

**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 September 30, 2020

OR

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

Commission file number 001-37359

BLUEPRINT MEDICINES CORPORATION

(Exact Name of Registrant as Specified in Its Charter)

Delaware
(State or Other Jurisdiction of
Incorporation or Organization)

45 Sidney Street
Cambridge, Massachusetts
(Address of Principal Executive Offices)

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

02139
(Zip Code)

(617) 374-7580

(Registrant's Telephone Number, Including Area Code)

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

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

Indicate by check mark whether the registrant has submitted electronically 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
Non-accelerated filer

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 October 26, 2020: 55,730,804

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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. Blueprint Medicines, AYVAKIT™, AYVAKYT®, GAVRETO™ and associated logos are trademarks of Blueprint Medicines Corporation. Other brands, names and trademarks contained in this Quarterly Report on Form 10-Q are the property of their respective owners.

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 “aim,” “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 timing or likelihood of regulatory actions, filings and approvals for our current and future drug candidates, including our ability to obtain marketing approval for avapritinib and pralsetinib for additional indications or in additional geographies;
- our ability and plans in continuing to build out our commercial infrastructure and successfully launching, marketing and selling AYVAKIT™ (avapritinib) (marketed in Europe under the brand name AYVAKYT®), GAVRETO™ (pralsetinib) and any current and future drug candidates for which we receive marketing approval;
- the rate and degree of market acceptance of AYVAKIT/AYVAKYT, GAVRETO and any current and future drug candidates for which we receive marketing approval;
- the pricing and reimbursement of AYVAKIT/AYVAKYT, GAVRETO and any current and future drug candidates for which we receive marketing approval;
- 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, pralsetinib, fisogatinib, BLU-263, BLU-945 and our research and development programs;
- our ability to advance drug candidates into, and successfully complete, clinical trials;
- our ability to successfully develop manufacturing processes for any of our current and future drugs or drug candidates and to secure manufacturing, packaging and labeling arrangements for development activities and commercial production;
- the implementation of our business model and strategic plans for our business, drugs, drug candidates, platform and technology;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our current and future drugs, drug candidates and technology;
- the potential benefits of our collaboration with F. Hoffmann-La Roche Ltd and Genentech, Inc. to develop and commercialize pralsetinib globally (excluding Greater China), our cancer immunotherapy collaboration with F. Hoffmann-La Roche Ltd and Hoffmann-La Roche Inc., and our collaboration with CStone Pharmaceuticals to develop and commercialize avapritinib, pralsetinib and fisogatinib in Greater China, as well as our ability to maintain these collaborations and establish additional strategic collaborations;
- the potential benefits of our exclusive license agreement with Clementia Pharmaceuticals, Inc. to develop and commercialize BLU-782 for fibrodysplasia ossificans progressiva;

- the development of companion diagnostic tests for our current or future drugs or drug candidates;
- our financial performance, estimates of our revenues, expenses and capital requirements and our needs for future financing, including our ability to achieve a self-sustainable financial profile;
- developments relating to our competitors and our industry;
- the actual or potential benefits of designations granted by the U.S. Food and Drug Administration, or FDA, such as orphan drug, fast track and breakthrough therapy designation or priority review, and the review of current or future new drug applications under the FDA's Oncology Center of Excellence Real-Time Oncology Review pilot program or the FDA's Project Orbis initiative; and
- the impact and scope of the COVID-19 pandemic on our business, operations, strategy, goals and anticipated milestones, including our ongoing and planned research and discovery activities, ability to conduct ongoing and planned clinical trials, clinical supply of current or future drug candidates, and the launch, marketing, sale and commercial supply of AYWAKIT/AYVAKYT, GAVRETO and any current or future drug candidates for which we receive marketing approval.

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.

For purposes of this Quarterly Report on Form 10-Q, including the footnotes to our condensed consolidated financial statements, (i) with respect to our collaboration for pralsetinib, Roche means F. Hoffmann-La Roche Ltd and Genentech, Inc., and (ii) with respect to our cancer immunotherapy collaboration, Roche means F. Hoffmann-La Roche Ltd and Hoffmann-La Roche Inc.

PART I – FINANCIAL INFORMATION**Item 1. Financial Statements****Blueprint Medicines Corporation**
Condensed Consolidated Balance Sheets
(in thousands, except share and per share data)
(Unaudited)

	September 30, 2020	December 31, 2019
Assets		
Current assets:		
Cash and cash equivalents	\$ 565,221	\$ 113,938
Investments, available-for-sale	192,209	369,616
Accounts receivable, net	44,369	663
Unbilled accounts receivable	16,887	22,749
Inventory	5,565	—
Prepaid expenses and other current assets	17,404	9,820
Total current assets	841,655	516,786
Investments, available-for-sale	598,470	64,406
Property and equipment, net	35,199	38,361
Operating lease right-of-use assets, net	69,020	72,753
Restricted cash	5,168	5,166
Other assets	8,666	10,222
Total assets	<u>\$ 1,558,178</u>	<u>\$ 707,694</u>
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	2,929	4,793
Accrued expenses	89,116	88,706
Current portion of operating lease liabilities	7,672	6,823
Current portion of deferred revenue	10,391	6,160
Total current liabilities	110,108	106,482
Operating lease liabilities, net of current portion	83,735	89,126
Deferred revenue, net of current portion	35,017	39,913
Other long-term liabilities	9,318	7,814
Total liabilities	238,178	243,335
Commitments (Note 15)		
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; 55,514,395 and 49,272,223 shares issued and outstanding at September 30, 2020 and December 31, 2019, respectively	56	49
Additional paid-in capital	1,867,572	1,412,083
Accumulated other comprehensive loss	(1,940)	(2,535)
Accumulated deficit	(545,688)	(945,238)
Total stockholders' equity	1,320,000	464,359
Total liabilities and stockholders' equity	<u>\$ 1,558,178</u>	<u>\$ 707,694</u>

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

	Three Months Ended		Nine Months Ended	
	September 30,		September 30,	
	2020	2019	2020	2019
Revenues:				
Product revenue, net	\$ 6,308	\$ —	\$ 15,446	\$ —
Collaboration revenue	738,810	9,139	744,183	14,979
Total revenues	745,118	9,139	759,629	14,979
Cost and operating expenses:				
Cost of sales	146	—	297	—
Research and development	74,230	81,453	249,456	242,804
Selling, general and administrative	37,375	25,647	115,203	64,123
Total cost and operating expenses	111,751	107,100	364,956	306,927
Other income (expense):				
Interest income, net	1,173	3,758	5,663	10,742
Other income (expense), net	(192)	(72)	(416)	(157)
Total other income	981	3,686	5,247	10,585
Income (loss) before income taxes	634,348	(94,275)	399,920	(281,363)
Income tax expense	370	—	370	—
Net income (loss)	\$ 633,978	\$ (94,275)	\$ 399,550	\$ (281,363)
Other comprehensive income (loss):				
Unrealized gain (losses) on available-for-sale investments	(777)	(287)	658	828
Currency translation adjustments	(43)	(3)	(64)	(10)
Comprehensive income (loss)	\$ 633,158	\$ (94,565)	\$ 400,144	\$ (280,545)
Net income (loss) per share - basic	\$ 11.49	\$ (1.93)	\$ 7.40	\$ (5.94)
Net income (loss) per share - diluted	11.16	(1.93)	7.20	(5.94)
Weighted-average number of common shares used in net income (loss) per share - basic	55,169	48,921	54,018	47,361
Weighted-average number of common shares used in net income (loss) per share - diluted	56,786	48,921	55,492	47,361

Blueprint Medicines Corporation
Condensed Consolidated Statements of Stockholders' Equity
(in thousands, except share data)
(Unaudited)

	Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Loss	Accumulated Deficit	Stockholders' Equity
	Shares	Amount				
Balance at December 31, 2019	49,272,223	\$ 49	\$ 1,412,083	\$ (2,535)	\$ (945,238)	\$ 464,359
Issuance of common stock under stock plan	186,166	1	1,612	—	—	1,613
Stock-based compensation expense	—	—	17,026	—	—	17,026
Follow on offering, net of issuance costs	4,710,144	4	308,419	—	—	308,423
Unrealized gain (loss) on available-for-sale securities	—	—	—	2,492	—	2,492
Cumulative translation adjustment	—	—	—	(26)	—	(26)
Net income (loss)	—	—	—	—	(110,954)	(110,954)
Balance at March 31, 2020	<u>54,168,533</u>	<u>\$ 54</u>	<u>\$ 1,739,140</u>	<u>\$ (69)</u>	<u>\$ (1,056,192)</u>	<u>\$ 682,933</u>
Issuance of common stock under stock plan	98,950	—	2,335	—	—	2,335
Purchase of common stock under ESPP	17,018	—	942	—	—	942
Stock-based compensation expense	—	—	19,675	—	—	19,675
Unrealized gain (loss) on available-for-sale securities	—	—	—	(1,057)	—	(1,057)
Cumulative translation adjustment	—	—	—	6	—	6
Net income (loss)	—	—	—	—	(123,474)	(123,474)
Other	—	—	7	—	—	7
Balance at June 30, 2020	<u>54,284,501</u>	<u>\$ 54</u>	<u>\$ 1,762,099</u>	<u>\$ (1,120)</u>	<u>\$ (1,179,666)</u>	<u>\$ 581,367</u>
Issuance of common stock under stock plan	194,375	1	6,279	—	—	6,280
Stock-based compensation expense	—	—	19,889	—	—	19,889
Issuance of common stock related to collaboration agreement	1,035,519	1	79,305	—	—	79,306
Unrealized gain (loss) on available-for-sale securities	—	—	—	(777)	—	(777)
Cumulative translation adjustment	—	—	—	(43)	—	(43)
Net income (loss)	—	—	—	—	633,978	633,978
Balance at September 30, 2020	<u>55,514,395</u>	<u>\$ 56</u>	<u>\$ 1,867,572</u>	<u>\$ (1,940)</u>	<u>\$ (545,688)</u>	<u>\$ 1,320,000</u>
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
Unrealized gain (loss) on available-for-sale securities	—	—	—	270	—	270
Cumulative translation adjustment	—	—	—	(15)	—	(15)
Net income (loss)	—	—	—	—	(87,407)	(87,407)
Balance at March 31, 2019	<u>44,171,465</u>	<u>\$ 44</u>	<u>\$ 1,029,046</u>	<u>\$ 75</u>	<u>\$ (684,952)</u>	<u>\$ 344,213</u>
Issuance of common stock under stock plan	215,299	—	5,813	—	—	5,813
Purchase of common stock under ESPP	10,718	—	522	—	—	522
Follow on offering, net of issuance costs	4,662,162	5	327,437	—	—	327,442
Stock-based compensation expense	—	—	13,666	—	—	13,666
Unrealized gain (loss) on available-for-sale securities	—	—	—	845	—	845
Cumulative translation adjustment	—	—	—	7	—	7
Net income (loss)	—	—	—	—	(99,681)	(99,681)
Balance at June 30, 2019	<u>49,059,644</u>	<u>\$ 49</u>	<u>\$ 1,376,484</u>	<u>\$ 927</u>	<u>\$ (784,633)</u>	<u>\$ 592,827</u>
Issuance of common stock under stock plan	115,798	—	3,089	—	—	3,089
Stock-based compensation expense	—	—	14,993	—	—	14,993
Follow on offering, net of issuance costs	—	—	—	—	—	—
Unrealized gain (loss) on available-for-sale securities	—	—	—	(287)	—	(287)
Cumulative translation adjustment	—	—	—	(3)	—	(3)
Net income (loss)	—	—	—	—	(94,275)	(94,275)
Balance at September 30, 2019	<u>49,175,442</u>	<u>\$ 49</u>	<u>\$ 1,394,566</u>	<u>\$ 637</u>	<u>\$ (878,908)</u>	<u>\$ 516,344</u>

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

	Nine Months Ended September 30,	
	2020	2019
Cash flows from operating activities		
Net income (loss)	\$ 399,550	\$ (281,363)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	4,887	3,685
Noncash lease expense	4,289	3,649
Stock-based compensation	56,022	38,954
Accretion of premiums and discounts on investments	245	(4,366)
Other	328	—
Changes in assets and liabilities:		
Accounts receivable	(43,705)	(2,350)
Unbilled accounts receivable	5,862	(2,417)
Inventory	(4,491)	—
Prepaid expenses and other current assets	(7,266)	(7,175)
Other assets	1,796	(58)
Accounts payable	(1,978)	(1,095)
Accrued expenses	1,573	26,408
Deferred revenue	(666)	(4,836)
Operating lease liabilities	(4,612)	(2,156)
Net cash provided by (used in) operating activities	411,834	(233,120)
Cash flows from investing activities		
Purchases of property and equipment	(2,472)	(10,122)
Purchases of investments	(796,980)	(597,514)
Maturities of investments	440,735	523,434
Net cash used in investing activities	(358,717)	(84,202)
Cash flows from financing activities		
Proceeds from public offerings of common stock, net of issuance cost	308,750	327,466
Net proceeds from stock option exercises and employee stock purchase plan	9,921	11,454
Issuance of common stock related to collaboration agreement	79,305	—
Other financing activities	(310)	(116)
Net cash provided by financing activities	397,666	338,804
Net increase in cash, cash equivalents, and restricted cash	450,783	21,482
Cash, cash equivalents and restricted cash at beginning of period	119,604	73,429
Effect of exchange rate changes on cash, cash equivalents and restricted cash	2	(10)
Cash, cash equivalents and restricted cash at end of period	\$ 570,389	\$ 94,901
Supplemental cash flow information		
Public offering costs incurred but unpaid at period end	\$ 6	\$ 25
Property and equipment purchases unpaid at period end	\$ 209	\$ 3,225
Cash paid for taxes, net	\$ 68	\$ 130

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 (in thousands).

	September 30, 2020	September 30, 2019
Cash and cash equivalents	\$ 565,221	\$ 89,237
Restricted cash included in prepaid expenses and other current assets	—	500
Restricted cash	5,168	5,164
Total cash, cash equivalents, and restricted cash shown in condensed consolidated statements of cash flows	\$ 570,389	\$ 94,901

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 has two approved precision therapies and is currently advancing multiple investigational medicines in clinical and pre-clinical development, along with a number of earlier stage research programs. The Company is devoting substantially all of its efforts to research and development for current and future drug candidates and commercialization of AYVAKIT/AYVAKYT, GAVRETO and any current or future drug candidates that obtain marketing approval.

As of September 30, 2020, the Company had cash, cash equivalents and investments of \$1,355.9 million. Based on the Company's current operating plans, the Company anticipates that its existing cash, cash equivalents and investments will be sufficient to enable it to fund its current operations for at least the next twelve months from the issuance of the financial statements.

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, 2019 and notes thereto included in the Company's Annual Report on Form 10-K for the year ended December 31, 2019, filed with the SEC on February 13, 2020 (the 2019 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 September 30, 2020, the results of its operations for the three and nine months ended September 30, 2020 and 2019, stockholder's equity for the three and nine months ended September 30, 2020 and 2019 and cash flows for the nine months ended September 30, 2020 and 2019. Such adjustments are of a normal and recurring nature. The results for the three and nine months ended September 30, 2020 are not necessarily indicative of the results for the year ending December 31, 2020 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, Blueprint Medicines (Netherlands) B.V., Blueprint Medicines (UK) Ltd, Blueprint Medicines (Germany) GmbH, Blueprint Medicines Spain, S.L., Blueprint Medicines (France) SAS and Blueprint Medicines (Italy) S.r.l. 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. The full extent to which the COVID-19 pandemic will directly or indirectly impact the Company's business, results of operations and financial condition, including sales, expenses, reserves and allowances, manufacturing, clinical trials, research and development costs and employee-related amounts, will depend on future developments that are highly uncertain, including as a result of new information that may emerge concerning COVID-19 and the actions taken to contain or treat COVID-19, as well as the economic impact thereof on local, regional, national and international customers and markets. The Company had made estimates of the impact of COVID-19 within its financial statements and there may be changes to those estimates in future periods. Actual results may differ from these estimates.

Significant Accounting Policies

The significant accounting policies used in preparation of these condensed consolidated financial statements for the three and nine months ended September 30, 2020 are consistent with those discussed in Note 2 to the consolidated financial statements in the 2019 Annual Report on Form 10-K, except as noted below with respect to the Company's accounting policies for product revenue, accounts receivable, and inventory.

Product Revenue

The Company generated product revenue from sales of AYVAKIT and GAVRETO to a limited number of specialty distributors and specialty pharmacy providers in the U.S. These customers subsequently resell the products or dispense the products directly to patients. In addition, the Company entered into arrangements with payors that provide for government mandated rebates, discounts and allowances with respect to the utilization of its products.

Product revenue is recognized when the customer takes control of the product, typically upon delivery to the customer. Product revenue is recorded at the net sales price, or transaction price, which includes estimated reserves for variable consideration resulting from chargebacks, government rebates, trade discounts and allowances, product returns and other incentives that are offered within the contract with customers, healthcare providers, payors and other indirect customers relating to the sales of the Company's product. Reserves are established based on the amounts earned or to be claimed on the related sales. Where appropriate, the Company utilizes the expected value method to determine the appropriate amount for estimates of variable consideration based on factors such as the Company's current contractual and statutory requirements, specific known market events and trends, industry data and forecasted customer buying and payment patterns. The amount of variable consideration that is included in the transaction price may be constrained and is included in net product revenues only to the extent that it is probable that a significant reversal in the amount of the cumulative revenue recognized will not occur in a future period. Actual amounts of consideration ultimately received may differ from the Company's estimates. If actual results vary from the Company's estimates, the Company adjusts these estimates, which would affect net product revenue and earnings in the period such variances become known.

Chargebacks: Chargebacks for fees and discounts represent the estimated obligations resulting from contractual commitments to sell product to qualified healthcare providers and government agencies at prices lower than the list prices charged to the customers who directly purchase the product from the Company. The customers charge the Company for the difference between what they pay for the product and the ultimate contractually committed or government required lower selling price to the qualified healthcare providers. These reserves are estimated using the expected value method based upon a range of possible outcomes and are established in the same period that the related revenue is recognized, resulting in a reduction of product revenue.

Government rebates: Government rebates consist of Medicare, Tricare and Medicaid rebates, which were estimated using the expected value method, based upon a range of possible outcomes for the estimated payor mix. These

reserves are recorded in the same period the related revenue is recognized, resulting in a reduction of product revenue. For Medicare, the Company also estimates the number of patients in the prescription drug coverage gap for whom it will owe a rebate under the Medicare Part D program.

Trade discounts and allowances: The Company provides the customers with discounts that are explicitly stated in the contracts and recorded as a reduction of revenue in the period the related product revenue is recognized. In addition, the Company also receives sales order management, inventory management and data services from the customers in exchange for certain fees.

Product returns: The Company estimates the amount of its product sales that may be returned by its customers and records this estimate as a reduction of revenue in the period the related product revenue is recognized. The Company currently estimates product return liabilities using expected value method based on available industry data and its visibility into the inventory remaining in the distribution channel.

Other deductions: Co-pay assistance relates to financial assistance provided to qualified patients, whereby the Company may assist them with prescription drug co-payments required by the patient's insurance provider. Reserves for co-pay assistance are recorded in the same period the related revenue is recognized, resulting in a reduction of product revenue.

Accounts Receivable, net

Accounts receivable arise from product sales and amounts due from the Company's collaboration partners. The amount from product sales represents amounts due from specialty pharmacy providers in the U.S. The Company monitors economic conditions to identify facts or circumstances that may indicate that its receivables are at risk of collection. The Company provides reserves against accounts receivable for estimated losses that may result from a customer's inability to pay based on the composition of its accounts receivable, current economic conditions and historical credit loss activity. Amounts determined to be uncollectible are charged or written-off against the reserve. For the three and nine months ended September 30, 2020, the Company did not record any expected credit losses related to outstanding accounts receivable.

