554 in combination with CS1001, a clinical stage anti-programmed death ligand-1 immunotherapy being developed by CStone, as a first-line therapy for the treatment of patients with HCC. The FDA has granted orphan drug designation to BLU-554 for the treatment of HCC.

BLU-782 is an orally available, potent and highly selective inhibitor that targets mutant activin-like kinase 2, or ALK2. We are developing BLU-782 for the treatment of fibrodysplasia ossificans progressiva, or FOP, a rare, severely disabling genetic disease caused by mutations in the ALK2 gene, ACVR1. FOP is characterized by progressive heterotopic ossification, which is the abnormal transformation of muscle, ligaments and tendons into bone. Heterotopic ossification may be spontaneous or associated with painful episodic disease flare-ups that are usually precipitated by soft tissue injury. As the disease progresses, extra-skeletal bone increasingly restricts joints, resulting in severe disability and

loss of mobility, compromised respiratory function and increased risk of early death. Currently, there are no approved therapies for FOP. In October 2018, we presented foundational pre-clinical data for our FOP program at the 2018 American Society for Bone and Mineral Research Annual Meeting, and we initiated a Phase 1 clinical trial in healthy volunteers in the first quarter of 2019. Based on the progress of the ongoing Phase 1 clinical trial of BLU-782 in healthy volunteers and input from clinical experts, we plan to initiate a Phase 2 clinical trial of BLU-782 in patients with FOP in the fourth quarter of 2019. The FDA has granted fast track designation to BLU-782 for the prevention of heterotopic ossification in patients with FOP.

We also 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 currently have four wholly-owned discovery programs for undisclosed kinase targets, and we anticipate nominating at least one additional wholly-owned discovery program in 2019.

We entered into collaborations with F. Hoffmann La Roche Ltd and Hoffmann La Roche Inc., which we collectively refer to as Roche, and CStone in March 2016 and June 2018, respectively. Under our collaboration agreement with Roche, we are seeking to discover, develop and commercialize up to five small molecule therapeutics targeting kinases believed to be important in cancer immunotherapy, as single products or possibly in combination with other therapeutics. Under our collaboration agreement with CStone, we are seeking to develop and commercialize BLU-554, avapritinib and BLU-667, including back-up forms and certain other forms, in Mainland China, Hong Kong, Macau and Taiwan, or the CStone territory, either as a monotherapy or as part of a combination therapy. We will continue to evaluate additional collaborations that could maximize the value for our programs and allow us to leverage the expertise of strategic collaborators. We are also focused on engaging in collaborations to capitalize on our discovery platform outside of our primary strategic focus area of cancer.

We currently have worldwide development and commercialization rights to avapritinib, BLU-667 and BLU-554 other than the rights licensed to CStone in the CStone territory. We currently have worldwide development and commercialization rights to BLU-782 and all of our discovery programs other than the discovery-stage programs under collaboration with Roche.

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 March 31, 2019, we have received an aggregate of $1.1 billion from such transactions, including $887.4 million in aggregate gross proceeds from the sale of common stock in our May 2015 initial public offering, or IPO, and December 2016, April 2017 and December 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 under our former collaboration with Alexion Pharma Holding, or Alexion, $55.0 million in upfront and milestone payments under our existing collaboration with Roche, a $40.0 million upfront payment under our existing collaboration with CStone, and $10.0 million in gross proceeds from the debt financing. In addition, we received aggregate gross proceeds of approximately $345.0 million from our April 2019 follow-on public offering.

Since inception, we have incurred significant operating losses. Our net losses were $87.4 million for the three months ended March 31, 2019 and $236.6 million, $148.1 million and $72.5 million for the years ended December 31, 2018, 2017 and 2016, respectively. As of March 31, 2019, we had an accumulated deficit of $685.0 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 to advance and initiate clinical development activities for our lead drug candidate, avapritinib, as well as our other most advanced drug candidates, BLU-667, BLU-554 and BLU-782;
- seek marketing approvals for our drug candidates that successfully complete clinical trials;
- establish a sales, marketing and distribution infrastructure to commercialize any medicines for which we may obtain marketing approval;
- continue to manufacture increasing quantities of drug substance and drug product material for use in pre-clinical studies, clinical trials and for any potential commercialization;

- continue to discover, validate and develop additional drug candidates;
- conduct research and development activities under our collaborations with Roche and CStone;
- conduct development and commercialization activities for companion diagnostic tests for current or future drug candidates;
- maintain, expand and protect our intellectual property portfolio;
- acquire or in-license other drug candidates or technologies;
- hire additional research, clinical, quality, manufacturing, regulatory, commercial and general and administrative personnel; and
- incur additional costs associated with operating as a public company.

Financial Operations Overview

Revenue

To date, we have not generated any revenue from drug sales. Our revenue consists of collaboration revenue under our collaborations with Roche and CStone, 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 revenues related to the supply of our drug candidates or products to CStone for development and commercialization activities in the CStone territory and additional milestone payments and royalties on any net product sales under our collaborations with Roche and CStone. We do not expect to generate any revenue from the sale of avapritinib until 2020, assuming we are able to file for regulatory approval for avapritinib in the United States in the second quarter of 2019 and receive marketing approval by 2020. We expect that any revenue we generate will fluctuate from quarter to quarter as a result of the timing and amount of product sales, if any, license fees, research and development services and related reimbursements, payments for manufacturing services, and milestone and other payments.

In the future, subject to obtaining marketing approval for one or more of our drug candidates, we expect to generate revenue from a combination of product sales, royalties on product sales and cost reimbursements, as well as upfront, milestone and royalty payments, if any, under any current or future collaborations.

Expenses

Research and Development Expenses

Research and development expenses consist primarily of costs incurred for our research and development 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;
- expenses incurred under agreements with third parties for the development and commercialization of companion diagnostic tests;
- the cost of consultants;
- the cost associated with regulatory quality assurance and quality control operations;

- the cost of lab supplies and acquiring, developing and manufacturing pre-clinical study materials, clinical trial materials and commercial supply materials; and

- facilities, depreciation, and other expenses, which include direct and allocated expenses for rent and maintenance of facilities, insurance, and other operating costs in support of research and development activities.

Research and development costs are expensed as incurred. Costs for certain activities are recognized based on an evaluation of the progress to completion of specific tasks. Nonrefundable advance payments for goods or services to be received in the future for use in research and development activities are capitalized. The capitalized amounts are expensed as the related goods are delivered or the services are performed.

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

- establishing an appropriate safety profile with IND-enabling toxicology studies;

- successful enrollment in, and completion of clinical trials;

- receipt of marketing approvals from applicable regulatory authorities;

- establishing commercial manufacturing capabilities or making arrangements with third-party manufacturers;

- obtaining and maintaining patent and trade secret protection and regulatory exclusivity for our drug candidates;

- commercializing the drug candidates, if and when approved, whether alone or in collaboration with others; and

- continued acceptable safety profile of the drugs following approval.

