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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, DC 20549

FORM 10-Q

(Mark One)

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

For the quarterly period ended September 30, 2023

OR

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

Commission file number 001-37359

BLUEPRINT MEDICINES CORPORATION
(Exact Name of Registrant as Specified in Its Charter)

Delaware	**26-3632015**
(State or Other Jurisdiction of Incorporation or Organization)	**(I.R.S. Employer Identification No.)**
45 Sidney Street Cambridge, Massachusetts	**02139**
(Address of Principal Executive Offices)	**(Zip Code)**

(617) 374-7580
(Registrant's Telephone Number, Including Area Code)

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

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

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

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

Large accelerated filer ☑	Accelerated filer ☐
Non-accelerated filer ☐	Smaller reporting company ☐
	Emerging growth company ☐

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

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

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

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

Number of shares of the registrant's common stock, $0.001 par value, outstanding on October 23, 2023: 60,789,712

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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 in additional geographies, particularly for indolent systemic mastocytosis (SM) in geographies outside of the U.S.;
- 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®) and any current and future drug candidates for which we receive marketing approval;
- our expectations regarding the potential benefits of AYVAKIT/AYVAKYT and any current and future drug candidates in treating patients with indolent SM and advanced SM;
- the rate and degree of market acceptance of AYVAKIT/AYVAKYT and any current and future drug candidates for which we receive marketing approval;
- the pricing and reimbursement of AYVAKIT/AYVAKYT and any current and future drug candidates for which we receive marketing approval;
- the anticipated impact of the termination of our collaboration with F. Hoffmann-La Roche Ltd and Genentech, Inc. to develop and commercialize pralsetinib globally (excluding Greater China), our expectations concerning the transition process with F. Hoffmann-La Roche Ltd and Genentech, Inc., and our plans to re-partner GAVRETO for future development and commercialization;
- the initiation, timing, progress and results of our preclinical studies and clinical trials, including our ongoing clinical trials and any planned clinical trials for our current and future drug candidates and 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 and length 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 CStone Pharmaceuticals to develop and commercialize avapritinib, pralsetinib and fisogatinib in Greater China, our collaboration with Zai Lab to develop and commercialize BLU-525 and BLU-945, and any respective back-up forms and certain other forms thereof, as inhibitors of epidermal growth factor receptor (EGFR) in Greater China, and our collaboration with Oncopia Therapeutics, Inc., d/b/a Proteovant Therapeutics, Inc. (Proteovant), to

research and advance novel targeted protein degrader therapies, 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., a wholly-owned subsidiary of Ipsen S.A. (Clementia), to develop and commercialize BLU-782 for fibrodysplasia ossificans progressiva;
- the potential benefits of our strategic financing transactions with Garnich Adjacent Investments S.a.r.l. and Tao Talents, LLC, both affiliates of Sixth Street Partners, and Royalty Pharma Investments 2019 ICAV (Royalty Pharma);
- our ability to realize the benefits of the collaboration compounds retained by us following the mutual termination of our cancer immunotherapy collaboration with F. Hoffmann-La Roche Ltd and Hoffman-La Roche Inc.;
- the potential benefits of our license agreement with IDRx, Inc. (IDRx) to develop our development candidate-stage KIT exon 13 inhibitor, IDRX-73, for the treatment of drug-resistant mutations of non-PDGFR-driven gastrointestinal stromal tumor (GIST);
- 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; and
- the actual or potential benefits of designations granted by the U.S. Food and Drug Administration (FDA), such as orphan drug, fast track and breakthrough therapy designation or priority review.

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 in Part II, Item 1A, 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., (ii) with respect to our terminated cancer immunotherapy collaboration, Roche means F. Hoffmann-La Roche Ltd and Hoffmann-La Roche Inc., and (iii) with respect to our financing transactions with Sixth Street Partners, Sixth Street Partners means Garnich Adjacent Investments S.a.r.l. and/or Tao Talents, LLC.

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, 2023	December 31, 2022
Assets		
Current assets:		
Cash and cash equivalents	$ 55,972	$ 119,709
Marketable securities	657,012	825,283
Accounts receivable	40,861	23,525
Unbilled accounts receivable	393	13,413
Inventory	16,457	29,697
Prepaid expenses and other current assets	37,477	35,024
Total current assets	808,172	1,046,651
Marketable securities	114,242	133,480
Property and equipment, net	40,619	33,344
Operating lease right-of-use assets, net	75,221	81,854
Restricted cash	9,696	5,195
Equity investment	27,789	27,789
Other assets	29,560	21,589
Total assets	$ 1,105,299	$ 1,349,902
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	6,963	2,729
Accrued expenses	110,436	131,123
Current portion of operating lease liabilities	11,617	10,579
Current portion of deferred revenue	3,010	4,667
Current portion of liabilities related to the sale of future royalties and revenues	35,137	17,285
Current portion of term loan	30,221	16,851
Total current liabilities	197,384	183,234
Operating lease liabilities, net of current portion	84,036	92,789
Deferred revenue, net of current portion	5,000	13,624
Liabilities related to the sale of future royalties and revenues, net of current portion	405,010	413,045
Term loan, net of current portion	208,157	122,232
Other long-term liabilities	3,101	10,301
Total liabilities	902,688	835,225
Commitments and Contingencies (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; 60,740,744 and 59,958,919 shares issued and outstanding at September 30, 2023 and December 31, 2022, respectively	61	60
Additional paid-in capital	2,434,258	2,358,018
Accumulated other comprehensive loss	(2,683)	(10,443)
Accumulated deficit	(2,229,025)	(1,832,958)
Total stockholders' equity	202,611	514,677
Total liabilities and stockholders' equity	$ 1,105,299	$ 1,349,902

See accompanying notes to the unaudited condensed consolidated financial statements.