Inventory

Inventories are stated at the lower of cost or estimated net realizable value with cost based on the first-in first-out method. Inventory that can be used in either the production of clinical or commercial products is expensed as research and development costs when identified for use in clinical trials.

Prior to the regulatory approval of its drug candidates, the Company incurs expenses for the manufacture of drug product supplies to support clinical development that could potentially be available to support the commercial launch of those drugs. Until the date at which regulatory approval has been received or is otherwise considered probable, the Company records all such costs as research and development expenses.

The Company performs an assessment of the recoverability of capitalized inventories during each reporting period and writes down any excess and obsolete inventory to its net realizable value in the period in which the impairment is first identified. Such impairment charges, should they occur, are recorded as a component of cost of product sales in the condensed consolidated statements of operations and comprehensive loss. The determination of whether inventory costs will be realizable requires the use of estimates by management. If actual market conditions are less favorable than projected by management, additional write-downs of inventory may be required.

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 condensed consolidated financial statements and disclosures.

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*. The FASB subsequently issued amendments to ASU 2016-13, which had the same effective date and transition date of January 1, 2020. These standards require that credit losses be reported using an expected losses model rather than the incurred losses model that is currently used, and establish additional disclosures related to credit risks. For available-for-sale debt securities with unrealized losses, these standards now require allowances to be recorded instead of reducing the amortized cost of the investment. This standard limits the amount of credit losses to be recognized for available-for-sale debt securities to the amount by which carrying value exceeds fair value and requires the reversal of previously recognized credit losses if fair value increases.

The Company adopted the new standard on a prospective basis on January 1, 2020 and has completed the assessment of the standard based on the composition of its accounts receivable, investment portfolio of financial instruments, current and forecasted economic conditions and historical credit loss activity as of January 1, 2020. The adoption of this standard did not have a significant impact on the Company's condensed consolidated financial statements and related disclosures.

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. The Company adopted the new standard on January 1, 2020 and the adoption of this standard did not have a material impact on related 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.

The Company adopted the new standard on January 1, 2020. 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 adoption of this standard did not have a material impact on its condensed 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. The standard is effective for interim and annual periods beginning after December 15, 2019, with early adoption permitted, and can be adopted prospectively or retrospectively.

The Company adopted the new standard on January 1, 2020 on a prospective basis. The adoption of this standard did not have a significant impact on the Company's condensed consolidated financial position and results of operations. However, the adoption of this standard will result in an increase in capitalized assets related to qualifying cloud computing arrangement implementation costs incurred after the adoption date.

Income Taxes

In December 2019, the FASB issued *ASU No. 2019-12, Income Taxes (Topic 740): Simplifying the Accounting for Income Taxes*, as part of its initiative to reduce complexity in the accounting standards. The amendments in ASU 2019-12 eliminate certain exceptions related to the approach for intraperiod tax allocation, the methodology for calculating income taxes in an interim period and the recognition of deferred tax liabilities for outside basis differences. ASU 2019-12 also clarifies and simplifies other aspects of the accounting for income taxes. The amendments in ASU 2019-12 are effective for the fiscal years beginning after December 15, 2020. Early adoption is permitted, including adoption in any interim period. The Company has early adopted this amendment as of January 1, 2020. The adoption of the standard did not have a material impact to the Company's condensed consolidated financial position and results of operations as well as related income tax disclosures.

Reclassification

Certain items in the prior year's condensed 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 September 30, 2020 and December 31, 2019 (in thousands):

	Amortized Cost	Unrealized Gain	Unrealized Losses	Fair Value
September 30, 2020				
Cash equivalents:				
Money market funds	\$ 565,221	\$ —	\$ —	\$ 565,221
U.S. treasury obligations	—	—	—	—
Investments, available-for-sale:				
U.S. government agency securities	643,513	598	(173)	643,938
U.S. treasury obligations	146,002	740	(1)	146,741
Total	\$ 1,354,736	\$ 1,338	\$ (174)	\$ 1,355,900

	Amortized Cost	Unrealized Gain	Unrealized Losses	Fair Value
December 31, 2019				
Cash equivalents:				
Money market funds	\$ 98,946	\$ —	\$ —	\$ 98,946
U.S. treasury obligations	14,992	—	—	14,992
Investments, available-for-sale:				
U.S. government agency securities	128,156	160	(4)	128,312
U.S. treasury obligations	305,360	358	(8)	305,710
Total	\$ 547,454	\$ 518	\$ (12)	\$ 547,960

As of September 30, 2020, the Company held 31 debt securities that were in an unrealized loss position with an aggregate fair value of \$383.4 million. As of December 31, 2019, the Company held 11 debt securities that were in an unrealized loss position with an aggregate fair value of \$82.1 million.

As of September 30, 2020, there was no securities 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 September 30, 2020.

As of September 30, 2020, 63 securities with an aggregate fair value of \$598.5 million have remaining maturities between one year and five years. As of December 31, 2019, nine securities with an aggregate fair value of \$64.4 million had remaining maturities greater than one year.

4. Fair Value of Financial Instruments

The following table summarizes cash equivalents and marketable securities measured at fair value on a recurring basis as of September 30, 2020 (in thousands):

Description	September 30, 2020	Active Markets (Level 1)	Observable Inputs (Level 2)	Unobservable Inputs (Level 3)
Financial Assets				
Cash equivalents:				
Money market funds	\$ 565,221	\$ 565,221	\$ —	\$ —
U.S. treasury obligations	—	—	—	—
Investments, available-for-sale:				
U.S. government agency securities	643,938	—	643,938	—
U.S. treasury obligations	146,741	146,741	—	—
Total	\$ 1,355,900	\$ 711,962	\$ 643,938	\$ —

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

Description	December 31, 2019	Active Markets (Level 1)	Observable Inputs (Level 2)	Unobservable Inputs (Level 3)
Financial Assets				
Cash equivalents:				
Money market funds	\$ 98,946	\$ 98,946	\$ —	\$ —
U.S. treasury obligations	14,992	14,992	—	—
Investments, available-for-sale:				
U.S. government agency securities	128,312	—	128,312	—
U.S. treasury obligations	305,710	305,710	—	—
Total	\$ 547,960	\$ 419,648	\$ 128,312	\$ —

5. Product Revenue Reserves and Allowances

In January 2020, the U.S. Food and Drug Administration (FDA) approved AYVAKIT for the treatment of adults with unresectable or metastatic gastrointestinal stromal tumor (GIST) harboring a PDGFRA exon 18 mutation, including PDGFRA D842V mutations. In September 2020, the FDA granted accelerated approval of GAVRETO for the treatment of adult patients with metastatic RET fusion-positive non-small cell lung cancer (NSCLC) as detected by an FDA approved test, and the European Commission granted conditional marketing authorization to AYVAKYT as a monotherapy for the treatment of adult patients with unresectable or metastatic GIST harboring the PDGFRA D842V mutation.

The Company has generated net product revenue from the U.S. sales of AYVAKIT and GAVRETO for a total of \$6.3 million and \$15.4 million for the three and nine months ended September 30, 2020, respectively. The following table summarizes activity in each of the product revenue allowance and reserve categories for the nine months ended September 30, 2020 (in thousands):

	Total
Beginning balance at January 1, 2020	\$ —
Provision related to sales in the current period	1,774
Adjustment related to prior periods sales	—
Credits and payments made	(824)
Ending balance at September 30, 2020	<u>\$ 950</u>

The total reserves above, which are included in the Company's condensed consolidated balance sheets, are summarized as follows (in thousands):

	September 30,
	2020
Reduction of accounts receivable, net	\$ 228
Component of accrued expenses	722
Total revenue-related reserves	<u>\$ 950</u>

6. Inventory

Capitalized inventory consists of the following at September 30, 2020 and December 31, 2019 (in thousands):

	September 30,	December 31,
	2020	2019
Work in process	\$ 5,415	\$ —
Finished goods	150	—
Total	<u>\$ 5,565</u>	<u>\$ —</u>

Inventory amounts written down as a result of excess, obsolescence, unmarketability or other reasons are charged to cost of sales and was zero for the three and nine months ended September 30, 2020 and 2019.

7. Restricted Cash

At September 30, 2020 and December 31, 2019, \$5.2 million and \$5.7 million, respectively, of the Company's cash is restricted by a bank primarily related to security deposits for the Company's building lease agreements.

8. Property and Equipment, Net

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

	Estimated Useful Life (Years)	September 30, 2020	December 31, 2019
Lab equipment	5	\$ 10,937	\$ 8,975
Furniture and fixtures	4	3,764	3,512
Computer equipment	3	1,572	1,558
Leasehold improvements	Term of lease	36,945	35,975
Software	3	350	417
Construction-in-progress		190	1,608
Total cost		53,758	52,045
Less: accumulated depreciation and amortization		(18,559)	(13,684)
Total		<u>\$ 35,199</u>	<u>\$ 38,361</u>

Property, plant and equipment are recorded at historical cost, net of accumulated depreciation. For the three and nine months ended September 30, 2020, depreciation expense totaled \$1.6 million and \$4.9 million, respectively, compared to \$1.3 million and \$3.7 million, respectively, for the three and nine months ended September 30, 2019.

9. Accrued Expenses

Accrued expenses consist of the following (in thousands):

	September 30, 2020	December 31, 2019
Research, development and commercial contract costs	\$ 56,658	\$ 59,420
Employee compensation	17,730	13,519
Accrued professional fees	11,049	12,042
Revenue-related reserves	722	—
Other	2,957	3,725
Total	<u>\$ 89,116</u>	<u>\$ 88,706</u>

10. Collaboration and License Agreements

Roche – Pralsetinib Collaboration

On July 13, 2020, the Company entered into a collaboration agreement (the Roche pralsetinib collaboration agreement) with F. Hoffmann-La Roche Ltd and Genentech, Inc., a member of the Roche Group (collectively, Roche), pursuant to which the Company granted Roche exclusive rights to develop and commercialize the Company's drug candidate pralsetinib worldwide, excluding the CStone territory (as defined below), and a co-exclusive license in the U.S. to develop and commercialize pralsetinib. In addition, Roche has the right to opt in to a next-generation RET compound co-developed by the Company and Roche.

Under the Roche pralsetinib collaboration agreement, the Company received an upfront cash payment of \$675.0 million in the third quarter of 2020. In addition, the Company is eligible to receive up to \$927.0 million in contingent payments, including specified development, regulatory and sales-based milestones for pralsetinib and any licensed product containing a next-generation RET compound. During the three months ended September 30, 2020, as a result of initial U.S. marketing approval for GAVRETO, the Company achieved \$40.0 million in specified regulatory and commercialization milestones.

In the U.S., the Company and Roche will work together to co-commercialize pralsetinib and will equally share responsibilities, profits and losses. In addition, the Company is eligible to receive tiered royalties ranging from high-teens to mid-twenties on annual net sales of pralsetinib outside the U.S., excluding Greater China (the Roche territory).

The Company and Roche have also agreed to co-develop pralsetinib globally in RET-altered solid tumors, including non-small cell lung cancer, medullary thyroid carcinoma and other thyroid cancers, as well as other solid tumors. The Company and Roche will share global development costs for pralsetinib at a rate of 45 percent for the Company and 55 percent for Roche up to a specified amount of aggregate joint development costs, after which the Company's share of global development costs for pralsetinib will be reduced by a specified percentage. The Company and Roche will also share specified global development costs for any next-generation RET compound co-developed under the collaboration in a similar manner.

Unless earlier terminated in accordance with its terms, the Roche pralsetinib collaboration agreement will expire on a licensed product-by-licensed product basis (i) in the U.S. upon the expiration of the gross profit sharing term for such licensed product and (ii) outside the U.S. on a country-by-country basis at the end of the applicable royalty term for such licensed product. Roche may terminate the agreement in its entirety or on a licensed product-by-licensed product or country-by-country basis subject to certain notice periods. Either party may terminate the Roche pralsetinib collaboration agreement for the other party's uncured material breach or insolvency. Subject to the terms of the Roche pralsetinib collaboration agreement, effective upon termination of the agreement, the Company is entitled to retain specified licenses to be able to continue to exploit the licensed products.

In connection with the Roche collaboration agreement, on July 13, 2020, the Company also entered into a stock purchase agreement with Roche Holdings, Inc. (Roche Holdings) pursuant to which the Company issued and sold an aggregate of 1,035,519 of shares of common stock to Roche Holdings at a purchase price of \$96.57 per share and received \$100.0 million in the third quarter of 2020. The closing for a minority portion of the equity investment occurred following the expiration of the waiting period under the Hart-Scott-Rodino Antitrust Improvements Act of 1976, as amended, and other customary closing conditions.

The Company considered the ASC 606 criteria for combining contracts and determined that the Roche pralsetinib collaboration agreement and stock purchase agreement should be combined into a single contract because they were negotiated and entered into in contemplation of one another. The Company accounted for the common stock issued to Roche Holdings based on the fair market value of the common stock on the dates of issuance. The fair market value of the common stock issued to Roche Holdings was \$79.3 million, based on the closing price of the Company's common stock on the dates of issuance, resulting in a \$20.7 million premium. The Company determined that the premium paid by Roche Holdings for the common stock should be attributed to the transaction price of the Roche pralsetinib collaboration agreement.

The Company determined that the Roche pralsetinib collaboration agreement contained four material components: (i) licenses granted to Roche to develop and commercialize pralsetinib worldwide, excluding the CStone territory (pralsetinib license); (ii) the Roche territory-specific commercialization activities for pralsetinib, including manufacturing Roche territory activities; (iii) the parties' joint development activities for pralsetinib worldwide, excluding the CStone territory; and (iv) the parties' joint commercialization activities for pralsetinib in the U.S. The Company considered the guidance in ASC 606 to determine which of the components of the Roche pralsetinib collaboration agreement are performance obligations with a customer and concluded that the pralsetinib license and the Roche territory activities are within the scope of ASC 606 because the Company is not exposed to significant risks and rewards, and Roche is a customer with regard to those components.

The Company evaluated the Roche pralsetinib license under ASC 606 and concluded that the pralsetinib license is a functional intellectual property license and is a distinct performance obligation. The transaction price for the pralsetinib license was determined to be \$695.7 million, which consisted of the upfront cash payment of \$675.0 million and the \$20.7 million premium on the sale of common stock to Roche Holdings. The Company determined that Roche benefited from the pralsetinib license at the time of grant, and therefore the related performance obligation is satisfied at a point in time. During the three months ended September 30, 2020, as a result of initial U.S. marketing approval for GAVRETO, the Company achieved \$40.0 million in specified regulatory and commercialization milestones and added the \$40.0 million to the estimated transaction price of the Roche pralsetinib agreement. The other potential milestone payments that the Company is eligible to receive under the Roche pralsetinib agreement have been excluded from the transaction price, as all the remaining 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, and any addition to the transaction price would be recognized as revenue when it becomes probable that inclusion would not lead to a significant revenue reversal.

The Company evaluated the Roche territory activities under ASC 606 and identified one material promise associated with manufacturing activities related to development and commercial supply of pralsetinib in the Roche territory. The Company concluded that the provision of manufacturing activities related to development and commercial supply of pralsetinib in Roche territory was an option for the purpose of ASC 606, was not issued at a significant and incremental discount and do not provide Roche with any material rights. Therefore, the manufacturing activities were excluded as performance obligations at the outset of the arrangement. Additionally, the Company is entitled to sales milestones and royalties from Roche upon future sales of pralsetinib in the Roche territory, and revenue will be recognized when the related sales occur. Costs that are incurred associated with the Roche territory activities are reimbursable from Roche and will be recognized as revenue.

The following table summarizes revenue recognized under the Roche pralsetinib collaboration during the three and nine months ended September 30, 2020 and 2019 (in thousands):

	Three Months Ended		Nine Months Ended	
	September 30,		September 30,	
	2020	2019	2020	2019
Upfront license revenue	\$ 695,694	\$ —	\$ 695,694	\$ —
License milestone revenue	40,000	—	40,000	—
Services related to Roche territory-specific activities	856	—	856	—
Total Roche pralsetinib collaboration revenue	<u>\$ 736,550</u>	<u>\$ —</u>	<u>\$ 736,550</u>	<u>\$ —</u>

For the parties' participation in global development for pralsetinib and the U.S. commercialization activities for GAVRETO, the Company concluded that those activities and cost-sharing payments related to such activities are within the scope of ASC 808, as both parties are active participants in the development, manufacturing and commercialization activities and are exposed to significant risks and rewards of those activities under the Roche pralsetinib collaboration agreement. Payments to or reimbursements from Roche related to the global development activities will be accounted for as an increase to or reduction of research and development expenses. Prior to the transition date as defined in the Roche pralsetinib collaboration agreement, the Company is the principal for product sales to customers in the U.S. and will recognize revenues on sales to third parties in product revenue, net in its consolidated statements of operations. After such transition, Roche will be the principal for product sales to customers in the U.S., and the Company will recognize its portion of the commercial profits and losses sharing as revenue (expenses) from the collaboration arrangement in its consolidated statements of operations.

During the three and nine months ended September 30, 2020, the Company recorded a \$5.3 million reduction in selling, general and administrative expenses in connection with the commercialization of GAVRETO in the U.S. and a \$9.7 million reduction in research and development expenses in connection with global development activities for pralsetinib.

The following table summarizes the contract assets associated with the Roche pralsetinib collaboration as of September 30, 2020 and December 31, 2019 (in thousands):

	September 30,	December 31,
	2020	2019
Accounts receivable, net	\$ 40,000	\$ —
Unbilled accounts receivable	\$ 15,888	\$ —

Clementia

On October 15, 2019, the Company entered into a license agreement (the Clementia agreement) with Clementia Pharmaceuticals, Inc. (Clementia), a wholly-owned subsidiary of Ipsen S.A. Under the Clementia agreement, the Company granted an exclusive, worldwide, royalty-bearing license to Clementia to develop and commercialize BLU-782, the Company's oral, highly selective investigational ALK2 inhibitor in Phase 1 clinical development for the

treatment of fibrodysplasia ossificans progressiva (FOP), as well as specified other compounds related to the BLU-782 program.

Under the Clementia agreement, the Company received an upfront cash payment of \$25.0 million and a \$20.0 million cash milestone payment in October 2019 and July 2020, respectively. Subject to the terms of the Clementia agreement, the Company is eligible to receive up to \$490.0 million in additional potential development, regulatory and sales-based milestone payments for licensed products. In addition, Clementia is obligated to pay to the Company royalties on aggregate annual worldwide net sales of licensed products at tiered percentage rates ranging from the low- to mid-teens, subject to adjustment in specified circumstances under the Clementia agreement, and Clementia purchased specified manufacturing inventory from the Company for a total of \$1.5 million.

Unless earlier terminated in accordance with the terms of the Clementia agreement, the agreement will expire on a country-by-country, licensed product-by-licensed product basis on the date when no royalty payments are or will become due. Clementia may terminate the agreement at any time on or after the second anniversary of the effective date of the agreement upon at least 12 months' prior written notice to the Company, which cannot be delivered before the first anniversary of the effective date. Either party may terminate the 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 Clementia licensed products.

The Company evaluated the Clementia agreement under ASC 606, as the agreement represented a transaction with a customer. The Company identified the following material promises under the agreement: (1) the exclusive license to develop, manufacture and commercialize BLU-782; (2) the technology transfer of BLU-782 program; (3) the transfer of existing manufacturing inventory; and (4) the transfer of in-process manufacturing inventory. In addition, the Company determined that the exclusive license and technology transfer were not distinct from each other, as the exclusive license has limited value without the corresponding technology transfer. As such, for the purposes of ASC 606, the Company determined that these four material promises, described above, should be combined into three performance obligations: (1) the exclusive license and the technology transfer; (2) the transfer of existing manufacturing inventory; and (3) the transfer of in-process manufacturing inventory.

The Company determined that the transaction price as of the outset of the arrangement was \$46.5 million, which consists of the upfront amount of \$25.0 million, the \$20.0 million cash milestone payment received in July 2020, the purchase of existing manufacturing inventory of \$1.2 million and the purchase of in-process manufacturing inventory of \$0.3 million. The other 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 transaction price was allocated to the three performance obligations on a relative stand-alone selling price basis. The Company satisfies the performance obligations upon delivery of the license and completion of the technology transfer and inventory transfers.