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

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

A significant portion of our research and development expenses have been external expenses, which we track on a program-by-program basis following nomination as a development candidate. Our internal research and development expenses are primarily personnel-related expenses, including stock-based compensation expense. Except for internal research and development expenses related to collaboration agreements, 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 months ended March 31, 2019 and 2018. Other development and pre-development candidate expenses, unallocated expenses and internal research and development expenses have been classified separately.

	Three Months Ended March 31,	
	2019	2018
	(in thousands)	
Avapritinib external expenses	$ 24,677	$ 17,783
BLU-554 external expenses	1,262	4,794
BLU-667 external expenses	16,059	5,585
BLU-782 external expenses	2,666	1,899
Other development and pre-development candidate expenses and unallocated expenses	13,528	9,732
Internal research and development expenses	16,058	10,161
Total research and development expenses	$ 74,250	$ 49,954

We expect that our research and development expenses will increase in future periods as we expand our operations and incur additional costs in connection with our clinical trials and preparing regulatory filings. These increases will likely include the costs related to the implementation and expansion of clinical trial sites and related patient enrollment, monitoring, program management and drug product and drug substance manufacturing expenses for current and future clinical trials. 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 collaboration with Roche, development activities under our collaboration with CStone and development activities for companion diagnostic tests for current and future drug candidates.

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, commercial, business development, information technology, legal and human resources functions. Other significant costs include facility costs not otherwise included in research and development expenses, pre-commercial development activities, legal fees relating to intellectual property 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 and planned commercialization activities, including establishing a sales, marketing and distribution infrastructure to commercialize any medicines for which we may obtain marketing approval. These increases will likely include increased costs related to the hiring of additional personnel, legal, auditing and filing fees and general compliance and consulting expenses, among other expenses. We have incurred and will continue to incur additional costs associated with operating as a public company and expanding the scope of our operations.

Other Income (Expense), net

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

Interest Expense

For the three months ended March 31, 2018, interest expense consisted primarily of interest expense on amounts outstanding under the loan and security agreement that we entered into with Silicon Valley Bank in May 2013 and amortization of debt discount. We repaid the loan in full in November 2018. For the three months ended March 31, 2019, interest expense consisted primarily of interest expense related to an insignificant finance lease.

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, leases and stock-based compensation.

For a description of our critical accounting policies, please see “Management’s Discussion and Analysis of Financial Condition and Results of Operations—Financial Operations Overview—Critical Accounting Policies and Estimates” in our Annual Report on Form 10-K for the year ended December 31, 2018. Other than as described below, there have been no significant changes to our critical accounting policies since December 31, 2018.

On January 1, 2019, we adopted *ASU No. 2016-02, Leases (Topic 84)*, or ASC 842, which requires the recognition of the right-of-use assets and related operating and finance lease liabilities on the balance sheet. We adopted ASC 842 using a modified retrospective approach for all leases existing at January 1, 2019. The adoption of ASC 842 had a substantial impact on our condensed consolidated balance sheet and no impact to our condensed consolidated statements of operations. Upon adoption of ASC 842, we recognized an adjustment of $54.2 million and $74.1 million to operating lease right-of-use assets and the related lease liabilities, respectively. The operating lease liabilities are based on the present value of the remaining minimum lease payments discounted using our secured incremental borrowing rate at the effective date of January 1, 2019.

For contracts entered into on or after the effective date, at the inception of a contract, we assess whether the contract is, or contains, a lease. The assessment is based on: (1) whether the contract involves the use of a distinct identified asset, (2) whether we obtain the right to substantially all the economic benefit from the use of the asset throughout the period, and (3) whether we have the right to direct the use of the asset. At inception of a lease, we allocate the consideration in the contract to each lease component based on its relative stand-alone price to determine the lease payments.

Leases are classified as either finance leases or operating leases. A lease is classified as a finance lease if any one of the following criteria are met: the lease transfers ownership of the asset by the end of the lease term, the lease contains an option to purchase the asset that is reasonably certain to be exercised, the lease term is for a major part of the remaining useful life of the asset or the present value of the lease payments equals or exceeds substantially all of the fair value of the asset. A lease is classified as an operating lease if it does not meet any of these criteria.

For all leases at the lease commencement date, a right-of-use asset and a lease liability are recognized. The right-of-use asset represents the right to use the leased asset for the lease term. The lease liability represents the present value of the lease payments under the lease.

The right-of-use asset is initially measured at cost, which primarily comprises the initial amount of the lease liability, plus any initial direct costs incurred if any, less any lease incentives received. All right-of-use assets are reviewed for impairment. The lease liability is initially measured at the present value of the lease payments, discounted using the interest rate implicit in the lease or, if that rate cannot be readily determined, our secured incremental borrowing rate for the same term as the underlying lease. For real estate leases and other operating leases, we use its secured incremental borrowing rate. For finance leases, we use the rate implicit in the lease or its secured incremental borrowing rate if the implicit lease rate cannot be determined.

Lease payments included in the measurement of the lease liability comprise the following: the fixed noncancelable lease payments, payments for optional renewal periods where it is reasonably certain the renewal period will be exercised, and payments for early termination options unless it is reasonably certain the lease will not be terminated early.

Lease expense for operating leases consists of the lease payments plus any initial direct costs, primarily brokerage commissions, and is recognized on a straight-line basis over the lease term. Included in lease expense are any variable lease payments incurred in the period that are not included in the initial lease liability and lease payments incurred in the period for any leases with an initial term of 12 months or less. Lease expense for finance leases consists of the amortization of the right-of-use asset on a straight-line basis over the lease term and interest expense determined on an amortized cost basis. The lease payments are allocated between a reduction of the lease liability and interest expense.

We made an accounting policy election to not recognize leases with an initial term of 12 months or less within our condensed consolidated balance sheets and to recognize those lease payments on a straight-line basis in our condensed consolidated statements of income over the lease term.

Results of Operations

Comparison of Three Months Ended March 31, 2019 and 2018

The following table summarizes our results of operations for the three months ended March 31, 2019 and 2018, together with the changes in those items in dollars and as a percentage:

	Year Ended March 31,			
	2019	2018	Dollar Change	% Change
	(in thousands)			
Collaboration revenue	$ 730	$ 954	$ (224)	(23)%
Operating expenses:				
Research and development	74,250	49,954	24,296	49
General and administrative	16,553	9,911	6,642	67
Total operating expenses	90,803	59,865	30,938	52
Other income (expense):				
Other income (expense), net	2,669	2,394	275	11
Interest expense	(3)	(32)	29	(91)
Total other income	2,666	2,362	304	13
Net loss	$ (87,407)	$ (56,549)	$ (30,858)	55 %

Collaboration Revenue

Collaboration revenue decreased by $0.2 million from $1.0 million for the three months ended March 31, 2018 to $0.7 million for the three months ended March 31, 2019. Collaboration revenue for the three months ended March 31, 2019 and 2018 was related to the Roche agreement. We entered into the CStone agreement on June 1, 2018 and did not record collaboration revenue under the CStone agreement for the three months ended March 31, 2019.