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

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2023	2022	2023	2022
Revenues:				
Product revenue, net	$ 54,228	$ 28,634	$ 133,173	$ 80,929
Collaboration and license revenue	2,338	9,843	44,250	56,826
License revenue - related party	—	27,500	—	27,500
Total revenues	56,566	65,977	177,423	165,255
Cost and operating expenses:				
Cost of sales	2,782	3,000	8,280	12,965
Collaboration loss sharing	1,771	1,665	4,301	7,076
Research and development	110,252	127,981	330,184	359,579
Selling, general and administrative	70,741	57,608	215,826	173,354
Total cost and operating expenses	185,546	190,254	558,591	552,974
Other income (expense):				
Interest expense, net	(3,808)	(8,396)	(13,624)	(7,527)
Other income (expense), net	(728)	396	(369)	575
Total other expense, net	(4,536)	(8,000)	(13,993)	(6,952)
Loss before income taxes	(133,516)	(132,277)	(395,161)	(394,671)
Income tax expense	197	886	907	4,200
Net loss	$ (133,713)	$ (133,163)	$ (396,068)	$ (398,871)
Other comprehensive loss:				
Unrealized gains (losses) on available-for-sale investments	1,443	(843)	7,624	(11,171)
Currency translation adjustments	95	265	136	478
Comprehensive loss	$ (132,175)	$ (133,741)	$ (388,308)	$ (409,564)
Net loss per share - basic and diluted	$ (2.20)	$ (2.23)	$ (6.55)	$ (6.70)
Weighted-average number of common shares used in net loss per share - basic and diluted	60,688	59,758	60,445	59,564

See accompanying notes to the unaudited condensed consolidated financial statements.

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, 2022	59,958,919	$ 60	$ 2,358,018	$ (10,443)	$ (1,832,958)	$ 514,677
Issuance of common stock under stock plan	457,416	—	—	—	—	—
Stock-based compensation expense	—	—	23,340	—	—	23,340
Other comprehensive income	—	—	—	5,841	—	5,841
Net loss	—	—	—	—	(129,560)	(129,560)
Balance at March 31, 2023	60,416,335	$ 60	$ 2,381,358	$ (4,602)	$ (1,962,518)	$ 414,298
Issuance of common stock under stock plan and stock purchase plan	221,940	$ 1	$ 5,298	$ —	$ —	$ 5,299
Stock-based compensation expense	—	—	23,945	—	—	23,945
Other comprehensive income	—	—	—	381	—	381
Net loss	—	—	—	—	(132,794)	(132,794)
Balance at June 30, 2023	60,638,275	$ 61	$ 2,410,601	$ (4,221)	$ (2,095,312)	$ 311,129
Issuance of common stock under stock plan	102,469	$ —	$ 445	$ —	$ —	$ 445
Stock-based compensation expense	—	—	23,212	—	—	23,212
Other comprehensive loss	—	—	—	1,538	—	1,538
Net loss	—	—	—	—	(133,713)	(133,713)
Balance at September 30, 2023	60,740,744	$ 61	$ 2,434,258	$ (2,683)	$ (2,229,025)	$ 202,611
Balance at December 31, 2021	59,141,086	$ 59	$ 2,250,250	$ (4,133)	$ (1,275,441)	$ 970,735
Issuance of common stock under stock plan	414,888	1	1,297	—	—	1,298
Stock-based compensation expense	—	—	23,609	—	—	23,609
Other comprehensive loss	—	—	—	(7,977)	—	(7,977)
Net loss	—	—	—	—	(105,999)	(105,999)
Balance at March 31, 2022	59,555,974	$ 60	$ 2,275,156	$ (12,110)	$ (1,381,440)	$ 881,666
Issuance of common stock under stock plan and stock purchase plan	132,321	$ —	$ 2,407	$ —	$ —	2,407
Stock-based compensation expense	—	—	25,524	—	—	25,524
Other comprehensive loss	—	—	—	(2,138)	—	(2,138)
Net loss	—	—	—	—	(159,709)	(159,709)
Balance at June 30, 2022	59,688,295	$ 60	$ 2,303,087	$ (14,248)	$ (1,541,149)	$ 747,750
Issuance of common stock under stock plan	120,197	—	2,030	—	—	2,030
Stock-based compensation expense	—	—	24,268	—	—	24,268
Other comprehensive income	—	—	—	(578)	—	(578)
Net loss	—	—	—	—	(133,163)	(133,163)
Balance at September 30, 2022	59,808,492	$ 60	$ 2,329,385	$ (14,826)	$ (1,674,312)	$ 640,307

See accompanying notes to the unaudited condensed consolidated financial statements.

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

	Nine Months Ended September 30,	
	2023	**2022**
Cash flows from operating activities		
Net loss	$ (396,068)	$ (398,871)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	10,134	4,719
Non-cash lease expense	6,759	6,212
Stock-based compensation	70,087	72,855
Non-cash interest expense	11,886	8,389
Non-cash customer consideration	—	(27,500)
Net (accretion of discount) amortization of premium on marketable securities	(11,527)	844
Other	2,342	(57)
Changes in assets and liabilities:		
Accounts receivable	(18,970)	5,553
Unbilled accounts receivable	13,019	9,282
Inventory	(5,195)	(20,653)
Prepaid expenses and other current assets	(2,449)	(15,575)
Other assets	(1,724)	(11,886)
Accounts payable	4,244	(2,031)
Accrued expenses	(15,100)	7,833
Other long-term liabilities	(7,235)	5,730
Deferred revenue	(10,280)	(19,952)
Operating lease liabilities	(7,842)	(5,764)
Net cash used in operating activities	(357,919)	(380,872)
Cash flows from investing activities		
Purchases of property and equipment	(11,389)	(7,438)
Purchases of investments	(648,705)	(258,654)
Maturities of investments	855,365	170,123
Other	—	(289)
Net cash provided by (used in) investing activities	195,271	(96,258)
Cash flows from financing activities		
Net proceeds from the sale of future royalties and revenues	—	415,836
Net proceeds from term loan facility	97,968	137,797
Net proceeds from stock option exercises and employee stock purchase plan	5,729	5,686
Net cash provided by financing activities	103,697	559,319
Net increase (decrease) in cash, cash equivalents, and restricted cash	(58,951)	82,189
Cash, cash equivalents and restricted cash at beginning of period	124,904	215,119
Effect of exchange rate changes on cash, cash equivalents and restricted cash	(285)	(685)
Cash, cash equivalents and restricted cash at end of period	$ 65,668	$ 296,623
Supplemental cash flow information		
Cash paid for interest	$ 25,455	$ 2,956
Property and equipment purchases unpaid at period end	$ 1,921	$ 195
Cash paid for taxes, net	$ 762	$ 4,018