During 2019, the Company completed the delivery of the license, the technology transfer and the transfer of existing manufacturing inventory and recognized a total of \$46.2 million as revenue.

During the three months ended September 30, 2020, no revenue was recognized from the Clementia collaboration. During the nine months ended September 30, 2020, the Company completed the transfer of the in-process manufacturing inventory and recognized revenue of \$0.3 million accordingly. No revenue was recognized during the nine months ended September 30, 2019. There was no revenue deferred as a contract liability associated with the Clementia agreement as of September 30, 2020 and December 31, 2019.

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 avapritinib, pralsetinib and fisogatinib, 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 received an upfront cash payment of \$40.0 million, and subject to the terms of the CStone agreement, is 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 fisogatinib 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 fisogatinib 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.

A summary of manufacturing and research and development services related to the global development activities net of cost sharing payments during the three and nine months ended September 30, 2020 and 2019 is as follows (in thousands):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2020	2019	2020	2019
Manufacturing and research and development services related to global development activities net of cost sharing payments	\$ 1,047	\$ 1,275	\$ 3,091	\$ 2,403

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 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.

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, and any addition to the transaction price would be recognized as revenue when it becomes probable that inclusion would not lead to a significant revenue reversal. During the nine months ended September 30, 2020, a development milestone was achieved and the associated cash consideration of \$2.0 million for such milestone was added to the estimated transaction price for the CStone agreement.

A summary of revenue recognized under the CStone agreement during the three and nine months ended September 30, 2020 and 2019 is as follows (in thousands):

	Three Months Ended		Nine Months Ended	
	September 30,		September 30,	
	2020	2019	2020	2019
License milestone revenue	\$ —	\$ 6,000	\$ 2,000	\$ 10,000
Manufacturing services related to CStone territory-specific activities	100	—	1,496	144
Total CStone collaboration revenue	<u>\$ 100</u>	<u>\$ 6,000</u>	<u>\$ 3,496</u>	<u>\$ 10,144</u>

The following table presents the contract assets associated with the CStone collaboration as of September 30, 2020 and December 31, 2019 (in thousands):

	September 30, 2020	December 31, 2019
Accounts receivable, net	\$ 1,050	\$ 663
Unbilled accounts receivable	\$ 270	\$ 2,749

As of September 30, 2020, the Company had \$2.1 million of deferred revenue as a contract liability associated with the CStone collaboration. This contract liability resulted from an advance payment made by CStone in connection with commercial supply of avapritinib for the CStone territory. There was no associated contract liability at December 31, 2019.

Roche – Immunotherapy Collaboration

In March 2016, the Company entered into a collaboration and license agreement (as amended, the Roche immunotherapy agreement) with F. Hoffmann-La Roche Ltd and Hoffmann-La Roche Inc. (collectively, Roche) for the discovery, development and commercialization of up to five small molecule therapeutics targeting kinases believed to be important in cancer immunotherapy (including the kinase target MAP4K1, which is believed to play a role in T cell regulation), as single products or possibly in combination with other therapeutics.

Under the Roche immunotherapy agreement, Roche was 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. As a result of an amendment to the Roche immunotherapy agreement in the fourth quarter of 2019, the parties are currently conducting activities for up to four programs under the collaboration. For up to two collaboration programs, if Roche exercises its option, Roche will receive worldwide, exclusive commercialization rights for the licensed products. For up to two collaboration programs, if Roche exercises its option, the Company will retain commercialization rights in the U.S. for the licensed products, and Roche will receive commercialization rights outside of the U.S. 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 immunotherapy 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 U.S.

The Company received an upfront cash payment of \$45.0 million in March 2016 upon execution of the Roche immunotherapy agreement, and subject to the terms of the Roche immunotherapy agreement, the Company is eligible to receive up to approximately \$940.0 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 \$190.0 million are for option fees and milestone payments for research, pre-clinical and clinical development events prior to licensing across all four potential collaboration programs.

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 U.S., 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 immunotherapy 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 immunotherapy agreement. Prior to its exercise of its first option, Roche may terminate the Roche immunotherapy 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 immunotherapy 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 immunotherapy 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 drugs 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 immunotherapy 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 immunotherapy 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 and October 2019, the Company achieved and received a \$10.0 million research milestone payment and an \$8.0 million research milestone payment related to the Roche immunotherapy agreement, respectively. These amounts were added to the estimated transaction price and allocated to the existing performance obligation as it became probable that a significant reversal of cumulative revenue would not occur for each of the research milestones achieved.

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.

A summary of revenue recognized under the Roche immunotherapy agreement during the three and nine months ended September 30, 2020 and 2019 is as follows (in thousands):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2020	2019	2020	2019
Roche immunotherapy collaboration research and development services revenue	\$ 2,161	\$ 3,139	\$ 3,845	\$ 4,836

During the three and nine months ended September 30, 2020 and 2019, the Company recognized the following revenue due to the changes in the contract liability balances (in thousands):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2020	2019	2020	2019
Amounts included in the contract liability at the beginning of the period	\$ 1,259	\$ 1,518	\$ 3,310	\$ 3,470

As of September 30, 2020, the Company had revenue deferred as a contract liability related to the Roche immunotherapy agreement of \$43.3 million, of which \$8.3 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 4.5 years.

11. 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, 2020, the number of shares reserved for issuance under the 2015 Plan was increased by 1,970,888 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 the Company's capitalization. As of September 30, 2020, there were 1,587,167 shares available for future grant under the 2015 Plan.

Stock options

The following table summarizes the stock option activity for the nine months ended September 30, 2020:

	Shares	Weighted-Average Exercise Price
Outstanding at December 31, 2019	5,795,710	\$ 58.82
Granted	1,386,743	59.65
Exercised	(385,696)	26.51
Canceled	(331,443)	76.55
Outstanding at September 30, 2020	6,465,314	\$ 60.01
Exercisable at September 30, 2020	3,280,686	\$ 49.45

As of September 30, 2020, the total unrecognized compensation expense related to unvested stock option awards was \$124.7 million, which is expected to be recognized over a weighted-average period of approximately 2.68 years.

Restricted stock units

The following table summarizes the restricted stock units activity for the nine months ended September 30, 2020:

	Shares	Weighted-Average Grant Date Fair Value
Unvested shares at December 31, 2019	419,755	\$ 82.50
Granted	903,460	57.62
Vested	(93,795)	85.67
Forfeited	(67,982)	66.81
Unvested shares at September 30, 2020	<u>1,161,438</u>	<u>\$ 63.81</u>

As of September 30, 2020, the total unrecognized compensation expense related to unvested restricted stock units was \$62.9 million, which is expected to be recognize over a weighted-average period of approximately 3.19 years.

2020 Inducement Plan

In March 2020, the Company's board of directors adopted the 2020 Inducement Plan (the Inducement Plan), pursuant to which the Company may grant, subject to the terms of the Inducement Plan and Nasdaq rules, nonstatutory stock options, stock appreciation rights, restricted stock awards, restricted stock units, and other stock-based awards. The Company initially reserved a total of 1,000,000 shares of common stock for the issuance of awards under the Inducement Plan. The number of shares reserved and available for issuance under the Inducement Plan can be increased at any time with the approval of the Company's board of directors. The Inducement Plan permits the board of directors or a committee thereof to use the stock-based awards available under the Inducement Plan to attract key employees for the growth of the Company. As of September 30, 2020, there were 159,514 shares issued under the Inducement Plan.

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 Company's initial public offering 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, 2020, the number of shares reserved for issuance under the 2015 ESPP was increased by 492,722 shares. The Company issued 17,018 and 10,718 shares under the 2015 ESPP during the nine months ended September 30, 2020 and 2019, respectively.

Stock-based compensation expense

The Company recognized stock-based compensation expense totaling \$19.6 million and \$56.0 million for the three and nine months ended September 30, 2020, respectively. Stock-based compensation expense by award type included within the unaudited condensed consolidated statements of operations and comprehensive income (loss) was as follows (in thousands):

	Three Months Ended		Nine Months Ended	
	September 30,		September 30,	
	2020	2019	2020	2019
Stock options	\$ 14,418	\$ 12,778	\$ 42,764	\$ 34,373
Restricted stock units	5,164	2,076	13,162	4,243
Employee stock purchase plan	306	139	664	338
Subtotal	19,889	14,993	56,590	38,954
Capitalized stock-based compensation costs	(254)	—	(568)	—
Stock-based compensation expense included in total cost and operating expenses	<u>\$ 19,635</u>	<u>\$ 14,993</u>	<u>\$ 56,022</u>	<u>\$ 38,954</u>

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

	Three Months Ended		Nine Months Ended	
	September 30,		September 30,	
	2020	2019	2020	2019
Research and development	\$ 8,634	\$ 7,678	\$ 25,141	\$ 20,971
Selling, general and administrative	11,001	7,315	30,881	17,983
Total	<u>19,635</u>	<u>14,993</u>	<u>56,022</u>	<u>38,954</u>

12. Earnings per Share

Basic earnings per share (EPS) is calculated by dividing net income (loss) by the weighted average number of shares of common stock outstanding during the period. Diluted EPS is calculated by adjusting weighted average shares outstanding for the dilutive effect of common stock equivalents outstanding for the period. For purposes of the diluted EPS calculation, the effect of stock options, unvested restricted stock units and ESPP shares on the weighted average number of shares is calculated using the treasury stock method. In periods with reported net operating losses, all common stock equivalents are deemed anti-dilutive such that basic net loss per share and diluted net loss per share are equal.

The calculation of net income (loss) and the number of shares used to compute basic and diluted net income (loss) per share for the three and nine months ended September 30, 2020 and 2019 are as follows (in thousands, except per share data):

	Three Months Ended		Nine Months Ended	
	September 30,		September 30,	
	2020	2019	2020	2019
Net income (loss) - basic and diluted	\$ 633,978	\$ (94,275)	\$ 399,550	\$ (281,363)
Weighted average shares outstanding - basic	55,169	48,921	54,018	47,361
Effect of dilutive securities:				
Stock options	1,289	—	1,265	—
Restricted stock units	328	—	209	—
Weighted average shares outstanding - diluted	56,786	48,921	55,492	47,361
Net income (loss) per share - basic	\$ 11.49	\$ (1.93)	\$ 7.40	\$ (5.94)
Net income (loss) per share - diluted	11.16	(1.93)	7.20	(5.94)

For the three and nine months ended September 30, 2020 and 2019, the following dilutive securities were not included in the computation of net income (loss) per share because the effect would be anti-dilutive (in thousands):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2020	2019	2020	2019
Stock options	4,704	5,631	4,543	4,459
Restricted stock units	—	382	68	12
ESPP	26	12	26	6
Total	4,730	6,025	4,637	4,477

13. Income Taxes

Coronavirus Aid, Relief and Economic Security Act

In response to the COVID-19 pandemic, the Coronavirus Aid, Relief and Economic Security Act (CARES Act) was signed into law in March 2020. The CARES Act lifts certain deduction limitations originally imposed by the Tax Cuts and Jobs Act of 2017 (2017 Tax Act). Corporate taxpayers may carryback net operating losses (NOLs) originating during 2018 through 2020 for up to five years, which was not previously allowed under the 2017 Tax Act. The CARES Act also eliminates the 80% of taxable income limitations by allowing corporate entities to fully utilize NOL carryforwards to offset taxable income in 2018, 2019 or 2020. Taxpayers may generally deduct interest up to the sum of 50% of adjusted taxable income plus business interest income (30% limit under the 2017 Tax Act) for tax years beginning in 2019 and 2020.

In addition, the CARES Act raises the corporate charitable deduction limit to 25% of taxable income and makes qualified improvement property generally eligible for 15-year cost-recovery and 100% bonus depreciation. The enactment of the CARES Act did not result in any material adjustments to the Company's income tax provision for the three and nine months ended September 30, 2020, or to its net deferred tax assets and related allowances as of September 30, 2020.

Roche Pralsetinib Collaboration

As a result of the Roche pralsetinib collaboration agreement, the Company received an upfront cash payment of \$675.0 million and \$100.0 million from the issuance and the sale of the Company's common stock to Roche Holdings. For the sale of common stock to Roche Holdings, \$20.7 million of the \$100.0 million is treated as a premium. The \$775.0 million in aggregate payments for the upfront payment and equity investment received in the third quarter of 2020 and the \$40.0 million in milestone payments received in October 2020 are expected to generate taxable income for the Company in 2020. The Company is currently performing an analysis to determine whether an ownership change under Section 382 of the Internal Revenue Code of 1986, as amended (the Code) has occurred from the Company's inception in 2008 and through December 31, 2020. If it is determined that the Company's U.S. subsidiaries underwent an "ownership change" for purposes of Section 382 of the Code at any time during this period, the effect of this change would result in the imposition of a limitation on the use of the Company's NOLs and other tax attributes.

14. Leases

The Company's building leases are comprised of office and laboratory spaces under non-cancelable operating leases. The lease agreements have remaining lease terms of two to nine years and contain various clauses for renewal at the Company's option. The renewal options were not included in the calculation of the operating lease assets and the operating lease as the renewal option is not reasonably certain of being exercised. The lease agreements do not contain residual value guarantees and the components of lease cost for the three and nine months ended September 30, 2020 and 2019 were as follows (in thousands):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2020	2019	2020	2019
Operating leases:				
Lease cost	\$ 4,303	\$ 4,167	\$ 13,014	\$ 11,906
Sublease income	(730)	(708)	(2,181)	(2,117)
Net lease cost	<u>\$ 3,573</u>	<u>\$ 3,459</u>	<u>\$ 10,833</u>	<u>\$ 9,789</u>

The Company has not entered into any material short-term leases or financing leases as of September 30, 2020.

Supplemental cash flow information related to leases for the three and nine months ended September 30, 2020 was as follows (in thousands):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2020	2019	2020	2019
Cash paid for amounts included in the measurement of lease liabilities:	\$ 3,616	\$ 3,485	\$ 10,789	\$ 8,727
Lease liabilities arising from obtaining right-of-use assets:				
Operating leases	\$ —	\$ —	\$ 486	\$ 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 in years	8.7
Weighted average discount rate	8.2%

15. Commitments

Manufacturing Agreements

In connection with the commercialization of AYVAKIT/AYVAKYT and GAVRETO, the Company has negotiated manufacturing agreements with certain vendors that require the Company to meet minimum purchase obligations on an annual basis. The aggregate amount of future minimum purchase obligations under these manufacturing agreements is approximately \$25.5 million as of September 30, 2020.

16. Subsequent Events

Manufacturing Agreements

In October 2020, in connection with the commercialization of GAVRETO, the Company negotiated an additional manufacturing agreement with certain vendor that requires the Company to meet minimum purchase obligations on an annual basis. The aggregate amount of future minimum purchase obligations under this manufacturing agreement is approximately \$10.0 million for a five year period.

Sublease Amendment

In October 2020, the Company amended the sublease agreement for the premises located at 38 Sidney Street, Cambridge, Massachusetts to extend the term of the sublease through December 31, 2020.

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, 2019, filed with the Securities and Exchange Commission, or the SEC, on February 13, 2020. 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 therapies 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. We have two approved precision therapies and are currently advancing multiple investigational medicines in clinical and pre-clinical development, along with a number of earlier stage research programs.

Avapritinib and BLU-263 — Systemic Mastocytosis and other Mast Cell Disorders

Avapritinib

We are developing and plan to commercialize avapritinib for the treatment of systemic mastocytosis, or SM, 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. Nearly all cases of SM are driven by the KIT D816V mutation, which aberrantly activates mast cells.

We are currently evaluating avapritinib in an ongoing registration-enabling Phase 1 clinical trial in advanced SM, which we refer to as our EXPLORER trial, and an ongoing registration-enabling Phase 2 clinical trial in advanced SM, which we refer to as our PATHFINDER trial. In June 2020, we presented data from the EXPLORER trial at the European Hematology Association 25th Annual Congress, and in September 2020, we reported top-line data from the EXPLORER trial and the PATHFINDER trial. We plan to submit a supplemental new drug application, or NDA, to the U.S. Food and Drug Administration, or FDA, for avapritinib for the treatment of advanced SM in the fourth quarter of 2020. We anticipate the supplemental NDA will be focused on data from patients in the EXPLORER and PATHFINDER trials who were treated with avapritinib at a starting dose of 200 mg once daily, or QD, supported by pooled data from all doses.

In addition, we are evaluating avapritinib in an ongoing registration-enabling Phase 2 clinical trial in indolent SM, which we refer to as our PIONEER trial. In March 2020, we reported updated data from the dose-finding portion (Part 1) of the PIONEER trial at an investor conference call and on a virtual forum established by the American Academy of Allergy, Asthma & Immunology, and in June 2020, we presented additional data from Part 1 of the PIONEER trial at the European Academy of Allergy and Clinical Immunology 2020 Congress. In the third quarter of 2020, we initiated the registration-enabling Part 2 of the PIONEER trial, activated multiple clinical sites in the United States and Europe, and are currently enrolling patients. Given uncertainty from the impact of the COVID-19 pandemic on activation of additional clinical trial sites and patient enrollment rates, we plan to provide an update in the first quarter of 2021 on expected timing for completing enrollment for Part 2 of the PIONEER trial.

The FDA has granted orphan drug designation to avapritinib for the treatment of mastocytosis, and the European Commission has granted orphan medicinal product designation to avapritinib for the treatment of mastocytosis. In addition, 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.

BLU-263

We are developing BLU-263 for the treatment of indolent SM and other mast cell disorders. BLU-263 is an investigational, orally available, potent and highly selective KIT inhibitor. BLU-263 is designed to have equivalent potency as avapritinib, improved selectivity for KIT, with low off-target activity, and lower penetration of the central nervous system relative to avapritinib based on preclinical data, which we believe will enable development of BLU-263 in a broad population of patients with indolent SM, including patients with lower disease burden requiring potentially life-long chronic therapy, as well as patients with other KIT-driven mast cell disorders. We are currently conducting a Phase 1 trial of BLU-263 in healthy volunteers.

Pralsetinib — RET-altered Cancers

We are developing and commercializing pralsetinib for the treatment of RET fusion-positive non-small cell lung cancer, or NSCLC, and developing and plan to commercialize pralsetinib for the treatment of RET-altered thyroid carcinoma, including medullary thyroid carcinoma, or MTC, and other solid tumors. We have exclusive licenses to Roche and CStone to develop and commercialize pralsetinib in their respective territories. See “—*Collaborations and Licenses*” below.

Pralsetinib is approved in the U.S. with accelerated approval under the brand name GAVRETO for the treatment of adult patients with metastatic RET fusion-positive NSCLC as detected by an FDA approved test. In addition, the European Medicines Agency, or EMA, is currently reviewing our marketing authorization application, or MAA, for pralsetinib for RET fusion-positive NSCLC. We plan to submit additional marketing applications for pralsetinib for RET fusion-positive NSCLC through the FDA’s Project Orbis initiative, which provides a framework for concurrent submission and review of marketing applications for oncology products among international health authorities. In addition, in September 2020, China’s National Medical Products Administration, or NMPA, accepted an NDA submitted by CStone Pharmaceuticals, or CStone, for pralsetinib for the treatment of RET fusion-positive NSCLC patients previously treated with platinum-based chemotherapy. In the second quarter of 2020, we submitted an NDA to the FDA for pralsetinib for the treatment of patients with advanced or metastatic RET mutant MTC and RET fusion-positive thyroid cancers, and the FDA set a Prescription Drug User Fee Act, or PDUFA, action date of February 28, 2021 for this NDA. This NDA was submitted under the FDA’s Oncology Center of Excellence Real-Time Oncology Review pilot program, or RTOR program, which aims to explore a more efficient review process to ensure that safe and effective treatments are available to patients as early as possible, while maintaining and improving review quality by the FDA.