Research and Development Expense

Research and development expense increased by $24.3 million from $50.0 million for the three months ended March 31, 2018 to $74.3 million for the three ended March 31, 2019. The increase in research and development expense was primarily related to the following:

- approximately $7.2 million in increased expenses for external clinical activities related to avapritinib, BLU-667 and BLU-782;
- approximately $7.0 million in increased expenses associated with clinical and commercial manufacturing activities;
- approximately $6.6 million in increased personnel expense, primarily due to an increase in headcount, which was driven by growth in the clinical and manufacturing organizations, and an increase of $2.8 million in stock-based compensation expense; and
- approximately $3.3 million in increased expenses associated with continuing to build our discovery platform and advance our discovery pipeline.

General and Administrative Expense

General and administrative expense increased by $6.6 million from $9.9 million for the three months ended March 31, 2018 to $16.6 million for the three months ended March 31, 2019. The increase in general and administrative expense was primarily related to the following:

- approximately $3.9 million in increased personnel expenses, primarily due to an increase in general and administrative headcount to support the overall growth of our business, and an increase of $2.0 million in stock-based compensation expense;
- approximately $2.2 million in increased professional fees including commercial planning activities; and

Other Income (Expense), Net

Other income, net, increased by $0.3 million from $2.4 million for the three months ended March 31, 2018 to $2.7 million for the three months ended March 31, 2019. The increase was primarily related to higher average investment balances and a higher rate of return on investments.

Interest Expense

Interest expense for the three months ended March 31, 2018 was less than $0.1 million and was primarily related to interest under our loan and security agreement with Silicon Valley Bank, which we repaid in full in November 2018. Interest expense for the three months ended March 31, 2019 was less than $0.1 million and was primarily related to interest expense for an insignificant finance lease.

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 March 31, 2019, we have received an aggregate of $1.1 billion from such transactions, including $887.4 million in aggregate gross proceeds from the sale of common stock in our May 2015 initial public offering, or IPO, and December 2016, April 2017 and December 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, $55.0 million in upfront and milestone payments from Roche, a $40.0 million upfront payment under our existing collaboration with CStone and $10.0 million in gross proceeds from debt financing. In addition, we received aggregate gross proceeds of approximately $345.0 million from our April 2019 follow-on public offering.

As of March 31, 2019, we had cash, cash equivalents and investments of $415.9 million.

Cash Flows

The following table provides information regarding our cash flows for the three months ended March 31, 2019 and 2018:

	Three Months Ended March 31,	
(in thousands)	**2019**	**2018**
Net cash used in operating activities	$ (80,188)	$ (49,563)
Net cash provided by (used in) investing activities	89,314	(219,128)
Net cash provided by financing activities	2,011	3,062
Net increase (decrease) in cash and cash equivalents	$ 11,137	$ (265,629)

Net Cash Used in Operating Activities. For the three months ended March 31, 2019, compared to the same period in 2018, the $30.6 million increase in net cash used in operating was primarily due to the increased net loss during

this period of $30.9 million, which was driven by increased payroll and payroll-related expenses and spending on pre-clinical, clinical and pre-commercial activities.

Net Cash Provided by (Used in) Investing Activities. For the three months ended March 31, 2019, compared to the same period in 2018, the $308.4 million increase in net cash provided by investing activities was primarily due to an increase in maturities of investments offset by purchases of investments.

Net Cash Provided by Financing Activities. For the three months ended March 31, 2019, compared to the same period in 2018, the $1.1 million decrease in net cash provided by financing activities was primarily due to less proceeds received from stock option exercises.

Borrowings

In May 2013, we entered into a loan and security agreement with Silicon Valley Bank. Under the terms of the loan and security agreement, we borrowed $5.0 million. Loan advances under the loan and security agreement 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, and we were required to pay a fee of 4% of the total loan advances at the end of the term of the loan. There were no financial covenants associated with the loan and security agreement. We repaid the loan in full in November 2018.

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 March 31, 2019, we had cash, cash equivalents and investments of $415.9 million. Based on our current plans, we believe that our existing cash, cash equivalents and investments, including the $327.2 million of estimated net proceeds from our April 2019 follow-on public offering but excluding any potential option fees and milestone payments under our existing collaborations with Roche and CStone, will be sufficient to enable us to fund our operating expenses and capital expenditure requirements into the middle of 2021. 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, timing and outcome of regulatory review of our drug candidates;
- the costs of establishing or contracting for sales, marketing and distribution capabilities if we obtain regulatory approvals to market 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 costs of securing manufacturing arrangements for development activities and commercial production;
- the scope, prioritization and number of our research and development programs;

- the success of our collaborations with Roche and CStone and our ability to establish and maintain collaborations on favorable terms, if at all;
- the achievement of milestones or occurrence of other developments that trigger payments to us under our collaboration agreements with Roche and CStone 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 extent to which we acquire or in-license other drug candidates and technologies;
- the success of our current or future companion diagnostic test collaborations for companion diagnostic tests;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;
- the costs of establishing operations outside the United States.

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. 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 other than potential funds to be earned under our collaborations with Roche and CStone. 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

As of March 31, 2019, there have been no 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, 2018.

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 March 31, 2019, and December 31, 2018, we had cash, cash equivalents and investments of $415.9 million and $494.0 million, respectively, consisting primarily of money market funds and investments in U.S. treasury obligations.

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

We are also exposed to market risk related to changes in foreign currency exchange rates. From time to time, we contract with vendors that are located Asia and Europe, which are denominated in foreign currencies. We are subject to fluctuations in foreign currency rates in connection with these agreements. We do not currently hedge our foreign currency exchange rate risk. As of March 31, 2019 and December 31, 2018, we had minimal or no liabilities denominated in foreign currencies.

Inflation generally affects us by increasing our cost of labor and clinical trial costs. We do not believe that inflation had a material effect on our business, financial condition or results of operations during the three months ended March 31, 2019 and 2018.

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 Chief Financial Officer (our principal executive officer and principal financial officer, respectively), evaluated the effectiveness of our disclosure controls and procedures as of March 31, 2019. Based upon such evaluation, our Chief Executive Officer and Chief Financial Officer have concluded that, as of March 31, 2019, our disclosure controls and procedures were effective at the reasonable assurance level.