See accompanying notes to the unaudited condensed consolidated financial statements.

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 unaudited condensed consolidated statements of cash flows (in thousands).

	September 30, 2023	September 30, 2022
Cash and cash equivalents	$ 55,972	$ 291,430
Restricted cash	9,696	5,193
Total cash, cash equivalents, and restricted cash shown in condensed consolidated statements of cash flows	$ 65,668	$ 296,623

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 and blood disorders. The Company's approach is to leverage its novel research engine to systematically and reproducibly identify drivers of diseases in genomically defined patient populations, and to craft highly selective and potent drug candidates that are intended to provide significant and durable clinical responses to patients.

The Company has brought its approved medicines, AYVAKIT®/AYVAKYT® (avapritinib) and GAVRETO® (pralsetinib), to patients in the U.S. and Europe, and the Company is globally advancing multiple programs for mast cell disorders, including SM and chronic urticaria, breast cancer and other cancers vulnerable to CDK2 inhibition, as well as EGFR-mutant lung cancer. 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, 2023, the Company had cash, cash equivalents and marketable securities of $827.2 million. Based on the Company's current operating plans, the Company anticipates that its existing cash, cash equivalents and marketable securities 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, 2022 and notes thereto included in the Company's Annual Report on Form 10-K for the year ended December 31, 2022, filed with the SEC on February 16, 2023 (2022 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, 2023, the results of its operations for the three and nine months ended September 30, 2023 and 2022, stockholder's equity for the three and nine months ended September 30, 2023 and 2022 and cash flows for nine months ended September 30, 2023 and 2022. Such adjustments are of a normal and recurring nature. The results for the three and nine months ended September 30, 2023 are not necessarily indicative of the results for the year ending December 31, 2023 or for any future period.

The accompanying unaudited interim 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, inventory, operating lease right-of-use assets, operating lease liabilities, stock-based compensation expense, accrued expenses, liabilities related to the sale of future royalties and future revenues, equity investment, and income taxes. 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, 2023 are consistent with those discussed in Note 2 to the consolidated financial statements in the 2022 Annual Report on Form 10-K, with the exception of the below new policy.

Performance-Based Restricted Stock Unit Awards

Fair value of performance-based restricted stock unit awards (PSUs) at the grant date are estimated using a lattice model with a Monte Carlo simulation. This valuation methodology utilizes several key assumptions, including defined consecutive trading day average closing stock price on the grant date, valuation date stock price, expected volatilities using historical volatilities, correlation coefficients based on the volatility data, risk-free rates of return and expected dividend yield. The probability of actual shares expected to be earned is considered in the grant date valuation and the expense is not adjusted to reflect the actual units earned. The PSUs cliff vest at the end of the service period and the compensation expense for PSUs is recognized straight-line over the applicable service period.

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. 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.

3. Financing Arrangements

Royalty Pharma Purchase and Sale Agreement

On June 30, 2022, the Company entered into a purchase and sale agreement (Royalty Purchase Agreement) with Royalty Pharma. Pursuant to the Royalty Purchase Agreement, the Company received an upfront payment of $175.0 million in consideration for the Company's rights to receive royalty payments on the net sales of GAVRETO worldwide excluding the CStone Territory (as defined below) and U.S. territory under the terms of the Roche pralsetinib collaboration agreement.

Although the Company sold all of the rights to receive royalties on the net sales of GAVRETO worldwide excluding the CStone Territory and U.S. territory to Royalty Pharma, the Company continues to co-develop pralsetinib with Roche globally and is therefore involved in the generation of these future royalties. Due to the Company's significant continuing involvement, the Company continues to account for any royalties and development and commercialization milestones earned related to the underlying territory under the Roche pralsetinib collaboration agreement as collaboration revenue on its consolidated statements of operations and comprehensive loss. Net proceeds from the transaction were recorded as a liability related to sale of future royalties and revenues on the consolidated balance sheet. The Company accretes the $175.0 million, net of transaction costs of $3.8 million, to the total of these royalties as interest expense using the effective interest method over the estimated life of the arrangement. These estimates contain assumptions that impact the amount recorded and the interest expense that will be recognized in future periods.

As payments are made to Royalty Pharma, the balance of the liability will be effectively repaid over the life of the Royalty Purchase Agreement. In order to determine the amortization of the liability, the Company estimates the total amount of future royalty payments to be paid to Royalty Pharma over the life of the arrangement. The exact amount of repayment is likely to change each reporting period. A significant increase or decrease in GAVRETO's net revenue of the underlying territory will impact interest expense and the liability related to this arrangement. The Company periodically assesses the expected payments to Royalty Pharma and prospectively adjusts the amortization of the liability related to this arrangement for material changes in such payments including the prospective impact around the uncertainty related to GAVRETO's commercial outlook in the underlying territory during the life of the arrangement.