We are currently evaluating pralsetinib in an ongoing registration-enabling Phase 1/2 clinical trial in patients with RET-altered NSCLC, MTC and other advanced solid tumors, which we refer to as our ARROW trial. In January 2020, we reported top-line data from the ARROW trial in RET fusion-positive NSCLC patients, and in April 2020, we reported top-line data from the ARROW trial in RET-mutant MTC patients. In June 2020, we presented additional data from the ARROW trial of pralsetinib in RET fusion-positive NSCLC and other RET-altered solid tumors at the American Society of Clinical Oncology Annual Meeting. In September 2020, we announced updated data from the ARROW trial in RET-mutant MTC patients at the European Society for Medical Oncology Virtual Congress 2020. We are also evaluating pralsetinib in an ongoing Phase 3 clinical trial in patients with first-line RET fusion-positive NSCLC, which we refer to as our AcceleRET Lung trial. Pursuant to our collaboration with Roche, we plan to co-develop pralsetinib globally in RET-altered solid tumors, including NSCLC, MTC and other thyroid cancers, as well as other solid tumors.

The FDA has granted orphan drug designation to pralsetinib for the treatment of RET-rearranged NSCLC, JAK1/2-positive NSCLC or TRKC-positive NSCLC, and the FDA has granted breakthrough therapy designation to pralsetinib for the treatment of patients with RET fusion-positive NSCLC that has progressed following platinum-based

chemotherapy and to pralsetinib for the treatment of patients with RET mutation-positive MTC that requires systemic treatment and for which there are no acceptable alternative treatments.

Avapritinib — Gastrointestinal Stromal Tumors

We are also developing and commercializing avapritinib for the treatment of patients with PDGFRA exon 18 mutant gastrointestinal stromal tumors, or GIST, a rare disease that is a sarcoma, or tumor of bone or connective tissue, of the gastrointestinal tract.

Avapritinib is approved in the U.S. under the brand name AYWAKIT for the treatment of adults with unresectable or metastatic GIST harboring a PDGFRA exon 18 mutation, including PDGFRA D842V mutations, and is approved in European Union with conditional marketing authorization under the brand name AYWAKYT as a monotherapy for the treatment of adult patients with unresectable or metastatic GIST harboring PDGFRA D842V mutation. The European Commission has granted orphan medicinal product designation to avapritinib for the treatment of GIST. In addition, in March 2020, the NMPA accepted an NDA submitted by CStone for avapritinib for the treatment of adults with unresectable or metastatic PDGFRA exon 18 mutant GIST and fourth-line GIST. CStone also submitted an NDA to the Taiwan Food and Drug Administration, or the TFDA, for avapritinib for the indication of adult patients with unresectable or metastatic GIST harboring a PDGFRA exon 18 mutation, including PDGFRA D842V mutations, and received priority review designation from the TFDA. As previously announced, we do not plan to further develop avapritinib for additional GIST indications beyond PDGFRA exon 18 mutant GIST.

BLU-945 — Treatment-Resistant EGFR-Mutated NSCLC

We are developing BLU-945 for the treatment of EGFR-mutated NSCLC. BLU-945 is selective investigational inhibitor designed to potently inhibit triple-mutant EGFR harboring either the activating L858R or exon 19 deletion mutations combined with the acquired T790M and C797S mutations, the most common on-target resistance to standard EGFR inhibitors. In addition, BLU-945 was designed to be wild-type EGFR and kinome selective with the potential for improved tolerability and combination strategies. Based on preclinical proof-of-concept data presented in September 2020, we plan to develop BLU-945 as a monotherapy and in combination with other agents for the treatment of patients with treatment-resistant EGFR-mutated NSCLC. We plan to initiate a global Phase 1 dose-escalation trial of BLU-945 in the first half of 2021.

Fisogatinib — Hepatocellular Carcinoma

We are developing fisogatinib for the treatment of advanced hepatocellular carcinoma, or HCC. Fisogatinib is an investigational, orally available, potent and highly selective inhibitor that targets FGFR4, a kinase that is aberrantly activated in a defined subset of patients with HCC, the most common type of liver cancer. We are currently evaluating fisogatinib in an ongoing Phase 1 clinical trial in patients with advanced HCC. As part of our collaboration with CStone, we are also evaluating fisogatinib in combination with CS1001, a clinical-stage anti-PDL1 immunotherapy being developed by CStone, for the treatment of locally advanced or metastatic HCC in an ongoing Phase 1b/2 trial conducted in multiple clinical sites in China. The FDA has granted orphan drug designation to fisogatinib for the treatment of HCC.

Discovery Platform

We plan to continue to leverage our discovery platform to systematically and reproducibly identify kinases that are drivers of diseases in genomically defined patient populations and craft drug candidates that potently and selectively target these kinases. We currently have four wholly-owned discovery programs consisting of the following: BLU-945, our development candidate for the treatment of resistant EGFR-positive triple mutant NSCLC; a pre-development candidate program targeting EGFR Exon 19/L858R+C797S, which we refer to as resistant EGFR-positive double mutant NSCLC; and two pre-development candidate programs for undisclosed kinase targets. We also have up to four discovery programs in cancer immunotherapy under our collaboration with Roche. See “—*Collaborations and Licenses*” below. In addition to BLU-945, we plan to nominate up to two additional development candidates by the end of 2020.

Development and Commercialization Rights

We currently have worldwide development and commercialization rights to avapritinib and fisogatinib, other than the rights licensed to CStone for these drug candidates in Mainland China, Hong Kong, Macau and Taiwan, or the CStone territory. We have worldwide development and commercialization rights to BLU-263. We currently have worldwide development and commercialization rights to all of our discovery programs, including BLU-945, other than the discovery-stage cancer immunotherapy programs under our collaboration with Roche.

We have granted Roche an exclusive license to develop and commercialize pralsetinib worldwide, excluding the CStone territory and the U.S., and a co-exclusive license in the U.S. to develop and commercialize pralsetinib. We have granted CStone an exclusive license to develop and commercialize pralsetinib in the CStone territory. We have granted an exclusive worldwide license to Clementia Pharmaceuticals, Inc., or Clementia, a wholly-owned subsidiary of Ipsen S.A., to develop and commercialize BLU-782.

Collaborations and Licenses

In addition to the collaborations and licenses described below, we will continue to evaluate potential additional collaborations, partnerships and licenses that could maximize the value of our programs and allow us to leverage the expertise of strategic collaborators, partners and licensors, including in additional geographies where we may not have current operations or expertise. We are also focused on engaging in collaborations, partnerships and license agreements to capitalize on our discovery platform outside of our primary strategic focus area of cancer and rare diseases. We may also explore opportunities to acquire or in-license additional businesses, technologies or drugs, form strategic alliances or create joint ventures with third parties that we believe will complement or augment our existing business.

Roche—Immunotherapy Collaboration. In March 2016, we entered into a collaboration with Roche to discover, develop and commercialize up to four small molecule therapeutics targeting kinases believed to be important in cancer immunotherapy (including the kinase target MAP4K1, which is believed to play a role in T cell regulation), as single products or possibly in combination with other therapeutics.

Roche—Pralsetinib Collaboration. In July 2020, we entered into a collaboration with Roche to develop and commercialize pralsetinib for the treatment of RET-altered cancers. Under the collaboration, we and Genentech are co-commercializing GAVRETO in the U.S., and Roche has exclusive commercialization rights for pralsetinib outside of the U.S., excluding the CStone territory. We and Roche also plan to co-develop pralsetinib globally in RET-altered solid tumors, including NSCLC, MTC and other thyroid cancers, and expand development of pralsetinib in multiple treatment settings. Further, we and Roche plan to explore development of a next-generation RET inhibitor as part of the collaboration.

CStone. In June 2018, we entered into a collaboration with CStone to develop and commercialize avapritinib, pralsetinib and fisogatinib, including back-up forms and certain other forms, in the CStone territory either as a monotherapy or as part of a combination therapy.

Clementia. In October 2019, we entered into a license agreement with Clementia and granted Clementia an exclusive, worldwide, royalty-bearing license to develop and commercialize BLU-782, as well as specified other compounds related to the BLU-782 program. BLU-782 is an investigational, orally available, potent and highly selective inhibitor that targets mutant activin-like kinase 2, or ALK2, in development for the treatment of fibrodysplasia ossificans progressiva, or FOP. The FDA has granted a rare pediatric disease designation, orphan drug designation and fast track designation to BLU-782, each for the treatment of FOP.

Note on the COVID-19 Pandemic

Due to the evolving and uncertain global impacts of the COVID-19 pandemic, we cannot precisely determine or quantify the impact this pandemic will have on our business, operations and financial performance for the remainder of our fiscal year ending December 31, 2020 and beyond. We initially established a work-from-home policy for all employees, other than those performing or supporting business-critical activities, such as certain members of our

laboratory and facilities staff. While the majority of employees continue to work from home, we have continued to evaluate and update this policy for each of our locations and field-based employees based on guidance from federal, state and local government authorities. For our ongoing and planned clinical trials, while we anticipate and have experienced some temporary delays or disruptions due to the COVID-19 pandemic, in particular with respect to activation of additional clinical trial sites and patient enrollment rates, we are working with any impacted clinical trial sites to ensure study continuity, enable medical monitoring, facilitate study procedures and maintain clinical data and records, including the use of local laboratories for testing and tumor imaging, home delivery of study drug and remote data and records monitoring. In addition, we currently have sufficient supply or plans for supply to meet our anticipated global commercial and clinical development needs for avapritinib, pralsetinib, fisogatinib and BLU-263 through 2021. However, depending on the length and ultimate impact of the COVID-19 pandemic, our suppliers could be adversely impacted, which may result in delays or disruptions in our current or future supply chain. For our commercial activities for AYVAKIT/AYVAKYT and GAVRETO, we are conducting commercial and medical affairs field activities across our portfolio in virtual formats where possible in order to allow us to continue to serve the needs of healthcare providers, patients and other stakeholders during this critical time. We will continue to assess the duration, scope and severity of the COVID-19 pandemic and the existing and potential impacts on our business, operations and financial performance, and we will continue to work closely with our third-party vendors, collaborators and other parties in order to seek to advance our pipeline of targeted therapies as quickly as possible, while making the health and safety of our employees and their families, healthcare providers, patients and communities a top priority. Please refer to our Risk Factors in Part II, Item IA of this Quarterly Report on Form 10-Q for further discussion of risks related to the COVID-19 pandemic.

Financial Operations Overview

To date, we have financed our operations primarily through public offerings of our common stock, private placements of our convertible preferred and common stock, collaborations, a license agreement, a debt financing and limited product revenue. Through September 30, 2020, we have received an aggregate of \$2.6 billion from such transactions, including \$1.7 billion in aggregate gross proceeds from the sale of common stock in our initial public offering, or IPO, follow-on public offerings and the equity investment by Roche, \$115.1 million in gross proceeds from the issuance of convertible preferred stock, \$855.8 million in upfront payments and milestone payments under our collaborations with Roche and CStone, our license agreement with Clementia and our former collaboration with Alexion Pharma Holding, or Alexion, and \$10.0 million in gross proceeds from a debt financing. In addition, in September 2020, we achieved \$40.0 million in specified regulatory and commercialization milestones as a result of the initial U.S. marketing approval for GAVRETO and received those milestone payments in October 2020.

Since inception, we have incurred significant operating losses, with the exception of the three and nine months ended September 30, 2020. Our net income was \$399.6 million for the nine months ended September 30, 2020 primarily due to the collaboration revenue recorded under our collaboration with Roche for pralsetinib. Our net losses were \$347.7 million, \$236.6 million and \$148.1 million for the years ended December 31, 2019, 2018 and 2017, respectively. As of September 30, 2020, we had an accumulated deficit of \$545.7 million. We expect to continue to incur significant expenses and operating losses over the next few years. However, as a result of our collaboration with Roche for pralsetinib, we expect to record net income for the year ended December 31, 2020. We anticipate that our expenses will continue to increase in connection with our ongoing activities, particularly as we:

- maintain and expand our sales, marketing and distribution infrastructure to continue to commercialize AYVAKIT/AYVAKYT, GAVRETO and any current or future drug candidates for which we may obtain marketing approval;
- seek marketing approval for avapritinib and pralsetinib for additional indications and in additional geographies and seek marketing approvals for any other current or future drug candidates;
- continue to advance clinical development activities for avapritinib and pralsetinib and initiate or advance clinical development activities for other current or future drug candidates;
- continue to discover, validate and develop additional drug candidates or development candidates, including BLU-945;

- continue to manufacture increasing quantities of drug substance and drug product material for use in pre-clinical studies, clinical trials and commercialization;
- conduct development and commercialization activities for companion diagnostic tests for AYWAKIT/AYVAKYT, GAVRETO and any other current or future drug candidates;
- conduct research and development activities under our collaborations with Roche and CStone;
- maintain, expand and protect our intellectual property portfolio;
- acquire or in-license additional businesses, technologies, drugs or drug candidates, form strategic alliances or create joint ventures with third parties;
- hire additional research, clinical, quality, manufacturing, regulatory, commercial and general and administrative personnel; and
- incur additional costs associated with operating as a public company.

Revenue

In January 2020, the FDA granted approval of avapritinib under the brand name AYWAKIT for the treatment of adults with unresectable or metastatic GIST harboring a PDGFRA exon 18 mutation, including PDGFRA D842V mutations. In September 2020, the FDA granted accelerated approval to pralsetinib under the brand name GAVRETO for the treatment of adult patients with metastatic RET fusion-positive NSCLC as detected by an FDA approved test, and the European Commission granted conditional marketing authorization to avapritinib under the brand name AYWAKYT as a monotherapy for the treatment of adult patients with unresectable or metastatic GIST harboring the PDGFRA D842V mutation.

Through September 30, 2020, our revenue consisted of sales of AYWAKIT, GAVRETO and collaboration revenue under our collaborations with Roche and CStone and license agreement with Clementia. Collaboration revenue includes amounts that were recognized related to upfront payments, milestone payments, the equity premium from Roche, and amounts due to us for supply of inventory (under our collaboration and license agreements), research and development services, and license revenue under our license agreement with Clementia.

In the future, we expect to record revenue from a combination of sales of AYWAKIT/AYVAKYT, GAVRETO and any current or future drug candidates for which we receive marketing approval, royalties on drug sales and cost reimbursements, as well as upfront, milestone, profit sharing, royalty and other payments, if any, under any current or future collaborations and licenses, including revenues related to the supply of our drug candidates or approved drugs to our various collaboration partners. We expect that any revenue we generate will fluctuate from quarter to quarter as a result of the timing and amount of product sales, license fees, research and development services and related reimbursements, payments for manufacturing services, and option fees, milestone payments or other payments under our collaboration or license agreements, if any.

Cost of Sales

Our cost of sales includes the cost of producing and distributing inventories that are related to product revenue during the respective period, including salary related and stock-based compensation expense for employees involved with production and distribution, freight, and indirect overhead costs. In addition, shipping and handling costs for product shipments are recorded in cost of sales as incurred. Cost of sales for newly launched products will not be significant until the initial pre-launch inventory is depleted, and additional inventory is manufactured. As a result, the gross margin of our product sales for the three and nine months ended September 30, 2020 was enhanced by use of

active pharmaceutical ingredients and components that were previously expensed as research and development expense in prior years.

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 initiation, 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 AYWAKIT/AYVAKYT, GAVRETO and our drug candidates;
- commercializing AYWAKIT/AYVAKYT, GAVRETO and our drug candidates, if and when approved, whether alone or in collaboration with others;

- market acceptance of AYVAKIT/AYVAKYT, GAVRETO and any future drug we may commercialize; 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 and nine months ended September 30, 2020 and 2019. Other development and pre-development candidate expenses, unallocated expenses and internal research and development expenses have been classified separately.

	<u>Three Months Ended September 30,</u>		<u>Nine Months Ended September 30,</u>	
	<u>2020</u>	<u>2019</u>	<u>2020</u>	<u>2019</u>
	<u>(in thousands)</u>		<u>(in thousands)</u>	
Avapritinib external expenses	\$ 17,477	\$ 18,290	\$ 56,412	\$ 69,953
Pralsetinib external expenses*	10,199	21,963	59,231	59,850
Fisogatinib external expenses	513	2,446	3,284	4,694
BLU-263 external expenses	4,318	1,654	10,382	2,019
Other development and pre-development candidate expenses and unallocated expenses*	17,313	17,550	48,314	51,892
Internal research and development expenses	24,410	19,550	71,833	54,396
Total research and development expenses	\$ 74,230	\$ 81,453	\$ 249,456	\$ 242,804

* Pralsetinib external expenses includes reimbursable expenses under our collaboration for pralsetinib with Roche, and other development and pre-development candidate expenses includes reimbursable expenses under our other collaboration agreements.

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 manufacturing expenses for active pharmaceutical ingredient, or API, drug product and drug substance for current and future clinical trials and commercial inventory. 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 immunotherapy collaboration with Roche, development activities under our collaboration with CStone, development activities under our collaboration for pralsetinib with Roche and development activities for companion diagnostic tests for our products and any current or future drug candidates.

Selling, General and Administrative Expenses

Selling, general and administrative expenses consist primarily of salaries and other related costs, including stock-based compensation, for pre-launch and post-launch commercial operations 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, commercial development activities, legal fees related to intellectual property and corporate matters and fees for accounting and consulting services.

We expect that our selling, general and administrative expenses will continue to increase in the future to support additional research and development activities and commercialization activities, including expanding our sales, marketing and distribution infrastructure to commercialize any drugs for which we may obtain marketing approval for additional indications or in additional geographies and expanding our operations. 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.

Interest Income, net

Interest income, net consists primarily of income earned on cash equivalents and investments. We expect our interest income, net will increase in future periods due to our increase in average investment balances following receipt of the upfront payments related to our collaboration with Roche for pralsetinib.

Other Income (Expense), net

Other income (expense), net consists primarily of foreign currency transaction gains or losses.

Income Tax Expense

Income tax expense consists primarily of income taxes related to the taxable income generated from our collaboration with Roche for pralsetinib and our product sales in the state jurisdictions where we conduct business. We expect our income taxes provisions will increase in future periods due to future taxable income generated from our collaboration with Roche for pralsetinib and the increase in our product sales in the respective state jurisdictions.

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, stock-based compensation and leases.

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, 2019. Other than as described below, there have been no significant changes to our critical accounting policies since December 31, 2019.

Product Revenue

We generated product revenue from sales of AYVAKIT and GAVRETO to a limited number of specialty distributors and specialty pharmacy providers in the U.S. These customers subsequently resell the products or dispense the products directly to patients. In addition, we entered into arrangements with payors that provide for government mandated rebates, discounts and allowances with respect to the utilization of our products.

Product revenue is recognized when the customer takes control of the product, typically upon delivery to the customer. Product revenue is recorded at the net sales price, or transaction price, which includes estimated reserves for variable consideration resulting from chargebacks, government rebates, trade discounts and allowances, product returns and other incentives that are offered within the contract with customers, healthcare providers, payors and other indirect customers relating to the sales of our product. Reserves are established based on the amounts earned or to be claimed on the related sales. Where appropriate, we utilize the expected value method to determine the appropriate amount for estimates of variable consideration based on factors such as our current contractual and statutory requirements, specific known market events and trends, industry data and forecasted customer buying and payment patterns. The amount of variable consideration that is included in the transaction price may be constrained and is included in net product revenues only to the extent that it is probable that a significant reversal in the amount of the cumulative revenue recognized will not occur in a future period. Actual amounts of consideration ultimately received may differ from our estimates. If actual results vary from our estimates, we adjust these estimates, which would affect net product revenue and earnings in the period such variances become known.

Chargebacks: Chargebacks for fees and discounts represent the estimated obligations resulting from contractual commitments to sell product to qualified healthcare providers and government agencies at prices lower than the list prices charged to the customers who directly purchase the product from us. The customers charge us for the difference between what they pay for the product and the ultimate contractually committed or government required lower selling price to the qualified healthcare providers. These reserves are estimated using the expected value method based upon a range of possible outcomes and are established in the same period that the related revenue is recognized, resulting in a reduction of product revenue.