Changes in Internal Control over Financial Reporting

There were no changes in our internal control over financial reporting that occurred during the fiscal quarter covered by this report that materially affected, or are 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 4 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 precision therapy 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 precision therapy 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 and preparing for additional planned clinical trials for our most advanced drug candidates, avapritinib, BLU-667, BLU-554 and BLU-782.

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 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 and commencing clinical development and pre-commercial activities. 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 March 31, 2019, we have received an aggregate of $1.1 billion from such transactions, including $887.4 million in aggregate gross proceeds from the sale of common stock in our May 2015 initial public offering, or IPO, and December 2016, April 2017 and December 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 under our former collaboration with Alexion Pharma Holding, or Alexion, $55.0 million in upfront and milestone payments under our existing collaboration with Roche, a $40.0 million upfront payment under our existing collaboration with CStone, and $10.0 million in gross proceeds from the debt financing. In addition, we received aggregate gross proceeds of approximately $345.0 million from our April 2019 follow-on public offering.

Since inception, we have incurred significant operating losses. Our net losses were $87.4 million for the three months ended March 31, 2019 and $236.6 million, $148.1 million and $72.5 million for the years ended December 31, 2018, 2017 and 2016, respectively. As of March 31, 2019, we had an accumulated deficit of $685.0 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' equity 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 most advanced drug candidates, avapritinib, BLU-667, BLU-554 and BLU-782. We do not expect to generate significant revenue unless and until we obtain marketing approval of, and begin to sell, avapritinib, BLU-667, BLU-554 or one of our other drug candidates. We do not expect to generate any revenue from the sale of avapritinib until 2020, assuming we are able to file for regulatory approval for avapritinib in the United States in the second quarter of 2019 and receive marketing approval by 2020. 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 most advanced drug candidates, avapritinib, BLU-667, BLU-554 and BLU-782, 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, manufacturing and distribution are not the responsibility of Roche, CStone 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. 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 March 31, 2019, we had cash, cash equivalents and investments of $415.9 million. Based on our current plans, we believe that our existing cash, cash equivalents and investments, including the $327.2 million of estimated net proceeds from our April 2019 follow-on public offering but excluding any potential option fees and milestone payments under our existing collaborations with Roche and CStone, will be sufficient to enable us to fund our operating expenses and capital expenditure requirements into the middle of 2021. 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 costs, timing and outcome of regulatory review of our drug candidates;
- the success of our collaborations with Roche and CStone;
- the success of our current or future collaborations for companion diagnostic tests;
- 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 agreements with Roche or CStone 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;
- the costs of securing manufacturing arrangements for development activities and commercial production;
- the costs of establishing operations outside the United States; and
- the costs of establishing or contracting for sales, marketing and distribution 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. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives.

Any additional fundraising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize our drug candidates. Dislocations in the financial markets have generally made equity and debt financing more difficult to obtain and may have a material adverse effect on our ability to meet our fundraising needs. We cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all. Moreover, the terms of any financing may adversely affect the holdings or the rights of our stockholders and the issuance of additional securities, whether equity or debt, by us, or the possibility of such issuance, may cause the market price of our shares to decline. The sale of additional equity or convertible securities

would dilute all of our stockholders. The incurrence of indebtedness would result in increased fixed payment obligations and we may be required to agree to certain restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. We could also be required to seek funds through arrangements with collaborators or otherwise at an earlier stage than otherwise would be desirable and we may be required to relinquish rights to some of our technologies or drug candidates or otherwise agree to terms unfavorable to us, any of which may have a material adverse effect on our business, operating results and prospects.

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

Raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our technologies or drug candidates.

Until such time, if ever, as we can generate substantial drug revenues, we expect to finance our cash needs through a combination of public and private equity offerings, debt financings, collaborations, strategic alliances and licensing arrangements. We do not have any committed external source of funds, other than our collaborations with Roche and CStone, which are limited in scope and duration and subject to the achievement of milestones or royalties on sales of licensed products, if any. 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 four drug candidates in clinical development: avapritinib, BLU-667, BLU-554 and BLU-782. 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 most advanced drug candidates or other drug candidates and ultimately commercialize our most advanced 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 four drug candidates in clinical development: avapritinib, BLU-667, BLU-554 and BLU-782. 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 drug candidates avapritinib, BLU-667, BLU-554 and BLU-782. Our ability to generate drug revenues, 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 do not expect to generate any revenue from the sale of avapritinib until 2020, assuming we are able to file for regulatory approval for avapritinib in the United States in the second quarter of 2019 and receive marketing approval by 2020 . 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 third parties to develop and commercialize companion diagnostics for avapritinib in order to identify GIST patients with the PDGFRA D842V mutation, BLU-554 in order to identify HCC patients with FGFR4 pathway activation and BLU-667 in order to identify NSCLC patients with RET fusions. 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 most advanced 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 clinical trials for avapritinib, BLU-667, BLU-554 and BLU-782;
- 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 current or future drug candidates;
- receipt of regulatory approvals from applicable regulatory authorities;
- establishing commercial manufacturing capabilities or making arrangements with third-party manufacturers for clinical supply and commercial manufacturing;
- obtaining and maintaining patent and trade secret protection or regulatory exclusivity for our drug candidates;
- launching commercial sales of our drug candidates, if and when approved, whether alone or in collaboration with others;
- acceptance of the drug candidates, if and when approved, by patients, the medical community and third-party payors;
- effectively competing with other therapies;
- obtaining and maintaining healthcare coverage and adequate reimbursement;
- enforcing and defending intellectual property rights and claims; and
- maintaining a continued acceptable safety profile of the drug candidates following approval.

If we do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize our drug candidates, which would materially harm our business. If we do not receive regulatory approvals for our drug candidates, we may not be able to continue our operations.

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.

Our drug candidates avapritinib, BLU-667, BLU-554 and BLU-782 are in clinical development, and all of our other drug candidates are in pre-clinical development. The risk of failure for our 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 clinical trials and future clinical trials may not be successful.

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 avapritinib, BLU-667, BLU-554, BLU-782 and our other drug candidates. We do not know whether any of our clinical trials for our 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;
- patients treated with our drug candidates may develop mutations that confer resistance to treatment, which may limit the market opportunity for our drug candidates or prevent us from completing our clinical trials, obtaining regulatory approval for or commercializing our drug candidates;
- 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 the FDA 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, deprioritize 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, deprioritize or terminate one or more of our discovery programs or pre-clinical drug candidates or programs. For example, we have previously determined to suspend our discovery program for inhibitors of neurotrophic tyrosine receptor kinase, or NTRK, and predicted NTRK resistant mutants, and to deprioritize our discovery program targeting protein kinase cAMP-activated catalytic subunit alpha fusions for the treatment of fibrolamellar carcinoma. If we

suspend, deprioritize 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, could delay 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 third parties to develop a companion diagnostic test for avapritinib in order to identify GIST patients with the PDGFRA D842V mutation, BLU-554 in order to identify HCC patients with FGFR4 pathway activation and BLU-667 in order to identify NSCLC patients with RET fusions. We plan to engage a third party to develop a companion diagnostic test for use in our planned COMPASS-2L trial, and we may engage third parties to develop companion diagnostic tests for use in some of our other current or future clinical trials. However, 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 for avapritinib in order to identify GIST patients with the PDGFRA D842V mutation, BLU-554 in order to identify HCC patients with FGFR4 pathway activation and BLU-667 in order to identify NSCLC patients with RET fusions, 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 for avapritinib, BLU-667 and BLU-554. 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 find deficiencies with or 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 avapritinib, 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.