In February 2023, the Company received written notice from Roche of their election to terminate for convenience the Roche pralsetinib collaboration agreement. The termination will become effective February 2024, at which time the Company will regain commercialization and development rights to GAVRETO from Roche worldwide excluding the CStone Territory. As of September 30, 2023, none of the derecognition conditions under ASC 405 *Liabilities* were met, and in consideration of the significant uncertainties related to GAVRETO's commercial outlook in the underlying territory during the life of the arrangement caused by the termination of the Roche pralsetinib collaboration agreement, during the three and nine months ended September 30, 2023, the Company did not accrete any interest expenses related to the liability. As of September 30, 2023, the net carrying value of the liability related to this arrangement was $175.3 million.

Pursuant to the Royalty Purchase Agreement, the Company is eligible to receive certain milestone payments totaling up to $165.0 million, subject to the achievement of specified net sales milestones by Roche. However, following the termination of the Roche pralsetinib collaboration agreement, if the specified net sales milestone thresholds under the Royalty Purchase Agreement with Royalty Pharma are not otherwise met, the Company may no longer be eligible to receive any of the contingent milestone payments under the Royalty Purchase Agreement. The potential milestone payments will be added to the carrying value of the liability related to this arrangement when and if the milestones are achieved and received.

Financing Arrangements with Sixth Street Partners

In July 2022, the Company closed two transactions pursuant to a purchase and sale agreement (Future Revenue Purchase Agreement) and a financing transaction for up to $660.0 million (as amended, Financing Agreement) with Sixth Street Partners. Because two transactions were entered into with the same parties and in contemplation of one another, the Company recorded these transactions based on the relative fair values of each freestanding financial instrument and allocated the proceeds in proportion to those fair value amounts.

Sixth Street Partners Purchase and Sale Agreement

Pursuant to the Future Revenue Purchase Agreement, the Company received gross proceeds of $250.0 million in exchange for future royalty payments at a rate of 9.75% on up to $900 million each year of (i) aggregate worldwide annual net product sales of AYVAKIT/AYVAKYT (avapritinib) and (ii), if it is approved, aggregate worldwide annual net product sales of BLU-263 (elenestinib), but excluding sales in Greater China, subject to a cumulative cap of 1.45 times the upfront invested capital or a total of $362.5 million. In the event that certain revenue targets are not achieved by specified dates, the royalty rate and cumulative cap shall be increased to 15% and 1.85 times the invested capital (or $462.5 million), respectively.

The Company continues to own the research, development, manufacturing and commercialization of AYVAKIT/AYVAKYT and if it is approved, elenestinib, and has significant continuing involvement in the generation of the cash flows under the Future Revenue Purchase Agreement. Therefore, the Company continues to account for any revenue earned from worldwide product sales of AYVAKIT/AYVAKYT and, if it is approved, elenestinib, on its consolidated statements of operations and comprehensive loss. Net proceeds received from the transaction were recorded as a liability related to sale of future royalties and revenues on the consolidated balance sheet. The Company accretes the $250.0 million, net of transaction costs of $5.4 million, to the total of these future payments as interest expense using the effective interest method over the estimated life of the arrangement.

As payments are made to Sixth Street Partners, the balance of the liability is effectively repaid over the life of the Future Revenue Purchase Agreement. In order to determine the amortization of the liability, the Company estimates the total amount of future revenue payments to be paid to Sixth Street Partners over the life of the arrangement. The

exact amount of repayment is likely to change each reporting period. A significant increase or decrease in worldwide product sales of AYVAKIT/AYVAKYT and, if it is approved, elenestinib, will materially impact the liability related to this arrangement, interest expense and the time period for repayment. The Company periodically assesses the expected payments to Sixth Street Partners and prospectively adjusts the amortization of the liability related to this arrangement for material changes in such payments. As of September 30, 2023, the Company's estimate of this total interest expense resulted in an effective annual interest rate of 10.8%. These estimates contain assumptions that impact the amount recorded and the interest expense that will be recognized in future periods.

As of September 30, 2023, the net carrying value of the liability related to this arrangement was $264.9 million. The following table shows the activity within the liability account (in thousands):

Carrying value as of January 1, 2023	$ 254,328
Interest expense recognized	21,043
Payments	(10,484)
Carrying value as of September 30, 2023	$ 264,887

Sixth Street Partners Term Loan

The Financing Agreement entered into by the parties in connection with the transaction provides for (i) a senior secured term loan facility of up to $150.0 million and (ii) a senior secured delayed draw term loan facility of up to $250.0 million to be funded in two tranches at the Company's choice subject to certain terms and conditions. The term loans will mature on June 30, 2028 and bear interest at a variable rate equal to either the Secured Overnight Financing Rate (SOFR) plus 6.50% or the base rate plus 5.50%, subject to a floor of 1% and 2% with respect to the SOFR and base rate, respectively.

As part of the Financing Agreement with Sixth Street Partners, the Company received gross proceeds of $150.0 million in July 2022 and incurred an aggregate of $12.2 million of debt discounts and transaction costs. In August 2023, the Company received the first tranche of the senior secured delayed draw term loan facility in the amount of $100.0 million in gross proceeds and incurred $2.0 million of transaction costs. Debt discounts and transaction costs have been recorded as a reduction to the carrying amount of the debt on the Company's consolidated balance sheet and are amortized as additional interest expenses using the effective interest rate method over the period from issuance through maturity. In addition, the Company may at any time request an incremental term loan in an amount not to exceed $260.0 million on terms to be agreed and subject to the consent of Sixth Street Partners providing such incremental term loan. As of September 30, 2023, the Company's estimate of the total interest expense resulted in an effective annual interest rate of 13.3%. The carrying amount of the debt as of September 30, 2023 is subject to variable interest rates, which are based on current market rates, and as such, approximates fair value.