Government rebates: Government rebates consist of Medicare, Tricare and Medicaid rebates, which were estimated using the expected value method, based upon a range of possible outcomes for the estimated payor mix. These reserves are recorded in the same period the related revenue is recognized, resulting in a reduction of product revenue. For Medicare, we also estimate the number of patients in the prescription drug coverage gap for whom we will owe a rebate under the Medicare Part D program.

Trade discounts and allowances: We provide the customers with discounts that are explicitly stated in the contracts and recorded as a reduction of revenue in the period the related product revenue is recognized. In addition, we also receive sales order management, inventory management and data services from the customers in exchange for certain fees.

Product returns: We estimate the amount of product sales that may be returned by our customers and records this estimate as a reduction of revenue in the period the related product revenue is recognized. We currently estimate product return liabilities using expected value method based on available industry data and our visibility into the inventory remaining in the distribution channel.

Other deductions: Co-pay assistance relates to financial assistance provided to qualified patients, whereby we may assist them with prescription drug co-payments required by the patient's insurance provider. Reserves for co-pay assistance are recorded in the same period the related revenue is recognized, resulting in a reduction of product revenue.

Accounts Receivable

Accounts receivables arise from product sales and amounts due from our collaboration partners. The amount from product sales represents amounts due from specialty pharmacy providers in the U.S. We monitor economic conditions to identify facts or circumstances that may indicate that our receivables are at risk of collection. We provide reserves against accounts receivable for estimated losses that may result from a customer's inability to pay based on the composition of our accounts receivable, current economic conditions and historical credit loss activity. Amounts determined to be uncollectible are charged or written-off against the reserve.

Inventory

Inventories are stated at the lower of cost or estimated net realizable value with cost based on the first-in first-out method. Inventory that can be used in either the production of clinical or commercial products is expensed as research and development costs when identified for use in clinical trials.

Prior to the regulatory approval of our drug candidates, we incur expenses for the manufacture of drug product supplies to support clinical development that could potentially be available to support the commercial launch of those drugs. Until the date at which regulatory approval has been received or is otherwise considered probable, we record all such costs as research and development expenses.

We perform an assessment of the recoverability of capitalized inventories during each reporting period and write down any excess and obsolete inventory to its net realizable value in the period in which the impairment is first identified. Such impairment charges, should they occur, are recorded as a component of cost of product sales in the condensed consolidated statements of operations and comprehensive loss. The determination of whether inventory costs will be realizable requires the use of estimates by management. If actual market conditions are less favorable than projected by management, additional write-downs of inventory may be required.

Results of Operations

Comparison of Three Months Ended September 30, 2020 and 2019

The following table summarizes our results of operations for the three months ended September 30, 2020 and 2019, together with the changes in those items in dollars and as a percentage:

	Three Months Ended September 30,		Dollar Change	% Change
	2020	2019 (in thousands)		
Revenues:				
Product revenue, net	\$ 6,308	\$ —	\$ 6,308	100 %
Collaboration revenue	738,810	9,139	729,671	7,984
Total revenues	745,118	9,139	735,979	8,053
Cost and operating expenses:				
Cost of sales	146	—	146	100
Research and development	74,230	81,453	(7,223)	(9)
Selling, general and administrative	37,375	25,647	11,728	46
Total cost and operating expenses	111,751	107,100	4,651	4
Other income (expense):				
Interest income, net	1,173	3,758	(2,585)	(69)
Other income (expense), net	(192)	(72)	(120)	(167)
Total other income	981	3,686	(2,705)	(73)
Income (loss) before income taxes	634,348	(94,275)	728,623	773
Income tax expense	370	—	370	100
Net income (loss)	\$ 633,978	\$ (94,275)	\$ 728,253	772 %

Product Revenue, Net

Product revenue, net was \$6.3 million for the three months ended September 30, 2020.

We started generating revenue from sales of AYVAKIT in the first quarter of 2020 following FDA approval of AYVAKIT for the treatment of adults with unresectable or metastatic GIST harboring a PDGFRA exon 18 mutation, including PDGFRA D842V mutations. For the three months ended September 30, 2020, we recorded net product revenue of \$6.1 million.

We started generating revenue from sales of GAVRETO in the third quarter of 2020 following FDA approval of GAVRETO for the treatment of adult patients with metastatic RET fusion-positive NSCLC. For the three months ended September 30, 2020, we recorded net product revenue of \$0.2 million.

Collaboration Revenue

Collaboration revenue increased by \$729.7 million from \$9.1 million for the three months ended September 30, 2019 to \$738.8 million for the three months ended September 30, 2020. For the three months ended September 30, 2020, our collaboration revenue consisted of \$736.6 million in revenue under our collaboration with Roche for pralsetinib and \$2.2 million in revenue under our immunotherapy collaboration with Roche. Revenue recognized under our collaboration with Roche for pralsetinib for the three months ended September 30, 2020 consisted of \$675.0 million upfront cash payment, \$20.7 million premium associated with the \$100.0 million equity investment by Roche, \$40.0 million in specified regulatory and commercialization milestone payments as a result of the initial U.S. marketing approval for GAVRETO and \$0.9 million associated with services related to Roche territory-specific activities. We recognized \$2.2 million in revenue under our cancer immunotherapy collaboration with Roche for the three months ended September 30, 2020, which was primarily related to amortization of the total \$63.0 million of upfront and milestone payments received as of such period.

For the three months ended September 30, 2019, our collaboration revenue mainly consisted of \$6.0 million in revenue under our CStone collaboration and \$3.1 million in revenue under our cancer immunotherapy collaboration with

Roche. Revenue recognized under the CStone collaboration for the three months ended September 30, 2019 consisted of \$6.0 million in milestone revenue related to development and regulatory milestones that were either achieved or deemed probable during the third quarter of 2019. We recognized \$3.1 million in revenue under our cancer immunotherapy collaboration with Roche for the three months ended September 30, 2019, which was primarily related to amortization of the total \$55.0 million of upfront and milestone payments received as of such period.

Cost of Product Sales

Cost of product sales was \$0.1 million for the three months ended September 30, 2020 and was related to manufacturing costs associated with our products sales. Costs associated with the manufacture of our products prior to FDA approval were expensed and, therefore, are not included in cost of sales during the current period.

Research and Development Expense

Research and development expense decreased by \$7.2 million from \$81.5 million for the three months ended September 30, 2019 to \$74.2 million for the three months ended September 30, 2020. The decrease in research and development expense was primarily related to a \$9.7 million reimbursement from global development cost sharing arrangement under our collaboration with Roche for pralsetinib. This decrease in research and development expense was offset primarily by an increase of approximately \$2.2 million in personnel expenses due to an increase in headcount, which was driven by growth in the clinical and manufacturing organizations, and an increase of \$1.0 million in stock-based compensation expense.

Selling, General and Administrative Expense

Selling, general and administrative expense increased by \$11.7 million from \$25.6 million for the three months ended September 30, 2019 to \$37.4 million for the three months ended September 30, 2020. The increase in selling, general and administrative expense was primarily related to an increase of \$10.2 million in personnel expenses, including an increase of \$3.7 million in stock-based compensation expense, as well as an increase of \$4.7 million in commercial expenses to build our commercial infrastructure for commercialization of AYWAKIT/AYVAKYT and GAVRETO. The increase in selling, general and administrative expense was partially offset by a \$5.3 million reimbursement in connection with the commercialization of GAVRETO in the U.S. under our collaboration with Roche for pralsetinib.

Interest Income, Net

Interest income, net, decreased by \$2.6 million from \$3.8 million for the three months ended September 30, 2019 to \$1.2 million for the three months ended September 30, 2020. The decrease was primarily due to a lower rate of return on investments caused by the severe liquidity crisis in the capital markets resulting from the COVID-19 pandemic.

Other Income (Expense), Net

Other expenses, net, increased by \$0.1 million from \$0.1 million for the three months ended September 30, 2019 to \$0.2 million for the three months ended September 30, 2020.

Income Tax Expense

Income tax expense consisted of \$0.4 million for the three months ended September 30, 2020, related to the income taxes provisions associated with the taxable income generated from our collaboration with Roche for pralsetinib and our product sales in certain state jurisdictions.

Comparison of Nine Months Ended September 30, 2020 and 2019

The following table summarizes our results of operations for the nine months ended September 30, 2020 and 2019, together with the changes in those items in dollars and as a percentage:

	Nine Months Ended September 30,		Dollar Change	% Change
	2020	2019		
(in thousands)				
Revenues:				
Product revenue, net	\$ 15,446	\$ —	\$ 15,446	100 %
Collaboration revenue	744,183	14,979	729,204	4,868
Total revenues	759,629	14,979	744,650	4,971
Cost and operating expenses:				
Cost of sales	297	—	297	100
Research and development	249,456	242,804	6,652	3
Selling, general and administrative	115,203	64,123	51,080	80
Total cost and operating expenses	364,956	306,927	58,029	19
Other income (expense):				
Interest income, net	5,663	10,742	(5,079)	(47)
Other income (expense), net	(416)	(157)	(259)	(165)
Total other income (expense), net	5,247	10,585	(5,338)	(50)
Income (loss) before income taxes	399,920	(281,363)	681,283	242
Income tax expense	370	—	370	100
Net income (loss)	<u>\$ 399,550</u>	<u>\$ (281,363)</u>	<u>\$ 680,913</u>	<u>242 %</u>

Product Revenue, Net

Product revenue, net was \$15.4 million for the nine months ended September 30, 2020.

We started generating revenue from sales of AYVAKIT in the first quarter of 2020 following FDA approval of AYVAKIT for the treatment of adults with unresectable or metastatic GIST harboring a PDGFRA exon 18 mutation, including PDGFRA D842V mutations. For the nine months ended September 30, 2020, we recorded net product revenue of \$15.2 million.

We started generating revenue from sales of GAVRETO in the third quarter of 2020 following FDA approval of GAVRETO for the treatment of adult patients with metastatic RET fusion-positive NSCLC. For the nine months ended September 30, 2020, we recorded net product revenue of \$0.2 million.

Collaboration Revenue

Collaboration revenue increased by \$729.2 million from \$15.0 million for the nine months ended September 30, 2019 to \$744.2 million for the nine months ended September 30, 2020. For the nine months ended September 30, 2020, our collaboration revenue mainly consisted of \$736.6 million in revenue under our collaboration agreement with Roche for pralsetinib, \$3.5 million in revenue under our CStone collaboration, and \$3.8 million revenue under our cancer immunotherapy collaboration with Roche. Revenue recognized under our collaboration with Roche for pralsetinib for the nine months ended September 30, 2020 consisted of \$675.0 million upfront cash payment, \$20.7 million premium associated with the \$100.0 million equity investment by Roche, \$40.0 million in specified regulatory and commercialization milestone payments as a result of the initial U.S. marketing approval for GAVRETO and \$0.9 million associated with services related to Roche territory-specific activities. Revenue recognized under our CStone collaboration for the nine months ended September 30, 2020 primarily consisted of \$2.0 million in milestone revenue related to a development milestone that was achieved as of such period and \$1.5 million associated with manufacturing services related to CStone territory-specific activities. We recognized \$3.8 million in revenue under our cancer immunotherapy collaboration with Roche for the nine months ended September 30, 2020, which was primarily related to amortization of the total \$63.0 million of upfront and milestone payments received as of such period.

For the nine months ended September 30, 2019, our collaboration revenue mainly consisted of \$10.1 million in revenue under our CStone collaboration and \$4.8 million in revenue under our cancer immunotherapy collaboration with Roche. Revenue recognized under our CStone collaboration for the nine months ended September 30, 2019 primarily consisted of \$10.0 million in milestone revenue related to development and regulatory milestones that were either achieved or deemed probable as of such period. We recognized \$4.8 million in revenue under our cancer immunotherapy collaboration with Roche for the nine months ended September 30, 2019, which was primarily related to amortization of the total \$55.0 million of upfront and milestone payments received as of such period.

Cost of Product Sales

Cost of product sales was \$0.3 million for the nine months ended September 30, 2020 and was related to manufacturing costs associated with our product sales. Costs associated with the manufacture of our products prior to FDA approval were expensed and, therefore, are not included in cost of sales during the current period.

Research and Development Expense

Research and development expense increased by \$6.7 million from \$242.8 million for the nine months ended September 30, 2019 to \$249.5 million for the nine months ended September 30, 2020. The increase in research and development expense was primarily related to an increase of approximately \$14.7 million in personnel expenses, primarily due to an increase in headcount, which was driven by growth in the clinical and manufacturing organizations and an increase of \$4.2 million in stock-based compensation expense. The increase in research and development expense was partially offset by a \$9.7 million reimbursement from global development cost sharing under our collaboration with Roche for pralsetinib.

Selling, General and Administrative Expense

Selling, general and administrative expense increased by \$51.1 million from \$64.1 million for the nine months ended September 30, 2019 to \$115.2 million for the nine months ended September 30, 2020. The increase in selling, general and administrative expense was primarily related to an increase of approximately \$39.2 million in personnel expenses, including an increase of \$12.9 million in stock-based compensation expense, as well as an increase of \$12.6 million in commercial expenses to build our commercial infrastructure for commercialization of AYWAKIT/AYWAKYT and GAVRETO. The increase in selling, general and administrative expense was partially offset by a \$5.3 million reimbursement in connection with the commercialization of GAVRETO in the U.S. under our collaboration with Roche for pralsetinib.

Interest Income, Net

Interest income, net, decreased by \$5.1 million from \$10.7 million for the nine months ended September 30, 2019 to \$5.7 million for the nine months ended September 30, 2020. The decrease was primarily due to a lower rate of return on investments caused by the severe liquidity crisis in the capital markets resulting from the COVID-19 pandemic.

Other Income (Expense), Net

Other expenses, net, increased by \$0.3 million from \$0.2 million for the nine months ended September 30, 2019 to \$0.4 million for the nine months ended September 30, 2020.

Income Tax Expense

Income tax expense consisted of \$0.4 million for the nine months ended September 30, 2020, related to the income taxes provisions associated with the taxable income generated from our collaboration with Roche for pralsetinib and our product sales in certain state jurisdictions.

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 and common stock, collaborations, a license agreement, a debt financing and limited product revenue. Through September 30, 2020, we have received an aggregate of \$2.6 billion from such transactions, including \$1.7 billion in aggregate gross proceeds from the sale of common stock in our IPO, follow-on public offerings and the equity investment by Roche, \$115.1 million in gross proceeds from the issuance of convertible preferred stock, \$855.8 million in upfront payments and milestone payments under our collaborations with Roche and CStone, our license agreement with Clementia and our former collaboration with Alexion, and \$10.0 million in gross proceeds from a debt financing. In addition, in September 2020, we achieved \$40.0 million in specified regulatory and commercialization milestones as a result of the initial U.S. marketing approval for GAVRETO and received those milestone payments in October 2020.

As of September 30, 2020, we had cash, cash equivalents and investments of \$1,355.9 million.

Cash Flows

The following table provides information regarding our cash flows for the nine months ended September 30, 2020 and 2019:

(in thousands)	Nine Months Ended September 30,	
	2020	2019
Net cash provided by (used in) operating activities	\$ 411,834	\$ (233,120)
Net cash used in investing activities	(358,717)	(84,202)
Net cash provided by financing activities	397,666	338,804
Net increase in cash and cash equivalents	<u>\$ 450,783</u>	<u>\$ 21,482</u>

Net Cash Provided by (Used in) Operating Activities. For the nine months ended September 30, 2020, compared to the same period in 2019, the \$645.0 million increase in net cash provided by operating activities was primarily due to the increased net income during this period of \$680.9 million, which was driven by the \$736.6 million collaboration revenue recognized under our collaboration agreement with Roche for pralsetinib.

Net Cash Used in Investing Activities. For the nine months ended September 30, 2020, compared to the same period in 2019, the \$274.5 million increase in net cash used in investing activities was primarily due to an increase in net purchases of available-for-sale investments.

Net Cash Provided by Financing Activities. For the nine months ended September 30, 2020, compared to the same period in 2019, the \$58.9 million increase in net cash provided by financing activities was primarily due to the \$79.3 million received from the issuance of common stock related to the collaboration agreement with Roche for pralsetinib, offset by an \$18.7 million decrease in net proceeds received from our January 2020 follow-on public offering as compared with our April 2019 follow-on public offering.

Funding Requirements

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, including marketing approval for avapritinib and pralsetinib for additional indications or in additional geographies. In addition, we expect to incur additional significant commercialization expenses for AYVAKIT/AYVAKYT, GAVRETO and other drug candidates, if approved, related to drug sales, marketing, manufacturing and distribution to the extent that such sales, marketing, manufacturing and distribution are not the responsibility of potential collaborators or licensors. We will also incur additional significant costs if we choose to pursue additional indications or geographies for any of our approved drugs or drug candidates or otherwise expand more rapidly than we presently anticipate. Accordingly, we may seek to obtain additional funding from time to time in connection with our continuing operations. If we are unable to

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

As of September 30, 2020, we had cash, cash equivalents and investments of \$1,355.9 million. Based on our current operating plans, we anticipate our existing cash, cash equivalents and investments, together with anticipated future product revenues, will provide sufficient capital to enable us to achieve a self-sustainable financial profile.

Our future capital requirements will depend on many factors, including:

- the success of our commercialization efforts and market acceptance for AYVAKIT/AYVAKYT, GAVRETO or any of our current or future drug candidates for which we receive marketing approval;
- the costs of maintaining, expanding or contracting for sales, marketing and distribution capabilities in connection with commercialization of AYVAKIT/AYVAKYT, GAVRETO and any of our current or future drug candidates for which we receive marketing approval;
- the costs of securing manufacturing, packaging and labeling arrangements for development activities and commercial production, including API, drug substance and drug product material for use in pre-clinical studies, clinical trials, our compassionate use program and for use as commercial supply, as applicable;
- the scope, progress, results and costs of drug discovery, pre-clinical development, laboratory testing and clinical trials for our approved drugs and drug candidates;
- the costs, timing and outcome of regulatory review of marketing applications for our drug candidates, including seeking marketing approval for avapritinib and pralsetinib for additional indications or in additional geographies;
- the success of our collaborations with Roche and CStone and our license agreement with Clementia, as well as our ability to establish and maintain additional collaborations, partnerships or licenses on favorable terms, if at all;
- the achievement of milestones or occurrence of other developments that trigger payments under our existing collaboration or license agreements, or any collaboration, partnership or license agreements that we may enter into in the future;
- the extent to which we are obligated to reimburse, or entitled to reimbursement of, research and development, clinical or other costs under future collaboration agreements, if any;
- the extent to which we acquire or in-license other approved drugs, drug candidates or technologies and the terms of any such arrangements;
- the success of our current or future collaborations for the development and commercialization of 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; and
- the costs of continuing to expand our operations.

Identifying potential drug candidates, conducting pre-clinical development and testing and clinical trials and, for any drug candidates that receive marketing approval, establishing and maintaining commercial infrastructure 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 additional marketing approvals, including for avapritinib and pralsetinib for additional indications or in additional geographies, and achieve substantial revenues for any of our drugs that receive marketing

approval, including for AYVAKIT/AYVAKYT and GAVRETO. In addition, our drugs and any current or future drug candidates that receive marketing approvals, including avapritinib or pralsetinib for additional indications or in additional geographies, may not achieve commercial success. Accordingly, we may need 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 primarily 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 and the license agreement with Clementia, 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, drugs 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 and drug candidates that we would otherwise prefer to develop and market ourselves.

Contractual Obligations

Our contractual obligations primarily consist of our obligations under non-cancellable operating leases and unconditional purchase obligations.

During the nine months ended September 30, 2020, except for minimum purchase obligations associated with certain commercial manufacturing agreements of approximately \$25.5 million disclosed in Note 15 to our condensed consolidated financial statements, there have been no other material changes to our contractual obligations and commitments from those described under “Management’s Discussion and Analysis of Financial Condition and Results of Operations” included in the Annual Report on Form 10-K for the year ended December 31, 2019.