The FDA has granted breakthrough therapy designation to avapritinib for the treatment of patients with unresectable or metastatic GIST harboring the PDGFRA D842V mutation, and the FDA has granted breakthrough therapy designation to avapritinib for the treatment of advanced SM, including the subtypes of aggressive SM, SM with an associated hematologic neoplasm and mast cell leukemia. In addition, the FDA has granted breakthrough therapy designation to BLU-667 for the treatment of patients with RET-fusion positive NSCLC that has progressed following platinum-based chemotherapy and to BLU-667 for the treatment of patients with RET mutation-positive MTC that requires systemic treatment and for which there are no acceptable alternative treatments. 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.

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 other drugs 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.

The FDA has granted fast track designation to avapritinib for (i) the treatment of patients with unresectable or metastatic GIST that progressed following treatment with imatinib and a second TKI and (ii) the treatment of patients with unresectable or metastatic GIST with the PDGFRA D842V mutation regardless of prior therapy, and the FDA has granted fast track designation to BLU-782 for the treatment of FOP. 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 avapritinib 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 PDGFRA 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. 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 our most advanced drug candidates, avapritinib, BLU-667 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.

The FDA has granted orphan drug designation to avapritinib for the treatment of GIST and the treatment of mastocytosis, to BLU-554 for the treatment of HCC and to BLU-667 for the treatment of RET-rearranged NSCLC, JAK1/2-positive NSCLC or TRKC-positive NSCLC. In addition, the European Commission has granted medicinal product designation to avapritinib for the treatment of GIST and the treatment of mastocytosis. 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 medicinal product designation after receiving the opinion of the EMA's Committee for Orphan Medicinal Products on an orphan medicinal product designation application. Orphan medicinal product 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 medicinal product 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 avapritinib for the treatment of GIST and the treatment of mastocytosis, BLU-554 for the treatment of HCC and BLU-667 for the treatment of RET-rearranged NSCLC, JAK1/2-positive NSCLC or TRKC-positive NSCLC, 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/or prevalence for GIST, SM, RET-altered NSCLC and MTC, HCC and FOP are unknown. Our projections of the number of people who have these diseases, the frequency of the genetic alterations targeted by our drug candidates and 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: 20,700 patients with SM, including 2,600 patients with advanced SM and 18,100 patients with ISM and SSM (regardless of severity of symptoms); 500 first-line patients with PDGFRA D842V mutant GIST (including resectable, metastatic and unresectable GIST); 7,500 second-line patients with GIST, including approximately 75%-80% of second-line patients with GIST who do not have a KIT V654A or T670I mutation; 7,400 third-line and later patients with GIST (regardless of alteration); 8,900 first- and second-line patients with RET-altered NSCLC; 1,300 patients with MTC (regardless of line of therapy or alteration); 25,900 first- and second-line patients with FGFR4-activated HCC; and 1,100 patients with FOP.

The total addressable market opportunity for avapritinib for the treatment of patients with GIST and SM, BLU-667 for the treatment of patients with RET-altered NSCLC and MTC, BLU-554 for the treatment of patients with advanced HCC and BLU-782 for the treatment of patients with FOP will ultimately depend upon, among other things, the diagnosis criteria included in the final label for each of avapritinib, BLU-667, BLU-554 and BLU-782, 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, patients treated with our drug candidates may develop mutations that confer resistance to treatment 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 we 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 avapritinib receives marketing approval for advanced SM, it will face competition from Novartis AG's midostaurin, a multi-kinase inhibitor with KIT D816V inhibitory activity. If avapritinib receives marketing approval for third line advanced GIST, it will face competition from Bayer AG's regorafenib, and if avapritinib receives marketing approval for second line advanced GIST, it will face competition from Pfizer Inc.'s sunitinib. In addition, if avapritinib receives marketing approval for advanced SM, GIST and/or for GIST patients with the PDGFRA 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., Allakos Inc., ARIAD Pharmaceuticals, Inc., a wholly-owned subsidiary of Takeda Pharmaceutical Company Limited, AROG Pharmaceuticals, Inc., Celldex Therapeutics, Inc., and Deciphera Pharmaceuticals, LLC.

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 AstraZeneca plc, Boston Pharmaceuticals, Inc., Eisai Inc., Exelixis, Inc., GlaxoSmithKline plc, Loxo Oncology, Inc., a wholly-owned subsidiary of Eli Lilly and Company, Mirati Therapeutics, Inc., Novartis AG, Pfizer Inc. Roche, Stemline Therapeutics, Inc., and Turning Point Therapeutics, Inc., as well as several approved multi-kinase inhibitors with RET activity being evaluated in clinical trials, including alectinib, apatinib, cabozantinib, dovitinib, lenvatinib, sorafenib, sunitinib and vandetinib.

If BLU-554 receives marketing approval for patients with FGFR4-activated HCC, it will face competition from Bristol-Myers Squibb Company's nivolumab and Merck & Co., Inc.'s pembrolizumab, immune checkpoint inhibitors approved by the FDA for the treatment of HCC, as well as sorafenib, cabozantinib, regorafenib and lenvatinib, multi-kinase inhibitors approved for the treatment of HCC. In addition, BLU-554 may face competition from other drug candidates in development by Abbisko Therapeutics Co., Ltd, AstraZeneca plc, Bayer AG, 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-782 receives marketing approval for FOP, it may face competition from drug candidates in development by BioCryst Pharmaceuticals, Inc., Clementia Pharmaceuticals Inc., a wholly-owned subsidiary of Ipsen Pharma, La Jolla Pharmaceutical Company and Regeneron Pharmaceuticals, Inc.