The following table shows the activity within the liability account (in thousands):

Carrying value as of January 1, 2023	$ 139,083
Net proceeds received from the delayed draw term loan	97,968
Interest expense recognized	15,557
Payments	(14,230)
Carrying value as of September 30, 2023	$ 238,378

The Company's obligations under the Financing Agreement are secured, subject to certain exceptions, by security interests in the substantially all of the Company's assets and the Company's certain subsidiaries. The Financing Agreement contains customary negative covenants that, among other things and subject to certain exceptions, could restrict the Company's ability to incur additional liens, incur additional indebtedness, make investments, including acquisitions, engage in fundamental changes, sell or dispose of assets that constitute collateral, including certain intellectual property, pay dividends or make any distribution or payment on or redeem, retire or purchase any equity interests, amend, modify or waive certain material agreements or organizational documents and make payments of certain subordinated indebtedness. The Financing Agreement also requires the Company to maintain a consolidated liquidity of at least (i) $50.0 million during the period commencing from the date on which the term loans are funded to the date which is the day before the next term loans are funded and (ii) $80.0 million for each day thereafter. As of

September 30, 2023, the Company was in compliance with the applicable terms and conditions of the covenants under the Financing Arrangement.

4. Marketable Securities

Marketable securities consisted of the following at September 30, 2023 and December 31, 2022 (in thousands):

September 30, 2023	Amortized Cost	Unrealized Gain	Unrealized Losses	Fair Value
Marketable securities, available-for-sale:				
U.S. government agency securities	$ 201,990	—	(1,127)	$ 200,863
U.S. treasury obligations	571,588	7	(1,204)	570,391
Total	$ 773,578	$ 7	$ (2,331)	$ 771,254

December 31, 2022	Amortized Cost	Unrealized Gain	Unrealized Losses	Fair Value
Marketable securities, available-for-sale:				
U.S. government agency securities	$ 377,519	—	(4,848)	$ 372,671
U.S. treasury obligations	591,193	22	(5,123)	586,092
Total	$ 968,712	$ 22	$ (9,971)	$ 958,763

The following table summarizes the estimated fair value (in thousands) and number of the Company's available-for-sale securities that are in loss position as of September 30, 2023 and December 31, 2022 by the length of time the security has been in loss position:

	September 30, 2023		December 31, 2022	
	Fair value	Number of securities	Fair value	Number of securities
Debt securities in unrealized loss position for 12 months or less	$ 624,319	116	$ 371,746	66
Debt securities in unrealized loss position for more than 12 months	56,975	10	550,561	56
Total debt securities in unrealized loss position	$ 681,294	126	$ 922,307	122

The Company has the intent and ability to hold its debt securities until recovery. As a result, the Company did not record any charges for credit-related impairments for its marketable debt securities for the three and nine months ended September 30, 2023 and 2022.

The following table summarizes the amortized cost basis and estimated fair value of the Company's available-for-sale securities by contractual maturity as of September 30, 2023 and December 31, 2022 (in thousands):

	September 30, 2023		December 31, 2022	
	Amortized Cost	Fair value	Amortized Cost	Fair value
Within one year	$ 658,760	$ 657,012	$ 834,440	$ 825,283
After one through five years	114,818	114,242	134,272	133,480
Total	$ 773,578	$ 771,254	$ 968,712	$ 958,763

The following table summarizes the proceeds from maturities of debt securities during the three and nine months ended September 30, 2023 and 2022 (in thousands):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2023	2022	2023	2022
Proceeds from maturities of debt securities	$ 237,600	$ 90,500	$ 855,365	$ 170,123

The Company did not realize any gains or losses from maturities of debt securities for the three and nine months ended September 30, 2023 and 2022.

5. Fair Value of Financial Instruments

The following table summarizes the Company's cash equivalents and marketable securities measured at fair value on a recurring basis as of September 30, 2023 (in thousands):

Description	September 30, 2023	Active Markets (Level 1)	Observable Inputs (Level 2)	Unobservable Inputs (Level 3)
Cash equivalents:				
Money market funds	$ 47,510	47,510	—	$ —
Marketable securities, available-for-sale:				
U.S. government agency securities	200,863	—	200,863	—
U.S. treasury obligations	570,391	570,391	—	—
Total	$ 818,764	$ 617,901	$ 200,863	$ —

The following table summarizes the Company's cash equivalents and marketable securities measured at fair value on a recurring basis as of December 31, 2022 (in thousands):

Description	December 31, 2022	Active Markets (Level 1)	Observable Inputs (Level 2)	Unobservable Inputs (Level 3)
Cash equivalents:				
Money market funds	$ 95,198	$ 95,198	$ —	$ —
U.S. treasury obligations	4,989	4,989	—	—
Marketable securities, available-for-sale:				
U.S. government agency securities	372,671	—	372,671	—
U.S. treasury obligations	586,092	586,092	—	—
Total	$ 1,058,950	$ 686,279	$ 372,671	$ —

6. 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 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. In June 2021, the FDA granted a subsequent approval for AYVAKIT, expanding the labeled indications to include adult patients with advanced SM, including aggressive SM (ASM), SM with an associated hematological neoplasm (SM-AHN) and mast cell leukemia (MCL). In March 2022, the European Commission expanded the marketing authorization for AYVAKYT to include the treatment of adult patients with ASM, SM-AHN, or MCL, after at least one systemic therapy. In May 2023, the FDA approved AYVAKIT for the treatment of adult patients with indolent SM.