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 September 30, 2020 and December 31, 2019, we had cash, cash equivalents and investments of \$1,355.9 million and \$548.0 million, respectively, consisting primarily of money market funds and investments in U.S. government agency and 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, including recent changes resulting from the impact of the COVID-19 pandemic. 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, including recent changes resulting from the impact of the COVID-19 pandemic. From time to time, we contract with vendors that are

located in 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 September 30, 2020 and December 31, 2019, we had minimal or no liabilities denominated in foreign currencies.

Inflation generally affects us by increasing our cost of labor, clinical trial and manufacturing costs. We do not believe that inflation had a material effect on our business, financial condition or results of operations during the three and nine months ended September 30, 2020 and 2019.

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 September 30, 2020. Based upon such evaluation, our Chief Executive Officer and Chief Financial Officer have concluded that, as of September 30, 2020, 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 the Section titled “Forward-Looking Statements” 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. 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. To date, we have not yet demonstrated our ability to conduct large-scale sales and marketing activities necessary for successful commercialization. We currently have two approved precision therapies and are transitioning to a company capable of supporting commercial activities. We may not be successful in such a transition.

We commenced operations in April 2011 and we have focused substantially all of our efforts and financial resources to date 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, conducting pre-clinical studies and clinical development for our drug candidates, commencing pre-commercial activities and the commercial launches for AYVAKIT/AYVAKYT and GAVRETO, and producing the active pharmaceutical ingredient, or API, drug substance and drug product material for use in pre-clinical studies and clinical trials for our drug candidates and commercial sale of AYVAKIT/AYVAKYT and GAVRETO. To date, we have financed our operations primarily through public offerings of our common stock, private placements of our convertible preferred and common stock, collaborations, a license agreement, a debt financing and limited product revenue. Through September 30, 2020, we have received an aggregate of \$2.6 billion from such transactions, including \$1.7 billion in aggregate gross proceeds from the sale of common stock in our initial public offering, follow-on public offerings and the equity investment by Roche, \$115.1 million in gross proceeds from the issuance of convertible preferred stock, \$855.8 million in upfront payments and milestone payments under our collaborations with Roche and CStone, our license agreement with Clementia and our former collaboration with Alexion Pharma Holding, and \$10.0 million in gross proceeds from a debt financing. In addition, in September 2020, we achieved \$40.0 million in specified regulatory and commercialization milestones as a result of the initial U.S. marketing approval for GAVRETO and received those milestone payments in October 2020.

Since inception, we have incurred significant operating losses, with the exception of the three and nine months ended September 30, 2020. Our net income was \$399.6 million for the nine months ended September 30, 2020 primarily due to the collaboration revenue recorded under our collaboration with Roche for pralsetinib, and our net losses were \$347.7 million, \$236.6 million, and \$148.1 million for the years ended December 31, 2019, 2018 and 2017, respectively. As of September 30, 2020, we had an accumulated deficit of \$545.7 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 few years. We anticipate that our expenses will continue to increase in connection with our ongoing activities. 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, we will incur significant sales, marketing and outsourced-manufacturing expenses in connection with the commercialization of any of our approved drugs. In addition, we have incurred and will continue to incur substantial costs associated with operating as a public company. 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 substantial revenue.

To date, we have not generated substantial revenue from drug sales. Our ability to generate substantial 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;
- continue to maintain and expand commercial manufacturing capabilities or make arrangements with third-party manufacturers for clinical supply and commercial manufacturing;
- establish and maintain a sales, marketing and distribution infrastructure to commercialize AYWAKIT/AYWAKYT, GAVRETO and any current or future drug candidates for which we obtain marketing approval; and
- achieve market acceptance in the medical community and with third-party payors for AYWAKIT/AYWAKYT, GAVRETO and any current or future drug candidates for which we receive marketing approval.

We expect to incur significant sales and marketing costs as we commercialize AYWAKIT/AYWAKYT, jointly commercialize GAVRETO with Roche and commercialize any current or future drug candidates for which we receive marketing approval. 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.

Our business, results of operations and future growth prospects could be materially and adversely affected by the COVID-19 pandemic.

Due to the evolving and uncertain global impacts of the COVID-19 pandemic, we cannot precisely determine or quantify the impact this pandemic will have on our business operations for the remainder of our fiscal year ending December 31, 2020 or beyond. The extent to which COVID-19 may impact our business, results of operations and future growth prospects will depend on a variety of factors and future developments, which are highly uncertain and cannot be predicted with confidence, including the duration, scope and severity of the pandemic, the duration and extent of travel restrictions and social distancing in the U.S. and other countries, business closures or business disruptions and the effectiveness of actions taken in the U.S. and other countries to contain and treat COVID-19.

For example, public health actions being undertaken globally in response to the COVID-19 pandemic, including quarantines, stay-at-home, executive and similar government orders and the prioritization of healthcare resources, could adversely impact our business, results of operations and future growth prospects. For ongoing and planned clinical trials, we anticipate and have experienced some temporary delays or disruptions due to the COVID-19 pandemic, including limited or reduced patient access to trial investigators, hospitals and trial sites, delayed initiation of new clinical trial sites and limited on-site personnel support at various trial sites, which could adversely impact our development plans, including the initiation of planned clinical trials, the rate of enrollment and our ability to conduct ongoing clinical trials. There may also be local orders affecting one or more trial sites, which may trigger mandated changes to our clinical trial protocols or temporary suspensions in the affected trial sites. In addition, quarantines, stay-at-home, executive and similar government orders, or the perception that such orders, shutdowns or other restrictions on the conduct of business operations have occurred and could continue to occur or be expanded in scope or duration,

which could adversely impact ongoing and planned clinical trials, our employees and business operations, personnel at our third-party suppliers and other vendors in the U.S. and other countries, the availability, cost or supply of materials, which may cause delays or disruptions to development plans for our drug candidates or clinical or commercial supply chains for our current or future approved drugs and drug candidates, and sales and marketing activities related to AYVAKIT/AYVAKYT, GAVRETO and any drug candidates for which we may receive marketing approval in the U.S. or other geographies in the future.

To the extent the COVID-19 pandemic adversely affects our business, results of operations and future growth prospects, it may also have the effect of heightening many of the other risks described in this “Risk Factors” section.

We may seek to raise additional funding from time to time. If we are unable to raise capital when needed, we may 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 multiple drug candidates and development programs through clinical and preclinical 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, including marketing approval for avapritinib for additional indications or in additional geographies and for pralsetinib. In addition, we expect to incur additional significant commercialization expenses for AYVAKIT/AYVAKYT, GAVRETO and other drug candidates, if approved, related to drug sales, marketing, manufacturing and distribution to the extent that such sales, marketing, manufacturing and distribution are not the responsibility of potential collaborators or licensors. We may also need to raise additional funds if we choose to pursue additional indications or geographies for any of our approved drugs or drug candidates or otherwise expand more rapidly than we presently anticipate. Accordingly, we may seek additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on attractive terms, we may be forced to delay, reduce or eliminate certain of our research and development programs or future commercialization efforts.

Our future capital requirements will depend on and could increase significantly as a result of many factors, including:

- the success of our commercialization efforts and market acceptance for AYVAKIT/AYVAKYT, GAVRETO or any of our current or future drug candidates for which we receive marketing approval;
- the costs of maintaining, expanding or contracting for sales, marketing and distribution capabilities in connection with commercialization of AYVAKIT/AYVAKYT, GAVRETO and any of our current or future drug candidates for which we receive marketing approval;
- the costs of securing manufacturing, packaging and labeling arrangements for development activities and commercial production, including API, drug substance and drug product material for use in pre-clinical studies, clinical trials, our compassionate use program and for use as commercial supply, as applicable;
- the scope, progress, results and costs of drug discovery, pre-clinical development, laboratory testing and clinical trials for our approved drugs and drug candidates;
- the costs, timing and outcome of regulatory review of marketing applications for our drug candidates, including seeking marketing approval for avapritinib and pralsetinib for additional indications or in additional geographies;
- the success of our collaborations with Roche and CStone and our license agreement with Clementia, as well as our ability to establish and maintain additional collaborations, partnerships or licenses on favorable terms, if at all;
- the achievement of milestones or occurrence of other developments that trigger payments under our existing collaboration or license agreements, or any collaboration, partnership or license agreements that we may enter into in the future;

- the extent to which we are obligated to reimburse, or entitled to reimbursement of, research and development, clinical or other costs under future collaboration agreements, if any;
- the extent to which we acquire or in-license other approved drugs, drug candidates or technologies and the terms of any such arrangements;
- the success of our current or future collaborations for the development and commercialization of 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; and
- the costs of continuing to expand our operations.

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 additional marketing approvals, including for avapritinib and pralsetinib for additional indications or in additional geographies, and achieve sales for any of our drug candidates that receive marketing approval. In addition, our approved drugs and drug candidates, if approved, may not achieve commercial success. Accordingly, we may need 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.

Any additional fundraising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize any of our approved drugs or 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 collaborations, partnerships, licensing arrangements or otherwise at an earlier stage than would be desirable and we may be required to relinquish rights to some of our technologies, drugs 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 of our approved drugs 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 primarily 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 and the license agreement with Clementia, 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, drugs 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 drugs and drug candidates that we would otherwise prefer to develop and market ourselves.

Risks Related to Drug Development and Regulatory Approval

If we are unable to advance our drug candidates to clinical development, obtain regulatory approval for our drug candidates, including for avapritinib and pralsetinib for additional indications or in additional geographies, and ultimately commercialize them, or experience significant delays in doing so, our business will be materially harmed.

We have four drug candidates currently in clinical development: avapritinib, pralsetinib, fisogatinib and BLU-263. All of our other drug candidates and development candidates are currently in pre-clinical or earlier stages of development. We have invested significant efforts and financial resources in the identification and pre-clinical development of kinase inhibitors, including the development of our drugs and drug candidates. Our ability to generate substantial drug revenues, if ever, will depend heavily on the successful development and commercialization of our drugs and drug candidates. Each of our drug candidates, including avapritinib and pralsetinib for additional indications or in additional geographies, 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 substantial revenues from drug sales. Further clinical development, manufacturing and regulatory activities, and substantial investment will be required before we may obtain marketing approval for avapritinib and pralsetinib for additional indications or in additional geographies, if at all. 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, or to identify appropriate patients for any drug candidates for which we obtain approval, we may be required or 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 or plan to enter into agreements with third parties to develop and/or commercialize companion diagnostics for avapritinib in order to identify GIST patients with the PDGFRA D842V mutation, fisogatinib in order to identify HCC patients with FGFR4 pathway activation and pralsetinib in order to identify NSCLC patients with RET fusions and medullary thyroid carcinoma, or MTC patients with RET mutations. Companion diagnostic tests are subject to regulation as medical devices and must themselves be cleared or approved for marketing by the FDA or certain other foreign regulatory agencies before we may commercialize our drug candidates. The success of our approved drugs and drug candidates will depend on several factors, including the following:

- successful enrollment in, and initiation and completion of, clinical trials, including our ongoing and planned clinical trials for avapritinib, pralsetinib, fisogatinib and BLU-263 and other current or future drug candidates;
- successful initiation and completion of pre-clinical studies for our other drug candidates;

- approval of INDs to commence 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-parties for clinical supply and commercial manufacturing, packaging and labeling and the receipt by such third-party manufacturers of requisite approvals to supply commercial inventories of our approved drugs and drug candidates;
- obtaining and maintaining patent and trade secret protection or regulatory exclusivity for our drugs and drug candidates;
- successful commercialization of our approved drugs and drug candidates, if and when approved, whether alone or in collaboration with others;
- acceptance of our approved drugs and 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 our approved drugs and 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.

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, including avapritinib for additional indications, 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 U.S. 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, we have experienced some temporary delays or disruptions in enrollment in our ongoing clinical trials due to the COVID-19 pandemic, and we anticipate we may experience additional delays or disruptions in the future due to the COVID-19 pandemic and changes in local site or IRB policies, availabilities of site staff, reprioritization of hospital resources, restricted access to healthcare professionals and testing sites and other containment measures or concerns among patients about participating in clinical trials during a pandemic. In addition, some of our competitors have ongoing clinical trials for drug candidates that treat the same indications as AYVAKIT/AYVAKYT, GAVRETO and 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 AYVAKIT/AYVAKYT, GAVRETO and our drug candidates are relatively small, it may be difficult to successfully identify patients, which could delay enrollment for our trials.

We focus our research and development on treatments for cancer and rare diseases, including genomically defined cancer and diseases driven by abnormal kinase activation. Because the target patient populations for AYVAKIT/AYVAKYT, GAVRETO and our drug candidates are relatively small, it may be difficult to successfully identify patients. We have entered into or plan to enter into agreements with third parties to develop a companion diagnostic test for avapritinib in order to identify GIST patients with the PDGFRA D842V mutation, fisogatinib in order to identify HCC patients with FGFR4 pathway activation and pralsetinib in order to identify NSCLC patients with RET fusions and MTC patients with RET mutations, and we may engage third parties to develop companion diagnostic tests for use in some of our other current or future clinical trials. However, we may experience delays in reaching, or fail to reach, agreement on acceptable terms to develop companion diagnostic tests with third parties, and any third parties whom we engage to develop companion diagnostic tests may experience delays or may not be successful in developing such companion diagnostic tests, furthering the difficulty in identifying patients for our clinical trials. In addition, current commercially available diagnostic tests to identify appropriate patients for our clinical trials or any approved drug candidates may become unavailable in the future.

Our inability to enroll a sufficient number of patients in our clinical trials, or to identify patients appropriate for enrollment 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.

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, such drug candidates, and our ability to generate revenue will be materially impaired.

Our drug candidates and any companion diagnostic tests related to our approved drugs or drug candidates, including the companion diagnostic tests that we are developing or have developed for AYVAKIT/AYVAKYT in order to identify GIST patients with the PDGFRA D842V mutation, pralsetinib in order to identify NSCLC patients with RET fusions and MTC patients with RET mutations and fisogatinib in order to identify HCC patients with FGFR4 pathway activation, 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 U.S. 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 clearance or approval for any related companion diagnostic tests, including the companion diagnostic tests that we are developing for avapritinib and fisogatinib.

We have 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 U.S. 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. We currently have marketing applications pending for pralsetinib in the U.S. and Europe.

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 U.S. 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;
- 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; and
- delays or disruptions impacting the FDA or comparable foreign regulatory authorities due to the COVID-19 pandemic.

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 other post-marketing requirements, 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 companion diagnostic tests related to our approved drugs and drug candidates, the commercial prospects for our approved drugs or drug candidates may be harmed and our ability to generate revenues will be materially impaired.

Our drugs and 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 any of our approved drugs or 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 approved drugs and 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 drugs or 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 clinical trials or result in potential product liability claims. Any of these occurrences may harm our business, financial condition and prospects significantly.

Further, our approved drugs and drug candidates could cause undesirable side effects in pre-clinical studies or 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 approved drugs or 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 drugs or drug candidates may only be uncovered with a significantly larger number of patients exposed to the drugs or drug candidate. If we or others identify undesirable side effects caused by any of our approved drugs or drug candidates (or any other similar drugs) after marketing approval, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw or limit their approval of such drug;
- 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 is distributed or administered, conduct additional clinical trials or change the labeling of such drug;
- 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 from the marketplace;
- we could be sued and held liable for injury caused to individuals exposed to or taking our drugs and 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 drugs or drug candidates and could substantially increase the costs of commercializing our approved drugs and drug candidates, if approved, and significantly impact our ability to successfully commercialize our approved drugs and drug candidates and generate revenues.

A breakthrough therapy designation by the FDA for our drug candidates, including avapritinib and pralsetinib, 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 pralsetinib for the treatment of patients with RET fusion-positive NSCLC that has progressed following platinum-based chemotherapy and to pralsetinib 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. As of June 23, 2020, the FDA noted it is continuing to ensure timely reviews of applications for medical products during the COVID-19 pandemic in line with its user fee performance goals; however, the FDA may not be able to continue its current pace and review timelines could be extended.

While we have received orphan drug designation for our drug candidates avapritinib, pralsetinib and fisogatinib 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 pralsetinib for the treatment of RET-rearranged NSCLC, JAK1/2-positive NSCLC or TRKC-positive NSCLC and to fisogatinib for the treatment of HCC. 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 U.S. 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 U.S., or a patient population greater than 200,000 in the U.S. where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the U.S. In the

U.S., 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 European Medicines Agency, or EMA, 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 drug 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 U.S. 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 U.S. 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 continue seek orphan drug designation for our drug candidates, 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.

Review of our NDA for pralsetinib for the treatment of patients with advanced or metastatic RET mutant MTC and RET fusion-positive thyroid cancers under the FDA's RTOR program and planned additional marketing applications for pralsetinib for RET fusion-positive NSCLC through the FDA's Project Orbis initiative may not lead to a faster regulatory review or approval for pralsetinib, and they do not increase the likelihood that pralsetinib will obtain marketing approval.

The FDA and other regulatory bodies periodically introduce pilot programs with the goal of a more efficient review of applications for drug or biologic approval, including the Oncology Center of Excellence Real-Time Oncology Review pilot program, or RTOR program, which is currently being tested by the FDA. The RTOR program aims to explore a more efficient review process to ensure that safe and effective treatments are available to patients as early as possible, while maintaining and improving review quality by the FDA. The FDA's Project Orbis initiative provides a framework for concurrent submission and review of marketing applications for oncology products among international health authorities.

Pralsetinib is approved in the U.S. with accelerated approval under the brand name GAVRETO for the treatment of adult patients with metastatic RET fusion-positive NSCLC as detected by an FDA approved test. In addition, the EMA is currently reviewing our MAA for pralsetinib for RET fusion-positive NSCLC. We plan to submit additional marketing applications for pralsetinib for RET fusion-positive NSCLC through the FDA's Project Orbis initiative, which provides a framework for concurrent submission and review of marketing applications for oncology products among international health authorities. In the second quarter of 2020, we submitted an NDA to the FDA for pralsetinib for the treatment of patients with advanced or metastatic RET mutant MTC and RET fusion-positive thyroid

cancers and the FDA set a Prescription Drug User Fee Act, or PDUFA, action date of February 28, 2021. This NDA was submitted under the FDA's Oncology Center of Excellence Real-Time Oncology Review pilot program, or RTOR program, which aims to explore a more efficient review process to ensure that safe and effective treatments are available to patients as early as possible, while maintaining and improving review quality by the FDA.

Acceptance into the RTOR program and Project Orbis initiative does not guarantee or influence approvability of any current or future marketing applications for pralsetinib in patients with RET fusion-positive NSCLC or patients with advanced or metastatic RET mutant MTC and RET fusion-positive thyroid cancers, which are subject to the standard benefit-risk evaluation by the FDA and any other applicable health authority. In addition, we may not derive any benefit, such as a more efficient review process compared to marketing applications submitted and reviewed under conventional procedures by the FDA or other health authorities, from inclusion in these programs. These programs are not formal regulatory pathways and may be changed, suspended, or halted at any time, including as a result of the FDA deciding not to continue these programs or determining that a current or future marketing application no longer meets the criteria for inclusion in one or both of these programs. The FDA's RTOR program and Project Orbis initiative do not change the scientific and medical standard for approval or the quality of evidence necessary to support approval. As a result, even if current or future marketing applications are subject to one or more of these programs, they may still be denied based on study data, study design, or other factors.

We are required to comply with comprehensive and ongoing regulatory requirements for our approved drugs and, if we receive regulatory approval, our drug candidates, including conducting confirmatory clinical trials of any drug that receives accelerated approval. In addition, our drugs and 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.

Any current or future drug candidate for which we receive accelerated approval from the FDA, including GAVRETO, or similar conditional approval from the EMA, including AVYAKYT, or comparable regulatory authorities in other jurisdictions may be required to undergo one or more confirmatory clinical trials. If such drug candidate fails to meet its safety and efficacy endpoints in such confirmatory clinical trials, the regulatory authority may withdraw its approval. There is no assurance that any such drug candidate will successfully advance through its confirmatory clinical trial(s). Therefore, even if a drug candidate receives accelerated approval from the FDA or similar conditional approval from the EMA or comparable regulatory authorities, such approval may be withdrawn at a later date.