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 face an inherent risk of product liability exposure related to the testing of our drug candidates in human clinical trials and use of our drug candidates through compassionate use programs, and we 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 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 third parties for avapritinib in order to identify GIST patients with the PDGFRA D842V mutation, BLU-554 in order to identify HCC patients with FGFR4 pathway activation and BLU-667 in order to identify NSCLC patients with RET fusions, and we expect to develop a companion diagnostic test with a third party for avapritinib for our planned COMPASS-2L trial in order to select patients with PDGFRA- and KIT-driven second-line GIST who do not test positive for the KIT V654A or T670I mutations. 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 are

relying on third parties to design, manufacture, obtain regulatory approval for and commercialize the companion diagnostic tests for avapritinib, BLU-667 and BLU-554, and we expect to rely in whole or in part on third parties to design, manufacture, obtain regulatory approval for and commercialize any other companion diagnostic tests for our drug candidates. We and our collaborators 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:

- 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 a companion diagnostic test; and
- may terminate their relationship with us.

Any delay or failure by us or our collaborators 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 have engaged or may in the future engage to assist us 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 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 2027 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 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.

Since its enactment, some of the provisions of the Affordable Care Act have yet to be fully implemented, while certain provisions have been subject to judicial, congressional, and executive challenges. In 2012, the U.S. Supreme Court upheld certain key aspects of the legislation, including a tax-based shared responsibility payment imposed on certain individuals who fail to maintain qualifying health coverage for all or part of a year, which is commonly the requirement that all individuals maintain health insurance coverage or pay a penalty, referred to as the "individual mandate." Though Congress has not passed repeal legislation to date, the 2017 Tax Reform Act included a provision which repealed the individual mandate effective January 1, 2019. On December 14, 2018, a U.S. District Court judge in the Northern District of Texas ruled that the individual mandate portion of the Affordable Care Act is an essential and inseverable feature of the Affordable Care Act, and therefore because the mandate was repealed as part of the 2017 Tax Reform Act, the remaining provisions of the Affordable Care Act are invalid as well. The Trump administration and CMS have both stated that the ruling will have no immediate effect, and on December 30, 2018 the same judge issued an order staying the judgment pending appeal. It is unclear how this decision and any subsequent appeals and other efforts to repeal and replace the Affordable Care Act will impact the Affordable Care Act and our business.

Further, on January 20, 2017, U.S. President Donald Trump signed an Executive Order directing federal agencies with authorities and responsibilities under the Affordable Care Act to waive, defer, grant exemptions from, or delay the implementation of any provision of the Affordable Care Act that would impose a fiscal burden on states or a cost, fee, tax, penalty or regulatory burden on individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices.

On October 13, 2017, President Trump signed an Executive Order terminating the cost-sharing subsidies that reimburse insurers under the Affordable Care Act. Several state Attorneys General filed suit to stop the administration from terminating these subsidies, but on October 25, 2017, a federal judge in California denied their request for a restraining order. In addition, the Centers for Medicare & Medicaid Services, the agency responsible for administering the Medicare program, or CMS, recently proposed regulations that would give states greater flexibility in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the health benefits required under the Affordable Care Act for plans sold through these marketplaces. For example, on November 30, 2018, CMS announced a proposed rule that would amend the Medicare Advantage and Medicare Part D prescription drug benefit regulations to reduce out of pocket costs for plan enrollees and allow Medicare plans to negotiate lower rates for certain drugs. Among other things, the proposed rule would allow Medicare Advantage plans to use pre-authorization and step therapy for six protected classes of drugs, with certain exceptions; permit plans to implement pre-authorization and step therapy in Medicare Part B drugs; change the definition of "negotiated prices"; and add a new definition of "price concession." It is unclear whether these proposed changes will be accepted, and if so, what effect such changes will have on our business. Congress will likely continue to consider subsequent legislation and further action to repeal, replace or modify the Affordable Care Act. It is unclear what impact any changes to the Affordable Care Act will have on the availability of healthcare and containing or lowering the 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.

Beyond challenges to the Affordable Care Act, other legislative measures have also been enacted that may impose additional pricing and product development pressures on our business. For example, on May 30, 2018, the Right to Try Act, was signed into law. Among other things, this law provides a federal framework for certain patients to access certain investigational new drug products that have completed a Phase 1 clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a drug manufacturer to make its drug products available to eligible patients as a result of the Right to Try Act, but the manufacturer must develop an internal policy and respond to patient requests according to that policy. We expect that additional foreign, federal and state 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 limited coverage and reimbursement and reduced demand for our products, once approved, or additional pricing pressures.

The delivery of healthcare in the European Union, including the establishment and operation of health services and the pricing and reimbursement of medicines, is almost exclusively a matter for national, rather than EU, law and policy. National governments and health service providers have different priorities and approaches to the delivery of health care and the pricing and reimbursement of products in that context. In general, however, the healthcare budgetary constraints in most EU member states have resulted in restrictions on the pricing and reimbursement of medicines by relevant health service providers. Coupled with ever-increasing EU and national regulatory burdens on those wishing to develop and market products, this could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to commercialize any products for which we obtain marketing approval.

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, overtly or covertly, 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 civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for, among other things, 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;

- the federal false statements statute, which prohibits knowingly and willfully falsifying, concealing, or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items, or services (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);

- federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers; 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.

On January 31, 2019, the Department of Health and Human Services, or HHS, and HHS Office of Inspector General, or OIG, proposed an amendment to one of the existing anti-kickback safe harbors (42 C.F.R. 1001.952(h)) that would prohibit certain pharmaceutical manufacturers from offering rebates to pharmacy benefit managers in the Medicare Part D and Medicaid managed care programs. The proposed amendment would remove protection for "discounts" from anti-kickback enforcement action and would include criminal and civil penalties for knowingly and willfully offering, paying, soliciting or receiving remuneration to induce or reward the referral of business reimbursable under federal health care programs. At the same time, HHS also proposed to create a new safe harbor to protect point-of-sale discounts that drug manufacturers provide directly to patients and add another safe harbor to protect certain administrative fees paid by manufacturers to pharmacy benefit managers. If this proposal is adopted, in whole or in part, it could affect the pricing and reimbursement for any products for which we receive approval in the future.

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, in 2016, the 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 agreements with Roche and CStone from entering into future agreements on certain terms with potential collaborators. Collaborations are complex and time-consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators.

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

In addition, our collaborations with Roche and CStone, 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, in the fourth quarter of 2017, Alexion terminated our collaboration related to fibrodysplasia ossificans progressiva for convenience following a strategic review by Alexion of its research and development portfolio. Any termination or expiration of our collaboration agreements with Roche and CStone or any 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 most advanced 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 substance and drug product used in our most advanced drug candidates are our sole source of supply, and the loss of any of these suppliers could significantly harm our business.