The following table summarizes revenue recognized from product sales for the three and nine months ended September 30, 2023 and 2022 (in thousands):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2023	2022	2023	2022
United States	$ 49,121	$ 25,054	$ 118,355	$ 70,888
Rest of World	5,107	3,580	14,818	10,041
Total product revenue	$ 54,228	$ 28,634	$ 133,173	$ 80,929

The Company primarily sells AYVAKIT/AYVAKYT through specialty distributors and specialty pharmacies. The following table summarizes the customers that represent 10% or greater of gross product revenue for the three and nine months ended September 30, 2023, and 2022 (in thousands):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2023	2022	2023	2022
Customer 1	42 %	45 %	42 %	46 %
Customer 2	11 %	10 %	11 %	11 %

The following table summarizes the customers with amounts due that represent 10% or greater of the accounts receivable associated with the Company's product sales as of September 30, 2023 and December 31, 2022 (in thousands):

	September 30, 2023	December 31, 2022
Customer 1	31 %	33 %
Customer 2	13 %	15 %
Customer 3	11 %	*
Customer 4	*	12 %

* Indicates the customer's share is under 10%.

The following table summarizes activity in each of the product revenue allowance and reserve categories for the nine months ended September 30, 2023 and 2022 (in thousands):

	Nine Months Ended September 30,	
	2023	2022
Beginning balance at January 1	$ 9,788	$ 4,345
Provision related to sales in the current period	25,874	13,606
Adjustment related to prior periods sales	(545)	(645)
Credits and payments made	(17,469)	(9,980)
Ending balance at September 30	$ 17,648	$ 7,326

The total reserves that are included in the Company's unaudited condensed consolidated balance sheets as of September 30, 2023 and December 31, 2022, are summarized as follows (in thousands):

	September 30, 2023	December 31, 2022
Reduction of accounts receivable, net	$ 1,547	$ 742
Component of accrued expenses	16,101	9,046
Total revenue-related reserves	$ 17,648	$ 9,788

7. Inventory

Capitalized inventory consists of the following at September 30, 2023 and December 31, 2022 (in thousands):

	September 30, 2023	December 31, 2022
Raw materials	$ 1,599	$ 4,967
Work in process	29,335	28,427
Finished goods	3,475	2,791
Total	$ 34,409	$ 36,185

Balance sheet classification

	September 30, 2023	December 31, 2022
Inventory	$ 16,457	$ 29,697
Other assets	17,952	6,488
Total	$ 34,409	$ 36,185

Inventory amounts written down as a result of excess, obsolescence, unmarketability or other reasons are charged to cost of sales. The Company recognized a write-down of $0.1 million and $2.2 million for the three and nine months ended September 30, 2023, respectively. The Company did not recognize any write-down for the three and nine months ended September 30, 2022. Long-term inventory, which primarily consists of work in process and raw materials, is included in other assets in the unaudited condensed consolidated balance sheets.

8. Restricted Cash

At September 30, 2023 and December 31, 2022, $9.7 million and $5.2 million, respectively, of the Company's cash is restricted by a financial institution primarily related to funds held to satisfy the requirements of certain government agreements and the security deposits for the lease agreements for the Company's office and laboratory spaces.

9. Accrued Expenses

Accrued expenses consist of the following (in thousands):

	September 30, 2023	December 31, 2022
Research, development and commercial contract costs	$ 38,699	$ 66,041
Employee compensation	34,517	30,744
Accrued professional fees	14,592	17,588
Revenue-related reserves	16,101	9,046
Other	6,527	7,704
Total	$ 110,436	$ 131,123

10. Collaboration and License Agreements

IDRx

In August 2022, the Company entered into a license agreement with IDRx, Inc. (IDRx), pursuant to which the Company granted IDRx an exclusive, worldwide, royalty-bearing license to exploit the Company's internally discovered KIT exon 13 inhibitor IDRX-73 (IDRx License Agreement). IDRx is a clinical-stage biopharmaceutical company and among IDRx's founders are Alexis Borisy, George Demetri, M.D., and Nicholas Lydon, Ph.D., who were each members of the Company's board of directors at the time. Due to these relationships, the transaction with IDRx is a related party transaction.

In connection with the IDRx License Agreement, the Company also entered into a stock purchase agreement with IDRx (IDRx Stock Purchase Agreement), pursuant to which the Company received 4,509,105 shares of IDRx's Series A preferred stock with the right to receive additional shares of IDRx's Series A preferred stock through an anti-dilution provision subject to a defined financing cap. In July 2023, the Company received 192,282 additional shares under the anti-dilution provision.

The Company is also eligible to receive up to $217.5 million in contingent cash payments, including specified development, regulatory and sales-based milestone payments. In addition, IDRx is obligated to pay to the Company royalties on aggregate annual worldwide net sales of licensed products at tiered percentage rates up to low-teens, subject to adjustments in specified circumstances under the IDRx License Agreement.

Unless earlier terminated, the IDRx License Agreement will expire on a country-by-country, licensed product-by-licensed product basis upon the latest of: (a) the expiration of the last valid claim within the licensed patents covering such licensed product in a such country, (b) the expiration of the regulatory exclusivity period for such licensed product in such country, or (c) the 10th anniversary of the first commercial sale of such licensed product in such country. Following the end of the term for any such licensed product and in such region by expiration, the license granted to IDRx will become exclusive, perpetual, irrevocable, fully paid-up and royalty-free. IDRx may terminate the IDRx License Agreement for convenience at any time upon at least twelve months' prior written notice to the Company. Either party may also terminate the IDRx License Agreement for material breach of the other party or for insolvency, and the Company may terminate the IDRx License Agreement for IDRx's breach of the anti-dilution provision in the IDRx Stock Purchase Agreement. Upon termination of the license agreement in its entirety, all rights and obligations under the license agreement will terminate and revert back to the Company, and the Company has a license under certain intellectual property of IDRx to continue to exploit the compound and terminated product, subject to a royalty that will be negotiated at the time of termination.

The Company considered the ASC 606 criteria for combining contracts and determined the IDRx License Agreement and the IDRx Stock Purchase Agreement should be combined into a single contract because they were negotiated and entered into in contemplation of one another. Therefore, the Company determined that the 4,509,105 shares of IDRx's Series A preferred stock and the anti-dilution right to receive additional shares should be attributed to the transaction price of the IDRx License Agreement.