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, "dear doctor" letters or 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 be successful in clinical trials or 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.

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 or 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 or 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 or clinical drug candidates or programs. 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.

Risks Related to Commercialization

We have limited experience as a commercial company and the marketing and sale of AYWAKIT/AYWAKYT, GAVRETO or any future approved drugs may be unsuccessful or less successful than anticipated.

We have two approved precision therapies, AYWAKIT/AYWAKYT and GAVRETO. While we have initiated the commercial launch of AYWAKIT and GAVRETO in the U.S. and AYWAKYT in Europe, we have limited experience as a commercial company and there is limited information about our ability to successfully overcome many of the risks and uncertainties encountered by companies commercializing drugs in the biopharmaceutical industry. Marketing applications for avapritinib and pralsetinib for additional indications are currently under review or planned in

the U.S. and Europe. To execute our business plan, in addition to successfully marketing and selling our approved drugs, we will need to successfully:

- establish and maintain our relationships with healthcare providers who will be treating the patients who may receive our drugs and any future drugs;
- obtain and maintain adequate pricing and reimbursement for AYVAKIT/AYVAKYT, GAVRETO and any future drugs;
- gain regulatory acceptance for the development and commercialization of the drug candidates in our pipeline;
- develop and maintain successful strategic alliances; and
- manage our spending as costs and expenses increase due to clinical trials, marketing approvals, and commercialization.

If we are unsuccessful in accomplishing these objectives, we may not be able to successfully develop drug candidates, commercialize AYVAKIT/AYVAKYT, GAVRETO or any future drugs, raise capital, expand our business or continue our operations.

The commercial success of our current and future drugs will depend upon the degree of market acceptance by physicians, patients, third-party payors and others in the medical community.

AYVAKIT/AYVAKYT, GAVRETO and any other drugs that we may bring to the market may not gain market acceptance by physicians, patients, third-party payors and others in the medical community. If these drugs do not achieve an adequate level of acceptance, we may not generate significant product revenue and may not become profitable. The degree of market acceptance of our approved drugs and any current or future drug candidates for which we receive marketing approval will depend on a number of factors, including:

- the potential efficacy and potential advantages over alternative treatments;
- the prevalence and severity of any side effects, including any limitations or warnings contained in a drug's approved labeling;
- relative convenience and ease of administration;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the length of time that patients who are prescribed our drugs remain on treatment;
- the pricing of our drugs and any current or future drug candidates for which we receive marketing approval;
- publicity concerning our current and future drugs, or competing products and treatments; and
- sufficient third-party insurance coverage or reimbursement.

Even if a potential drug displays a favorable efficacy and safety profile in preclinical and clinical studies, market acceptance of the drug will not be known until after it is launched. Our efforts to educate the medical community and third-party payors on the benefits of our drugs may require significant resources and may never be successful. Our efforts to educate the marketplace may require more resources than are required by the conventional technologies marketed by our competitors. Any of these factors may cause our approved drugs or any current or future drug candidates for which we receive marketing approval to be unsuccessful or less successful than anticipated.

If we are unable to establish additional commercial capabilities and infrastructure, we may be unable to generate sufficient revenue to sustain our business.

Although we have established our initial commercial infrastructure, we are continuing to build out our commercial capabilities and infrastructure and have limited sales and distribution experience and limited capabilities for marketing and market access. To successfully commercialize our approved drugs or any current or future drug candidates for which we receive marketing approval, we will need to develop these capabilities and further expand our infrastructure to support commercial operations in the U.S., Europe and other regions, either on our own or with others. We may be competing with many companies that currently have extensive and well-funded marketing and sales operations. Without a significant internal team or the support of a third party to perform these functions, including marketing and sales functions, we may be unable to compete successfully against these more established companies.

We cannot be sure that we will be able to recruit, hire and retain a sufficient number of sales representatives or that they will be effective at promoting our drugs. In addition, we will need to commit significant additional management and other resources to maintain and grow our sales organization. We may not be able to achieve the necessary development and growth in a cost-effective manner or realize a positive return on our investment. We will also have to compete with other companies to recruit, hire, train and retain sales and marketing personnel.

Factors that may inhibit our efforts to commercialize our drugs include:

- our inability to recruit, train and retain adequate numbers of sales and marketing personnel;
- the inability of sales personnel to obtain access to or to persuade adequate numbers of physicians to prescribe our drugs;
- unforeseen costs and expenses associated with maintaining an independent sales and marketing organization; and
- delays or disruptions to sales and marketing activities due to the COVID-19 pandemic.

In the event that we are unable to effectively deploy our sales organization or distribution strategy on a timely and efficient basis, if at all, the commercialization of our drug candidates could be delayed which would negatively impact our ability to generate product revenues.

Our reliance on single-source third-party suppliers could harm our ability to commercialize our drugs or any other drug candidates that may be approved in the future.

We do not currently own or operate manufacturing facilities for the production of our drugs or any other drug candidates that may be approved in the future. We rely on single-source third-party suppliers to manufacture and supply our drugs, which may not be able to produce sufficient inventory to meet commercial demand in a timely manner, or at all. Our third-party suppliers may not be required to provide us with any guaranteed minimum production levels or have dedicated capacity for our drugs. As a result, there can be no assurances that we will be able to obtain sufficient quantities of our drugs or any other drug candidates that may be approved in the future, which could have a material adverse effect on our business as a whole.

The incidence and prevalence for target patient populations of our approved drugs and drug candidates have not been established with precision. If the market opportunities for our approved drugs or 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, and HCC 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 U.S., France, Germany, Italy, Spain, the United Kingdom and Japan, or the Major Markets, there are approximately: 75,000 patients with SM, including 3,750 patients with advanced SM and 71,250 patients with indolent SM or smoldering SM (regardless of severity of symptoms); 500

first-line patients with PDGFRA D842V mutant GIST (including resectable, metastatic and unresectable GIST); 8,900 first- and second-line patients with RET-altered NSCLC; 1,300 patients with MTC (regardless of line of therapy or alteration); and 25,900 first- and second-line patients with FGFR4-activated HCC.

The total addressable market opportunity for avapritinib for the treatment of patients with GIST and SM, pralsetinib for the treatment of patients with RET-altered NSCLC and thyroid cancers, including MTC, and fisogatinib for the treatment of patients with advanced HCC will ultimately depend upon, among other things, the diagnosis criteria included in the final label for our current and future drugs 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 drugs and 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 drugs and current clinical-stage drug candidates, and we will face competition with respect to any drugs and 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. In addition, if avapritinib is approved for advanced SM or if avapritinib or BLU-263 are approved for indolent SM, they may face competition from other drug candidates in development for these indications, including drug candidates being developed by AB Science S.A., Allakos Inc. and Cogent Biosciences, Inc. (formerly known as Unum Therapeutics).

AYVAKIT/AYVAKYT may face competition from drug candidates in development for GIST, including those being developed by AB Science S.A., ARIAD Pharmaceuticals, Inc., a wholly-owned subsidiary of Takeda Pharmaceutical Company Limited, AROG Pharmaceuticals, Inc., AstraZeneca plc, Celldex Therapeutics, Inc., Cogent Biosciences, Inc., Deciphera Pharmaceuticals, LLC, Exelixis, Inc., Ningbo Tai Kang Medical Technology Co. Ltd. and Xencor, Inc.

GAVRETO faces competition for RET fusion-positive NSCLC from Eli Lilly and Company's selpercatinib, which was approved by the FDA in May 2020 for the treatment of RET-driven NSCLC, MTC and thyroid cancer. If pralsetinib receives marketing approval for patients with RET-altered thyroid carcinoma, including MTC, and other solid tumors, it will also face competition from selpercatinib for these additional indications. In addition, pralsetinib may face competition from other drug candidates in development, including those being developed by AstraZeneca plc, Boston Pharmaceuticals, Inc., Eisai Inc., Exelixis, Inc., GlaxoSmithKline plc, 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 fisogatinib 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, fisogatinib 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.

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 of our approved drugs or drug candidates that we may develop.

We face an inherent risk of product liability exposure related to the testing of our approved drugs and drug candidates in human clinical trials and use of our drug candidates through compassionate use programs, and an even greater risk in connection with our commercialization of our current and future drugs. If we cannot successfully defend ourselves against claims that any of our approved drugs or drug candidates caused injuries, we could incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for any of our approved drugs or drug candidates that we may develop and commercialize;
- 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 of approved drugs or 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 may need to further increase our insurance coverage as we begin additional clinical trials or if we successfully commercialize additional drug candidates. 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 drugs and drug candidates, or experience significant delays in doing so we may not realize the full commercial potential of our drugs and drug candidates.

Because we are focused on precision medicine, in which predictive biomarkers will be used to identify the right patients for our drugs and 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 or plan to enter into agreements to develop and/or commercialize companion diagnostic tests with third parties for AYVAKIT in order to identify GIST patients with the PDGFRA D842V mutation, pralsetinib in order to identify NSCLC patients with RET fusions and MTC patients with RET mutations and fisogatinib in order to identify HCC patients with FGFR4 pathway activation. 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 limited 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 our approved drugs or drug candidates that receive marketing approval. In addition, current commercially available diagnostic tests may become unavailable in the future. Companion diagnostic tests are subject to regulation by the FDA and similar regulatory authorities outside the U.S. as medical devices and require separate regulatory clearance or 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 clearance or approval for and commercialize the companion diagnostic tests for avapritinib, pralsetinib and fisogatinib, and we expect to rely in whole or in part on third parties to design, manufacture, obtain regulatory clearance or approval for and commercialize any other companion diagnostic tests for our drugs and drug candidates. We and our collaborators may encounter difficulties in developing and obtaining clearance or 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 clearances or 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 clearance or 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 drugs and drug candidates, or experience delays in doing so:

- the development of our approved drugs and 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;
- regulatory authorities may impose post-marketing requirements regarding the development and commercialization of companion diagnostic tests for our drugs and drug candidates; and
- we may not realize the full commercial potential of any of our approved drugs or 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 current and future drugs. 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 approved drugs and 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 drugs and drug candidates or do so on commercially reasonable terms, which could adversely affect and/or delay the development or commercialization of our drugs and drug candidates.

Even if we are able to commercialize any of our approved drugs or drug candidates, if approved, such drug or drug candidate 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. In the U.S. and markets in other countries, patients generally rely on third-party payors to reimburse all or part of the costs associated with their treatment. Adequate coverage and reimbursement from governmental healthcare programs, such as Medicare and Medicaid, and commercial payors is critical to new product acceptance. Our ability to successfully commercialize our products will depend in part on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers and other organizations. Government authorities and other third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. In the United States, the principal decisions about reimbursement for new medicines are typically made by the Centers for Medicare & Medicaid Services, or CMS, an agency within the U.S. Department of Health and Human Services, or HHS. CMS decides whether and to what extent a

new medicine will be covered and reimbursed under Medicare and private payors tend to follow CMS to a substantial degree. The availability of coverage and extent of reimbursement by governmental and private payors is essential for most patients to be able to afford treatments. Sales of these or other products that we may identify will depend substantially, both domestically and abroad, on the extent to which the costs of our products will be paid by health maintenance, managed care, pharmacy benefit and similar healthcare management organizations, or reimbursed by government health administration authorities, private health coverage insurers and other third-party payors. If coverage and adequate reimbursement is not available, or is available only to limited levels, we may not be able to successfully commercialize our products. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish or maintain pricing sufficient to realize a sufficient return on our investment. 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 U.S. 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 U.S. Private 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 U.S., 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 healthcare 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 (increased to 70% by the Bipartisan Budget Act of 2018, effective January 1, 2019) 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 U.S. 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 2030 unless additional Congressional action is taken.

However, the Medicare sequester reductions under the Budget Control Act of 2011 will be suspended from May 1, 2020 through December 31, 2020 due to the COVID-19 pandemic. 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, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

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

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. Since January 2017, President Trump has signed two executive orders and other directives designed to delay the implementation of certain provisions of the Affordable Care Act. Concurrently, Congress has considered legislation that would repeal or repeal and replace all or part of the Affordable Care Act. While Congress has not passed repeal legislation to date, it has enacted laws that modify certain provisions of the Affordable Care Act. The Tax Cuts and Jobs Act of 2017, or TCJA, included a provision which repealed, effective January 1, 2019, the tax-based shared responsibility payment imposed by the Affordable Care Act on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the “individual mandate.” 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 inseparable feature of the Affordable Care Act, and therefore because the mandate was repealed as part of the TCJA, the remaining provisions of the Affordable Care Act are invalid as well. On December 18, 2019, the Fifth Circuit U.S. Court of Appeals held that the individual mandate is unconstitutional, and remanded the case to the lower court to reconsider its earlier invalidation of the full Affordable Care Act. On March 2, 2020, the United States Supreme Court granted the petitions for writs of certiorari to review this case, and has allotted one hour for oral arguments, which are expected to occur in the fall. Pending review, the Affordable Care Act remains in effect, but it is unclear at this time what effect the latest ruling will have on the status of the Affordable Care Act. Litigation and legislation over the Affordable Care Act are likely to continue, with unpredictable and uncertain results. We will continue to evaluate the effect that the Affordable Care Act and its possible repeal and replacement has on 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. On June 14, 2018, U.S. Court of Appeals for the Federal Circuit ruled that the federal government was not required to pay more than \$12 billion in Affordable Care Act risk corridor payments to third-party payors who argued were owed to them. On April 27, 2020, in *Moda Health Plan, Inc. v. United States* the U.S. Supreme Court reversed the judgment, holding the risk corridors program created a government obligation to pay insurers the full amount set out in the Affordable Care Act and remanded for further proceeding. The effects of this gap in reimbursement on third-party payors, the viability of the Affordable Care Act marketplace, providers, and potentially our business, are not yet known.

Moreover, on January 22, 2018, President Trump signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain Affordable Care Act-mandated fees, including the so called “Cadillac” tax on certain high cost employer-sponsored insurance plans, the annual fee imposed on certain health insurance providers based on market share. However, on December 20, 2019, President Trump signed into law the Further Consolidated Appropriations Act (H.R. 1865), which repeals the Cadillac tax, the health insurance provider tax, and the medical device excise tax. In December 2018, CMS published a final rule permitting further collections and

payments to and from certain Affordable Care Act qualified health plans and health insurance issuers under the Affordable Care Act risk adjustment program in response to the outcome of federal district court litigation regarding the method CMS uses to determine this risk adjustment. Since then, the Affordable Care Act risk adjustment program payment parameters have been updated annually. In addition, CMS published 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. Congress and the Trump administration 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.

There has been increasing legislative and enforcement interest in the U.S. with respect to drug pricing practices. Specifically, there have been several recent U.S. Congressional inquiries and proposed federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. For example, at the federal level, the U.S. government's budget proposal for fiscal year 2021 includes a \$135 billion allowance to support legislative proposals seeking to reduce drug prices, increase competition, lower out-of-pocket drug costs for patients, and increase patient access to lower-cost generic and biosimilar drugs. While some proposed measures may require additional authorization to become effective, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs.

We may face competition in the U.S. for our current and future drug candidates and approved drugs from therapies sourced from foreign countries that have placed price controls on pharmaceutical products. In the United States, the Medicare Modernization Act, or MMA, contains provisions that call for the promulgation of regulations that expand pharmacists' and wholesalers' ability to import cheaper versions of an approved drug and competing products from Canada, where there are government price controls. Further, the MMA provides that these changes to U.S. importation laws will not take effect, unless and until the Secretary of the HHS certifies that the changes will pose no additional risk to the public's health and safety and will result in a significant reduction in the cost of products to consumers. On September 23, 2020, the Secretary of the HHS made such certification to Congress, and on October 1, 2020, the FDA published a final rule that allows for the importation of certain prescription drugs from Canada. Under the final rule, states and Indian tribes, and in certain future circumstances pharmacists and wholesalers, may submit importation program proposals to the FDA for review and authorization. On September 25, 2020, CMS stated drugs imported by states under this rule will not be eligible for federal rebates under Section 1927 of the Social Security Act, and manufacturers would not report these drugs for "best price" or Average Manufacturer Price purposes. Since these drugs are not considered covered outpatient drugs, CMS further stated it will not publish a National Average Drug Acquisition Cost for these drugs. Separately, the FDA also issued a final guidance document outlining a pathway for manufacturers to obtain an additional National Drug Code for an FDA-approved drug that was originally intended to be marketed in a foreign country and that was authorized for sale in that foreign country. The market implications of the final rule and guidance are unknown at this time. Proponents of drug reimportation may attempt to pass legislation that would directly allow reimportation under certain circumstances. Legislation or regulations allowing the reimportation of drugs, if enacted, could decrease the price we receive for any products that we may develop and adversely affect our future revenues and prospects for profitability.

On March 10, 2020, the U.S. government sent "principles" for drug pricing to Congress, calling for legislation that would, among other things, cap Medicare Part D beneficiary out-of-pocket pharmacy expenses, provide an option to cap Medicare Part D beneficiary monthly out-of-pocket expenses, and place limits on pharmaceutical price increases. Additionally, the Trump administration previously released a "blueprint" to lower drug prices and reduce out of pocket costs of drugs that contains additional proposals to increase drug manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products, and reduce the out of pocket costs of drug products paid by consumers. HHS has already started the process of soliciting feedback on some of these measures and, at the same time, is immediately implementing others under its existing authority. For example, in May 2019, CMS issued a final rule to allow Medicare Advantage Plans the option of using step therapy for Part B drugs beginning January 1, 2020. This final rule codified CMS's policy change that was effective January 1, 2019.

In addition, individual states have also become increasingly active in passing legislation and implementing regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures and, in some cases, to encourage importation from other countries and bulk purchasing.

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 current and future drugs. 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.

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 drugs and drug candidates, if approved, or additional pricing pressures.

We are currently unable to predict what additional legislation or regulation, if any, relating to the healthcare 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 commercialization of our approved drugs and drug candidates.

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

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.

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 current or future drugs ourselves. In addition, we may not be successful in entering into arrangements with third parties to sell and market our current and future drugs 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 drugs 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 drugs and drug candidates, if approved. 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.

We are 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 of our approved drugs and 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 drugs and drug candidates for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations include, but are not limited to, 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. Manufacturers can be held liable under the False Claims Act even when they do not submit claims directly to government payors if they are deemed to “cause” the submission of false or fraudulent claims;
- 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 regardless of the payor (e.g., public or private), 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 (as defined by the statute) and their immediate family members. Effective January 1, 2022, these reporting obligations will extend to include transfers of value made to certain non-physician providers such as physician assistants and nurse practitioners;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, 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. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil

actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys' fees and costs associated with pursuing federal civil actions;

- 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 healthcare 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.

In the U.S., to help patients who have no or inadequate insurance access our drug, we have a patient assistance program that we administer in conjunction with our patient support program vendor. If we or our vendors are deemed to fail to comply with relevant laws, regulations or evolving government guidance in the operation of these programs, we could be subject to damages, fines, penalties or other criminal, civil or administrative sanctions or enforcement actions. We cannot ensure that our compliance controls, policies and procedures will be sufficient to protect against acts of our employees, business partners or vendors that may violate the laws or regulations of the jurisdictions in which we operate. Regardless of whether we have complied with the law, a government investigation could impact our business practices, harm our reputation, divert the attention of management, increase our expenses and reduce the availability of assistance to our patients.

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, manufacturing, commercial sales, pricing and distribution of our drug candidates, and we cannot predict success in these jurisdictions. If we seek to

develop our drug candidates or 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, including the European General Data Protection Regulation 2016/679, commonly referred to as GDPR;
- 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 U.S. 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 licensing arrangements, 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 commercialization of any of our approved drugs and drug candidates will require substantial additional cash to fund expenses. We may decide to collaborate with additional pharmaceutical and biotechnology companies for the development and commercialization of certain approved drugs or drug candidates or to license the development and commercialization rights of certain approved drugs or drug candidates to third parties.