The API, drug substance and drug product used in our most advanced 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 substance and drug product 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 most advanced 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 substance and drug product 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 substance and drug product 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 substance and drug product used in our drug candidates, any interruption or delay in the supply of components or materials, or our inability to obtain such API, drug substance and drug product 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 lead drug candidate, avapritinib, as well as our other most advanced drug candidates, BLU-667, BLU-554 and BLU-782, 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 compounds, technologies, inventions and improvements that are important to the development and implementation of our business. We also rely on copyright, 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 avapritinib, BLU-667, BLU-554 and BLU-782 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, composition of matter for inhibitors of RET, including predicted RET resistance mutations, with multiple compound families, and composition of matter for inhibitors of ALK2, with multiple compound families, as well as methods of use for these novel compounds. The issued U.S. patent directed to avapritinib composition of matter has a statutory expiration date in 2034, the issued U.S. patent directed to BLU-554 composition of matter has a statutory expiration date in 2034, the issued U.S. patent directed to BLU-667 composition of matter has a statutory expiration date in 2036 and the issued U.S. patent directed to BLU-782 composition of matter has a statutory expiration date in 2037.

As of April 30, 2019, we owned nine issued U.S. patents, six issued foreign patents, including one European patent validated in 38 countries, two pending U.S. non-provisional patent applications, four pending U.S. provisional patent applications, 39 pending foreign patent applications and one pending Patent Cooperation Treaty, or PCT, international patent application directed to our KIT program, including avapritinib. Our foreign patent filings are in a number of jurisdictions, including Australia, Argentina, Brazil, Bolivia, Canada, China, the European Union, Hong Kong, Israel, India, Japan, Lebanon, Mexico, New Zealand, Pakistan, Paraguay, Philippines, Russia, Singapore, South Africa, South Korea, Taiwan, Uruguay and Venezuela. Any U.S. or ex-U.S. patents issuing from the pending applications covering avapritinib will have a statutory expiration date between October 2034 and April 2040. Patent term adjustments or patent term extensions could result in later expiration dates.

As of April 30, 2019, we owned five issued U.S. patents, two pending U.S. non-provisional patent applications, two pending PCT international applications, 28 pending foreign patent applications and three pending U.S. provisional patent applications directed to our RET program, including BLU-667. Our foreign patent filings are in a number of jurisdictions, including Argentina, Australia, Brazil, Canada, China, Chile, Ecuador, Eurasia, the European Union, Israel, India, Japan, Lebanon, Malaysia, Mexico, New Zealand, Philippines, Saudi Arabia, Singapore, South Africa, South Korea, Taiwan, Thailand, the United Arab Emirates and Uruguay. Any U.S. or ex-U.S. patent issuing from the pending applications covering BLU-667 will have a statutory expiration date between November 2036 and August 2039. Patent term adjustments or patent term extensions could result in later expiration dates.

As of April 30, 2019, we owned eight issued U.S. patents, three pending U.S. non-provisional patent applications, ten issued foreign patents and 40 pending foreign patent applications directed to our FGFR4 program, including BLU-554. Our foreign patent filings are in a number of jurisdictions, including Argentina, Australia, Bolivia, Brazil, Canada, China, Egypt, the European Union, Hong Kong, Israel, India, Indonesia, Japan, South Korea, Lebanon, Mexico, New Zealand, Pakistan, Paraguay, Philippines, Russia, Singapore, South Africa, Taiwan, Thailand, Uruguay, Venezuela and Vietnam. Any U.S. or ex-U.S. patent issuing from the pending applications covering BLU-554 will have a statutory expiration date between July 2033 and September 2037. Patent term adjustments or patent term extensions could result in later expiration dates.

As of April 30, 2019, we owned one issued U.S. patent, one pending U.S. non-provisional patent application, one pending PCT international application and 15 pending foreign patent applications directed to our ALK2 program,

including BLU-782. Our foreign patent filings are in a number of jurisdictions, including Australia, Brazil, Canada, China, Chile, the European Union, Israel, Japan, South Korea, Mexico, New Zealand, Eurasia and South Africa. Any U.S. or ex-U.S. patent issuing from pending applications covering BLU-782 will have a statutory expiration date of April 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 April 30, 2019, we owned one issued U.S. patent, nine pending U.S. non-provisional patent applications, nine pending European Union patent applications and one issued European patent (validated in the UK) directed to this technology. Any U.S. or ex-U.S. patent issuing from the pending applications directed to this technology, 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 avapritinib, BLU-667, BLU-554, BLU-782 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 patents owned by third parties that have generic composition of matter, method of inhibition and method of treatment claims that may cover BLU-554 or generic method of treatment claims that may cover BLU-667. If the claims of any of these third-party patents are asserted against us, we do not believe BLU-554, BLU-667 or our proposed activities related to such compounds would be found to infringe any valid claim of these patents. While we may decide to initiate proceedings to challenge the validity of these patents 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 patents. 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 some 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 patents owned by third parties that have generic composition of matter, method of inhibition and method of treatment claims that may cover BLU-554 or generic method of treatment claims that may cover BLU-667. If the claims of any of these third-party patents are asserted against us, we do not believe BLU-554, BLU-667 or our proposed activities related to such compounds would be found to infringe any valid claim of these patents. While we may decide to initiate proceedings to challenge the validity of these patents 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 patents. 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 Operating Officer, Michael Landsittel, our Chief Financial Officer, Tracey McCain, our Chief Legal and Compliance Officer, Christopher Murray, our Senior Vice President of Technical Operations, and Christina Rossi, our Chief Commercial 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, 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 April 30, 2019, we had 239 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. Physical expansion of our operations in the future 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.

Following its June 23, 2016 vote to leave the European Union, on March 29, 2017, the United Kingdom invoked Article 50 of the Lisbon Treaty and formally began the process of exiting the European Union. Although 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 resulting immediate changes in foreign currency exchange rates have had a limited overall impact due to natural hedging. Given the lack of comparable precedent, it is unclear what financial, trade and legal implications the withdrawal of the United Kingdom from the European Union would have and how such withdrawal would affect us. 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, and we are closely monitoring the Brexit developments in order to determine, quantify and proactively address changes as they become clear.

For example, Brexit could result in the United Kingdom or the European Union significantly altering its regulations affecting the clearance or approval of our product candidates that are developed in the United Kingdom. Any new regulations could add time and expense to the conduct of our business, as well as the process by which our products receive regulatory approval in the United Kingdom, the European Union and elsewhere. In addition, the announcement of Brexit and the withdrawal of the United Kingdom from the European Union have had and may continue to have a material adverse effect on global economic conditions and the stability of global financial markets, and may significantly reduce global market liquidity and restrict the ability of key market participants to operate in certain financial markets. Any of these effects of Brexit, among others, could adversely affect our business, our results of operations, liquidity and financial condition.

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 collaborators, service providers, contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our drug candidates' development programs and have a material adverse effect on our reputation, business, financial condition or results of operations.