The Company evaluated the IDRx License Agreement under ASC 606. The Company identified the following material promises under the agreement: (1) the exclusive license and (2) the initial know-how transfer. The Company determined that the exclusive license and the initial know-how transfer were not distinct from each other, as the exclusive license has limited value without the corresponding know-how transfer. As such, for the purposes of ASC 606, the Company determined that these two material promises, the exclusive license and the initial know-how transfer, should be combined into one distinct performance obligation. The Company concluded that the license is a functional intellectual property license. The Company determined that IDRx benefited from the license along with the initial know-how transfer at the time of grant, and therefore the related performance obligation is satisfied at a point in time.

For the purposes of ASC 606, the transaction price of the IDRx License Agreement at the contract inception was determined to be $27.5 million and recorded as license revenue-related party on the consolidated statements of operations and comprehensive loss during the year ended December 31, 2022. The fair value was derived from IDRx's most recent financing transaction with unrelated investors. All potential milestone payments that the Company is eligible to receive under the IDRx License Agreement have been excluded from the transaction price. The Company reevaluates the transaction price for inclusion of milestone payments and royalties at the end of each reporting period and as uncertain events are resolved or other changes in circumstances occur, and if necessary, the Company adjusts 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. Additionally, the Company is entitled to sales milestones and royalties from the sales of the licensed products, and revenue are recognized when the related sales occur.

The Company concluded the preferred stock investment should be accounted for as an equity investment as it is not mandatorily redeemable nor does the Company have the unilateral right to redeem the preferred stock, and the Company, along with its related parties, do not have a controlling financial interest in IDRx nor have the ability to influence the financial and operating policies through the ownership of preferred stock. IDRx's preferred stock is not

exchange-traded and does not have a readily determinable fair value. Therefore, the Company accounts for the preferred stock investment under the measurement alternative for equity investments that do not have a readily determinable fair value, which is at cost of $27.8 million including transaction costs of $0.3 million. As of September 30, 2023, the cost of the investment in IDRx's preferred stock was $27.8 million and was recorded as equity investment on the condensed consolidated balance sheets. As of September 30, 2023, no adjustments have been recognized related to the preferred stock investment as a result of the application of the measurement alternative.

Proteovant

In February 2022, the Company entered into an exclusive collaboration agreement (the Proteovant collaboration agreement) with Oncopia Therapeutics, Inc., d/b/a Proteovant Therapeutics, Inc. (Proteovant), to jointly research and advance up to two novel protein degrader therapies into development candidates, as well as up to two additional novel protein degrader target programs as may be mutually agreed to by the Company and Proteovant (each program is referred to as a target program). On a target program-by-target program basis, the Company has an exclusive option to obtain a worldwide, exclusive license to develop and commercialize any licensed compound and licensed product under each target program. Proteovant has the right to opt into the global development and U.S. commercialization of certain licensed compounds and licensed products under the second target program that the Company options, and if the parties add additional target programs, Proteovant will have the same opt-in right for the fourth target program that the Company options.

The Company paid Proteovant an upfront payment of $20.0 million in connection with the execution of the agreement and Proteovant will be eligible to receive up to an additional $632.0 million in contingent milestone payments including specified research, development, regulatory and commercialization milestones and tiered percentage royalties on a licensed product-by-licensed product basis ranging from the mid- to high-single digits on net sales on the first two target programs, subject to adjustment in specified circumstances. If Proteovant opts in to the second target program, the parties will split profits and losses of that program equally in the U.S. along with development costs and the milestone payments for the program will be reduced accordingly. Proteovant will be eligible to receive milestone payments and royalties on ex-U.S. sales. In addition, the parties may jointly extend the collaboration, with the same structure and financial terms, to two additional program targets through additional funding by the Company.

The Company concluded that Proteovant is providing the Company with research services throughout the period until the Company can exercise its option to obtain a worldwide, exclusive license to develop and commercialize any licensed compound. Therefore, the Company recorded the $20.0 million upfront payment as an asset on the unaudited condensed consolidated financial statements and records it as research and development expense over the expected research period. The Company reevaluates the expected research period at the end of each reporting period and prospectively adjusts the amortization of the asset for changes in the expected research period. Each research and development milestone payment is accrued and expensed when probable. During the three and nine months ended September 30, 2023, the Company recorded research and development expense of $0.6 million and $6.2 million, respectively, under the Proteovant collaboration agreement. During the three and nine months ended September 30, 2022, the Company recorded research and development expense of $1.4 million and $2.9 million, respectively, under the Proteovant collaboration agreement.

Zai Lab

In November 2021, the Company entered into a collaboration (the Zai Lab agreement) with Zai Lab (Shanghai) Co., Ltd., (Zai Lab) to develop and commercialize certain licensed products for the treatment of EGFR-driven non-small cell lung cancer in Greater China, including Mainland China, Hong Kong, Macau and Taiwan (collectively, the Zai Lab Territory). The collaboration aims to accelerate and expand global development of the licensed products, which currently include BLU-945 and BLU-525 (which served as a back-up candidate for BLU-701). The Company retains exclusive rights to the licensed products outside the Zai Lab Territory.

Under the Zai Lab agreement, the Company received an upfront cash payment of $25.0 million and, in addition to the upfront payment received, the Company is eligible to receive up to $590.0 million in contingent payments, including specified development, regulatory and sales-based milestones and tiered percentage royalties on a licensed product-by-licensed product basis ranging from the low-teens to mid-teens on annual net sales of each licensed product in the Zai Lab Territory, subject to adjustment in specified circumstances. Zai Lab is responsible for costs related to

clinical trials in the Zai Lab Territory, other than the specified shared services costs as defined in the Zai Lab agreement which are shared by the Company and Zai Lab.