We face significant competition in seeking appropriate collaborators and licensing partners. Whether we reach a definitive agreement for a collaboration or license will depend, among other things, upon our assessment of the collaborator's or licensing partner's resources and expertise, the terms and conditions of the proposed agreement and the proposed partner'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 U.S., the potential market for the subject drug or drug candidate, the costs and complexities of manufacturing and delivering such drug or 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 or licensing partner may also consider alternative drug candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration or licensing arrangement could be more attractive than the one with us for our drug candidate. The terms of any additional collaborations, licenses 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 and our license agreement with Clementia 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 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 and licensing arrangements 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 or license, 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 or licenses with Roche, CStone and Clementia, as well as any future collaborations or licenses that we enter into, may not be successful. The success of these arrangements will depend heavily on the efforts and activities of our collaborators and licensing partners. 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. Licensors generally have sole discretion in determining the efforts and resources that they will apply to the licensed products. Collaborations and licenses 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 or license agreements with Roche, CStone or Clementia, or of any future collaboration or license agreement, could adversely affect us financially or harm our business reputation.

We rely on third parties to conduct our clinical trials for our approved drugs and 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 approved drugs and 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 approved drugs and drug candidates. We rely heavily on these parties for execution of clinical trials for our drugs and 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 approved drugs and 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.

Some of these factors may be beyond our control. For example, the performance of our CROs may also be delayed or disrupted by the ongoing COVID-19 pandemic, including due to travel or quarantine policies, availabilities of staff, exposure of CRO staff to COVID-19 or re-prioritization of CRO resources as a result of the pandemic. 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 approved drugs for additional indications and 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 for additional indications or our drug candidates. As a result, we believe that our financial results and the commercial prospects for our drugs or our drug candidates in the subject indication would be harmed, our costs could increase and our ability to generate substantial revenue could be delayed.

We contract with third parties for the manufacture of our drug candidates for pre-clinical development and clinical trials, and for the manufacture of AYWAKIT/AYVAKYT and GAVRETO for commercialization. This reliance on third parties increases the risk that we will not have sufficient quantities of our drugs or drug candidates 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 current and future drugs. This reliance on third parties increases the risk that we will not have sufficient quantities of our drugs or drug candidates 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 drugs and 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 drugs and 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 drugs and drug candidates or is unable to conduct inspections necessary to approve these facilities due to delays or disruptions caused by the COVID-19 pandemic, or if the FDA or a comparable regulatory authority withdraws any such approval in the future, we may be delayed in obtaining approval of these facilities for the manufacture of our drugs and drug candidates or 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 drugs and drug candidates.

In response to the COVID-19 pandemic, on March 10, 2020, the FDA announced its intention to postpone most inspections of foreign manufacturing facilities and products while local, national and international conditions warrant. On March 18, 2020, the FDA announced its intention to temporarily postpone routine surveillance inspections of domestic manufacturing facilities and provided guidance regarding the conduct of clinical trials which the FDA continues to update. As of June 23, 2020, the FDA noted it was conducting mission critical domestic and foreign inspections to ensure compliance of manufacturing facilities with FDA quality standards. On July 10, 2020, the FDA announced its goal of restarting domestic on-site inspections during the week of July 20, 2020, but such activities will

depend on data about the virus' trajectory in a given state and locality and the rules and guidelines that are put in place by state and local governments. The FDA has developed a rating system to assist in determining when and where it is safest to conduct prioritized domestic inspections. Should the FDA determine that an inspection is necessary for approval and an inspection cannot be completed during the review cycle due to restrictions on travel, the FDA has stated that it generally intends to issue a complete response letter. Further, if there is inadequate information to make a determination on the acceptability of a facility, the FDA may defer action on the application until an inspection can be completed. Regulatory authorities outside the U.S. may adopt similar restrictions or other policy measures in response to the COVID-19 pandemic and may experience delays in their regulatory activities.

We do not have long-term supply agreements with all of our contract manufacturers, and purchase our required drug supply, including the API, drug product and drug substance used in our drug candidates, on a purchase order basis with certain contract manufacturers. 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.

Any of our approved drugs and drug candidates that we may develop may compete with other approved drugs and drug candidates 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. On March 27, 2020, President Trump signed into law the Coronavirus Aid, Relief, and Economic Security (CARES) Act in response to the U.S. COVID-19 pandemic. Throughout the COVID-19 outbreak, there has been public concern over the availability and accessibility of critical medical products, and the CARES Act enhances FDA's existing authority with respect to drug shortage measures. Under the CARES Act, we must have in place a risk management plan in place that identifies and evaluates the risks to the supply of approved drugs for certain serious diseases or conditions for each establishment where the drug or API is manufactured. The risk management plan will be subject to FDA review during an inspection.

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 all of our bulk drug substances. If our current contract manufacturers cannot perform as agreed, we may experience shortages that require reporting to the FDA or foreign regulatory authorities and may be required to replace such manufacturers. Although we believe that there are several potential alternative manufacturers who could manufacture our approved drugs and 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 drugs or drug candidates could result in significant delays or gaps in availability of such drugs or drug candidates 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 API, drug substance and drug product used in avapritinib and pralsetinib 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 avapritinib and pralsetinib 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 avapritinib and pralsetinib, 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, including as a result of the COVID-19 pandemic, it could significantly and adversely affect our business, the supply of our drug candidates or approved drugs 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. In addition, we currently have sufficient supply or plans for supply to meet our anticipated global commercial and clinical development needs for avapritinib, pralsetinib, fisogatinib and BLU-263 through 2021. However, the COVID-19 pandemic could adversely impact our suppliers and result in delays or disruptions in our current or future supply chain.

Establishing additional or replacement suppliers for the API, drug substance and drug product used in our drug candidates or approved drugs, 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 and approved drugs, 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.

Certain of our research and development, clinical trials and manufacturing and supply for certain raw materials used in our drugs and our drug candidates takes place in China through third-party CROs, collaborators or manufacturers. A significant disruption in the operation of those CROs, collaborators or manufacturers, could materially adversely affect our business, financial condition and results of operations.

We have relied on certain third parties located in China to manufacture and supply certain raw materials used in our drugs and our drug candidates, and we expect to continue to use such third party manufacturers for such purposes. In addition, certain of our drug candidates are being evaluated at clinical trial sites in China under our collaboration with CStone and through CROs located in China. A natural disaster, epidemic or pandemic disease outbreaks, including the recent COVID-19 pandemic, trade war, political unrest or other events in China could disrupt the business or operations of CROs, collaborators, manufacturers or other third parties with whom we conduct business now or in the future. Any disruption in China that significantly impacts such third parties, including services provided by CROs for our research and development programs, clinical trial operations conducted by CROs or our collaborators, or our manufacturers ability to produce raw materials in adequate quantities to meet our needs could impair our ability to operate our business on a day-to-day basis and impede, delay, limit or prevent the research, development or commercialization of our current and future approved drugs or drug candidates. In addition, for any activities conducted in China, we are exposed to the possibility of product supply disruption and increased costs in the event of changes in the policies of the U.S. or Chinese governments, political unrest or unstable economic conditions in China, and we may be exposed to fluctuations in the value of the local currency in China for goods and services. Our costs for any of these services or activities could also increase as a result of future appreciation of the local currency in China or increased labor costs if the demand for skilled laborers increases in China and the availability of skilled labor declines in China.

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 U.S. and other countries for our drugs and drug candidates, including avapritinib and pralsetinib, 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 U.S. 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 the composition of matter for avapritinib, pralsetinib, fisogatinib and BLU-263. We also own applications relating to composition of matter for KIT and PDGFRA inhibitors with multiple compound families, composition of matter for FGFR4 inhibitors with multiple compound families, and composition of matter for inhibitors of RET, including predicted RET resistance mutations, 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 pralsetinib composition of matter has a statutory expiration date in 2036, and the issued U.S. patent directed to fisogatinib composition of matter has a statutory expiration date in 2034. Patent term adjustments or patent term extensions could result in later expiration dates.

As of October 15, 2020, we owned nine issued U.S. patents, 13 issued foreign patents, including one European patent validated in 38 countries, three pending U.S. non-provisional patent applications, five pending U.S. provisional patent applications, four pending PCT international applications and 23 pending foreign patent applications directed to our KIT and PDGFRA program, including avapritinib and BLU-263. The patents that have issued or will issue covering our KIT and PDGFRA program will have a statutory expiration date between 2034 and 2041. Patent term adjustments or patent term extensions could result in later expiration dates for avapritinib or BLU-263.

As of October 15, 2020, we owned seven issued U.S. patents, five pending U.S. non-provisional patent applications, three U.S. provisional patent applications, two pending PCT international applications, two issued foreign patents and 38 pending foreign patent applications directed to our RET program, including pralsetinib. The patents that have issued or will issue covering our RET program will have a statutory expiration date between 2036 and 2041. Patent term adjustments or patent term extensions could result in later expiration dates.

As of October 15, 2020, we owned eight issued U.S. patents, three pending U.S. non-provisional patent applications, two pending PCT international applications, 26 issued foreign patents and 29 pending foreign patent applications directed to our FGFR4 program, including fisogatinib. The patents that have issued or will issue covering our FGFR4 program will have a statutory expiration date between 2033 and 2039. 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 October 15, 2020, we owned seven issued U.S. patents, six pending U.S. non-provisional patent applications, five pending European Union patent applications and six issued European patents 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 any of our approved drugs and 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, pralsetinib, fisogatinib or BLU-263. In addition, the laws of foreign countries may not protect our rights to the same extent as the laws of the U.S. Furthermore, patents have a limited lifespan. In the U.S., 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 drugs and drug candidates, including generic versions of such drugs or drug candidates.

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 U.S. 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 fisogatinib or generic method of treatment claims that may cover pralsetinib. If the claims of any of these third-party patents are asserted against us, we do not believe fisogatinib, pralsetinib 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 U.S. and abroad could uphold the validity of any such patents. If we were to challenge the validity of any issued U.S. patent in court, we would need to overcome a statutory presumption of validity that attaches to every U.S. 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. 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 U.S. 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, consultants, advisors, and other third parties who have access to our proprietary know-how 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, drugs and drug candidates. Such challenges may also result in our inability to manufacture or commercialize our drugs or drug candidates, if approved, 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 drugs and drug candidates.

Even if they are unchallenged, our issued patents and our pending patent applications, 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 drugs and 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 drugs and drug candidates is not sufficiently broad to impede such competition, our ability to successfully commercialize our drugs or drug candidates, if approved, 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 current and future drugs 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 drugs, 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 fisolgatinib or generic method of treatment claims that may cover pralsetinib. If the claims of any of these third-party patents are asserted against us, we do not believe fisolgatinib, pralsetinib 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 U.S. and abroad could uphold the validity of any such patents. If we were to challenge the validity of any issued U.S. patent in court, we would need to overcome a statutory presumption of validity that attaches to every U.S. 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 drugs and drug candidates. If a patent holder believes any of our approved drugs or drug

candidate infringes on its patent, the patent holder may sue us even if we have received patent protection for our drugs, drug candidates and 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, drugs 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 current and future drugs 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 U.S., 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 any of our approved drugs or drug candidates, we would lose at least part, and perhaps all, of the patent protection covering such drug or 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 drugs or 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 drugs and 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 U.S. 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 U.S. 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 drugs and 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 drugs and 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 U.S. and other jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our drugs and 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 U.S. 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 U.S. 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 U.S. 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 drugs and 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 drugs and drug candidates, if approved. 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 drugs and drug candidates, if approved, 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, Fouad Namouni, M.D., our President, Research & Development, Anthony L. Boral, our Chief Medical Officer, Debra Durso-Bumpus, our Chief People 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. In addition, insurance coverage is increasingly expensive, including with respect to directors and officers liability insurance, or D&O insurance. We may not be able to maintain D&O insurance at a reasonable cost or in an amount adequate to satisfy any liability that may arise. An inability to secure and maintain D&O insurance may make it difficult for us to retain and attract talented and skilled directors and officers to serve our company, which could adversely affect our business. 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, regulatory, manufacturing and sales and marketing personnel is 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 October 15, 2020, we had 420 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 COVID-19 pandemic has caused extreme volatility and disruptions in the capital and credit markets. A severe or prolonged economic downturn 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.

For example, the departure of the United Kingdom from the European Union, commonly referred to as Brexit, could result in the United Kingdom or the European Union significantly altering its regulations affecting the clearance or approval of our drug 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 drug candidates 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 clinical trial sites or 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 drugs' and 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 drugs' and drug candidates' development programs and

significant reputational, financial, legal, regulatory, business or operational harm. For example, the loss of clinical trial data for our drugs or 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 physician data, patient data, or any 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.

Interruptions in the availability of server systems or communications with Internet or cloud-based services, or failure to maintain the security, confidentiality, accessibility or integrity of data stored on such systems, could harm our business.

We rely upon a variety of Internet service providers, third-party hosting facilities and cloud computing platform providers to support our business. Failure to maintain the security, confidentiality, accessibility or integrity of data stored on such systems could damage our reputation in the market, cause us to lose revenue or market share, increase our service costs, cause us to incur substantial costs, subject us to liability for damages and/or fines and divert our resources from other tasks, any one of which could materially adversely affect our business, financial condition, results of operations and prospects. Any damage to, or failure of, such systems, or communications to and between such systems, could result in interruptions in our operations. If our security measures or those of our third-party data center hosting facilities, cloud computing platform providers, or third-party service partners, are breached, and unauthorized access is obtained to our data or our information technology systems, we may incur significant legal and financial exposure and liabilities.

We do not have control over the operations of the facilities of our cloud service providers and our third party providers may be vulnerable to damage or interruption from natural disasters, cybersecurity attacks, terrorist attacks, power outages and similar events or acts of misconduct. In addition, any changes in our cloud service providers' service levels may adversely affect our ability to meet our requirements and operate our business.

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 U.S., 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, which is commonly referred to as 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 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 are subject to the California Consumer Privacy Act, or CCPA, which took effect on January 1, 2020 and imposes 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. While there is currently an exception for protected health information that is subject to HIPAA and clinical trial regulations, as currently written, the CCPA may impact our business activities. The CCPA became enforceable as of July 1, 2020, but there continues to be uncertainty about how the law will be interpreted and enforced. 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 U.S. 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 or in-license businesses, technologies or drugs, or form strategic alliances, in the future, and we may not realize the benefits of such acquisitions.

We may acquire or in-license additional businesses, technologies 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.

For example, on December 22, 2017, 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. Additionally, on March 27, 2020, President Trump signed into law the CARES Act, which included certain changes in tax law intended to stimulate the U.S. economy in light of the COVID-19 pandemic, including delaying the effective date of the net operating loss restrictions imposed by the TJCA, temporarily relaxing (but not eliminating) the TJCA's interest deductibility limitations, and making temporary beneficial changes to the payroll tax regime. We continue to examine the impact this tax reform legislation may have on our business. The impact of these and other future changes in tax laws is uncertain and could have an adverse effect on our business, cash flow, financial condition or results of operations.

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. 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 October 28, 2020. As a result of this volatility, our stockholders could incur substantial losses.

The stock market in general has recently experienced relatively large price and volume fluctuations, particularly in response to the COVID-19 outbreak. In particular, the market prices of securities of Nasdaq listed and biopharmaceutical companies have experienced extreme fluctuations that often have been unrelated or disproportionate to the operating results of these companies. Continued market fluctuations could result in extreme volatility in the price of our common stock, which could include a decline in the value of our common stock. In addition, the market price for our common stock may be influenced by many factors, including:

- the success of commercialization of our drugs and drug candidates, if approved;
- 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 U.S. 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;
- natural disasters, epidemic or pandemic disease outbreaks, including the COVID-19 pandemic, trade wars, political unrest or other similar events;
- general economic, industry and market conditions; and
- the other factors described in this “Risk Factors” section.

Future sales or issuances of common stock or other equity related securities may also adversely affect the market price of our common stock. In July 2020, we entered into a sales agreement with Cowen through which we may, from time to time, issue and sell shares of our common stock having an aggregate offering price of up to \$250.0 million, subject to the terms and conditions of the sales agreement. If we sell our common stock under the sales agreement, seek authorization to sell additional shares of common stock under the sales agreement, enter into new “at-the-market” stock offering programs, or through other means, it could lead to additional dilution for our stockholders and may impact our stock price adversely.

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. Because of the potential volatility of our stock price, we may become the target of securities litigation in the future. 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.

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.

Our bylaws contain exclusive forum provisions, which may limit a stockholder's ability to bring a claim in a judicial forum it finds favorable and may discourage lawsuits with respect to such claims.

Our amended and restated bylaws, as amended, or bylaws, provide that unless we consent in writing to an alternative forum, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for state law claims for (1) any derivative action, (2) any claim of breach of fiduciary duty, (3) any claim against a current or former director, officer, employee or stockholder, and (4) any action against our company governed by the internal affairs doctrine, which we refer to collectively as the Delaware forum provision. The Delaware forum provision does not apply to any claims arising under the Securities Exchange Act of 1934 or the Securities Act of 1933, as amended, or the Securities Act. Our bylaws further provide that, unless we consent in writing to an alternative forum, the United States District Court for the District of Massachusetts will be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act, which we refer to as the federal forum provision. We have chosen the United States District Court for the District of Massachusetts as the exclusive forum for such Securities Act causes of action because our principal executive offices are located in Massachusetts. In addition, our bylaws provide that any person or entity purchasing or otherwise acquiring any interest in shares of our common stock is deemed to have notice of and consented to the Delaware forum provision and the federal forum provision.

The Delaware forum provision and the federal forum provision may impose additional litigation costs on stockholders who assert the provision is not enforceable and may impose more general additional litigation costs in pursuing any such claims, particularly if the stockholders do not reside in or near the State of Delaware or the Commonwealth of Massachusetts. In addition, these forum selection clauses in our bylaws may limit our stockholders' ability to bring a claim in a judicial forum that they find favorable for disputes with us or our directors, officers or employees, which may discourage such lawsuits against us and our directors, officers and employees even though an action, if successful, might benefit our stockholders. The federal forum provision may also impose additional litigation costs on stockholders who assert the provision is not enforceable or invalid. Alternatively, if the federal forum provision is found inapplicable to, or unenforceable in respect of, one or more of the specified types of actions or proceedings, we may incur additional costs associated with resolving such matters in other jurisdictions, which could have an adverse effect on our business, financial condition or results of operations. The Court of Chancery of the State of Delaware and the United States District Court for the District of Massachusetts may also reach different judgments or results than would other courts, including courts where a stockholder considering an action may be located or would otherwise choose to bring the action, and such judgments may be more or less favorable to us than our stockholders.

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, 2019, we had federal net operating loss carryforwards of \$812.2 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 (as modified by the CARES Act), we may not use net operating loss carry-forwards generated in taxable years beginning after December 31, 2017 to reduce our taxable income in any year beginning after December 31, 2020 by more than 80%, and we may not carry back any net operating losses generated in taxable years beginning after December 31, 2020 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 – the instance document does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL 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
104	Cover Page Interactive Data File – The cover page interactive data file does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL 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 of 1933, as amended, 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: October 29, 2020

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

Date: October 29, 2020

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

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: October 29, 2020

By: /s/ Jeffrey W. Albers

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

CERTIFICATIONS

I, Michael Landsittel, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Blueprint Medicines Corporation;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer(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: October 29, 2020

By: /s/ Michael Landsittel

Michael Landsittel
Chief Financial Officer
(Principal Financial Officer)

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

In connection with the Quarterly Report on Form 10-Q of Blueprint Medicines Corporation (the "Company") for the period ended September 30, 2020 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: October 29, 2020

By: /s/ Jeffrey W. Albers

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

Date: October 29, 2020

By: /s/ Michael Landsittel

Michael Landsittel
Chief Financial Officer
(Principal Financial Officer)