Our internal computer systems and those of our current or future third-party collaborators, service providers, contractors and consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. Attacks on information technology systems are increasing in their frequency, levels of persistence, sophistication and intensity, and they are being conducted by increasingly sophisticated and organized groups and individuals with a wide range of motives and expertise. In addition to extracting sensitive information, such attacks could include the deployment of harmful malware, ransomware, denial-of-service attacks, social engineering and other means to affect service reliability and threaten the confidentiality, integrity and availability of information. The prevalent use of mobile devices also increases the risk of data security incidents. While we have not experienced any material system failure, accident or security breach to date, if such an event were to occur and cause interruptions in our operations or the operations of third-party collaborators, service providers, contractors and consultants, it could result in a material disruption of our drug candidates' development programs and significant reputational, financial, legal, regulatory, business or operational harm. 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. In addition, our liability insurance may not be sufficient in type or amount to cover us against claims related to security breaches, cyberattacks and other related breaches.

Any failure or perceived failure by us or any third-party collaborators, service providers, contractors or consultants to comply with our privacy, confidentiality, data security or similar obligations to third parties, or any data security incidents or other security breaches that result in the unauthorized access, release or transfer of sensitive information, including personally identifiable information, may result in governmental investigations, enforcement actions, regulatory fines, litigation or public statements against us, could cause third parties to lose trust in us or could result in claims by third parties asserting that we have breached our privacy, confidentiality, data security or similar obligations, any of which could have a material adverse effect on our reputation, business, financial condition or results of operations. Moreover, data security incidents and other security breaches can be difficult to detect, and any delay in identifying them may lead to increased harm. While we have implemented data security measures intended to protect our information technology systems and infrastructure, there can be no assurance that such measures will successfully prevent service interruptions or data security incidents.

Compliance with global privacy and data security requirements could result in additional costs and liabilities to us or inhibit our ability to collect and process data globally, and the failure to comply with such requirements could have a material adverse effect on our business, financial condition or results of operations.

Privacy and data security have become significant issues in the United States, Europe and in many other jurisdictions where we conduct or may in the future conduct our operations. The regulatory framework for the collection, use, safeguarding, sharing and transfer of information worldwide is rapidly evolving and is likely to remain uncertain for the foreseeable future. Globally, virtually every jurisdiction in which we operate has established its own data security and privacy frameworks with which we must comply. On May 25, 2018, the European General Data Protection Regulation 2016/679, or GDPR, took effect. The GDPR applies to any company established in the European Union as well as any company outside the European Union that collects or otherwise processes personal data in connection with the offering goods or services to individuals in the European Union or the monitoring of their behavior. The GDPR enhances data protection obligations for processors and controllers of personal data, including, for example, expanded disclosures about how personal information is to be used, limitations on retention of information, mandatory data breach

notification requirements and onerous new obligations on services providers. The GDPR imposes additional obligations and risk upon our business and substantially increase the penalties to which we could be subject in the event of any non-compliance, including fines of up to €20 million or 4% of total worldwide annual turnover, whichever is higher. Given the breadth and depth of changes in data protection obligations, preparing for and complying with the GDPR's requirements has required and will continue to require significant time, resources and a review of our technologies, systems and practices, as well as those of any third-party collaborators, service providers, contractors or consultants that process or transfer personal data collected in the European Union. If enacted, we will be subject to the EU ePrivacy Regulation, which is a proposed regulation of privacy and electronic communications. In addition, we will be subject to the California Consumer Privacy Act, which takes effect January 1, 2020 and will impose sweeping privacy and security obligations on many companies doing business in California and provides for substantial fines for non-compliance and, in some cases, a private right of action to consumers who are victims of data breaches involving their unredacted or unencrypted personal information. The GDPR and other changes in laws or regulations associated with the enhanced protection of certain types of sensitive data, such as healthcare data or other personal information from our clinical trials, could lead to government enforcement actions and significant penalties against us and could have a material adverse effect on our business, financial condition or results of operations.

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.

On December 22, 2017, the Tax Cuts and Jobs Act, or TCJA, was enacted. The TCJA significantly reforms the Internal Revenue Code of 1986, as amended. The TCJA, among other things, includes changes to U.S. federal tax rates, imposes significant additional limitations on the deductibility of interest and net operating loss carryforwards and allows for the expensing of capital expenditures. Our net deferred tax assets and liabilities were revalued as of December 31, 2017 at the newly enacted U.S. corporate rate, and the impact was recognized in our tax expense in the year of enactment but was offset by a corresponding reduction to the valuation allowance. We continue to examine the impact this tax reform legislation may have on our business. The impact of this tax reform is uncertain and could be adverse.

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 may in the future 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 $109.00 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 May 6, 2019. 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 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. 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 acquiror 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.

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, we have incurred and expect to continue to incur significant legal, accounting and other expenses. 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 costlier.

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. To achieve compliance with Section 404 within the prescribed period, we have been and will continue to 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 in the future 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 or that we will not be able to comply with the requirements of Section 404 in a timely manner. If this were to occur, the market price of our stock could decline and we could be subject to sanctions or investigations by the SEC or other regulatory authorities, which would require additional financial and management resources. Furthermore, investor perceptions of our company may suffer if deficiencies are found, and this could cause a decline in the market price of our stock. Irrespective of compliance with Section 404, any failure of our internal control over financial reporting could have a material adverse effect on our stated operating results and harm our reputation. If we are unable to implement these requirements effectively or efficiently, it could harm our operations, financial reporting, or financial results and could result in an adverse opinion on our internal control over financial reporting from our independent registered public accounting firm.

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, 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, 2018, we had federal net operating loss carryforwards of approximately $464.9 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. In addition, pursuant to the TCJA, we may not use net operating loss carry-forwards to reduce our taxable income in any year by more than 80%, and we may not carry back any net operating losses to prior years. These new rules apply regardless of the occurrence of an ownership change.

Item 6. Exhibits

EXHIBIT INDEX

Exhibit Number	Description of Exhibit
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

* 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.

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: May 9, 2019

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

Date: May 9, 2019

By: /s/ Michael Landsittel
Michael Landsittel
Chief Financial Officer
(Principal Financial Officer)

Exhibit 31.1

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(s) 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)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) 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) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

(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(s) 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: May 9, 2019

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

Exhibit 31.2

CERTIFICATIONS

I, Michael Landsittel, certify that:

1. I have reviewed this 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(s) 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)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) 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) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

(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(s) 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: May 9, 2019

By: /s/ Michael Landsittel
Michael Landsittel
Chief Financial Officer
(Principal Financial Officer)

Exhibit 32.1

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

In connection with the Quarterly Report on Form 10-Q of Blueprint Medicines Corporation (the "Company") for the period ended March 31, 2019 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: May 9, 2019

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

Date: May 9, 2019

By: /s/ Michael Landsittel
Michael Landsittel
Chief Financial Officer
(Principal Financial Officer)