Pursuant to the terms of the Zai Lab agreement, Zai Lab is responsible for conducting all development and commercialization activities in the Zai Lab Territory related to the licensed drug candidates. In addition, under the Zai Lab agreement, each party has granted the other party specified intellectual property licenses to enable the other party to perform its obligations and exercise its rights under the Zai Lab agreement, including license grants to enable each party to conduct research, development and commercialization activities pursuant to the terms of the Zai Lab agreement.

The Zai Lab agreement will continue on a licensed product-by-product and region-by-region basis until the later of (i) the 12th anniversary of the date of the first commercial sale of a licensed product in the Zai Lab Territory, (ii) the date of expiration of the last valid patent claim related to the Company's patent rights of the product in the Zai Lab Territory, and (iii) the expiration of the last regulatory exclusivity for that product in a region in the Zai Lab Territory. Zai Lab may terminate the agreement for convenience by giving a written notice after the second anniversary of the effective date (a) at least 12 months after the date of notice, in the event such notice is given after the first commercial sale of a licensed product in the Zai Lab Territory or (b) at least nine months after the date of such notice, in the event such notice is given prior to the first commercial sale of the first licensed product in the Zai Lab Territory. Either party may terminate the Zai Lab agreement for the other party's uncured material breach or insolvency. Upon termination, all licenses and all other rights granted by the Company to Zai Lab will terminate. Each party will retain its joint ownership interests in any joint collaboration technology.

The Company evaluated the Zai Lab agreement to determine whether it is a collaborative arrangement in the scope of ASC 808. The Company concluded that the Zai Lab agreement is a collaborative agreement under ASC 808 as both parties are active participants in the clinical trials and are exposed to significant risks and rewards of those activities under the Zai Lab agreement. The Company determined that the Zai Lab agreement contained two material components: (i) licenses granted to Zai Lab to exploit and develop each licensed product in the Zai Lab Territory and related activities in the Zai Lab Territory, including manufacturing, and (ii) the parties' participation in the global development of the licensed products. The Company used the criteria specified in ASC 606 to determine which of the components of the Zai Lab agreement are performance obligations with a customer and concluded that Zai Lab is the Company's customer for the licenses and related activities in the Zai Lab Territory under ASC 606. The global development activities under the agreement does not present a transaction with a customer and the payments received by the Company for global development activities, including manufacturing, are accounted for as a reduction of related expenses. During the three and nine months ended September 30, 2023, the Company did not record such reductions of expenses under the Zai Lab agreement. During the three and nine months ended September 30, 2022, the Company recorded $0.2 million and $0.5 million, respectively, in reductions of expenses under the Zai Lab agreement.

The Company evaluated the Zai Lab Territory specific licenses and related activities under ASC 606 as these transactions are considered transactions with a customer and identified three material promises at the outset of the Zai Lab agreement, which consists of the following for each licensed product: (1) the exclusive license, (2) the initial know-how transfer and (3) manufacturing activities related to development and commercial supply of the licensed product in the Zai Lab Territory. The Company determined that the exclusive license and the initial know-how transfer were not distinct from each other, as the exclusive license has limited value without the corresponding know-how transfer. As such, for the purposes of ASC 606, the Company determined that these two material promises, the exclusive license and the initial know-how, should be combined into one distinct performance obligation. The Company further evaluated the material promise associated with manufacturing activities related to development and commercial supply of the licensed products in the Zai Lab Territory, given Zai Lab is not obligated to purchase any minimum amount or quantities of the development and commercial supply from the Company, the Company concluded that, for the purpose of ASC 606, the provision of manufacturing activities related to development and commercial supply of the licensed product in Zai Lab Territory was an option but not a performance obligation of the Company at the inception of the Zai Lab collaboration agreement and will be accounted for if and when exercised. The Company also concluded that there is no separate material right in connection with the development and commercial supply of the licensed product, as the expected pricing was not issued at a significant and incremental discount. Therefore, the manufacturing activities were excluded as performance obligation at the outset of the arrangement.

The Company evaluated the license under ASC 606 and concluded that the license is a functional intellectual property license. The Company determined that Zai Lab benefited from the license along with the initial know-how

transfer at the time of grant, and therefore the related performance obligation is satisfied at a point in time. Additionally, the Company is entitled to sales milestones and royalties from Zai Lab upon future sales of the licensed products in the Zai Lab Territory, and revenue will be recognized when the related sales occur. Costs that are incurred associated with Zai Lab Territory specific activities are reimbursable from Zai Lab and are recognized as revenue. The revenue recognized under the Zai Lab agreement during the three and nine months ended September 30, 2023 was negligible. During the three and nine months ended September 30, 2022, the Company recorded $0.2 million and $0.8 million, respectively, in revenue related to Zai Lab Territory specific activities.

For the purposes of ASC 606, the transaction price of the Zai Lab agreement at the outset of the arrangement was determined to be $25.0 million, which consisted of the upfront cash payment. 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 Company satisfied the performance obligation upon delivery of the licenses and initial know-how transfer, and recognized the upfront payment of $25.0 million as revenue in 2021.

The Company reevaluates 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 adjusts 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.

Roche – Pralsetinib Collaboration

In July 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.

Under the Roche pralsetinib collaboration agreement, the Company received an upfront cash payment of $675.0 million, and through September 30, 2023, the Company received an aggregate of $105.0 million in specified regulatory and commercialization milestones. In February 2023, the Company received written notice from Roche of their election to terminate for convenience the Roche pralsetinib collaboration agreement. The termination will become effective in February 2024, at which time the Company will regain commercialization and development rights to GAVRETO from Roche worldwide excluding the CStone Territory. Until the termination of the collaboration agreement is effective, the parties continue to perform their respective obligations under the collaboration agreement, including with respect to the development and commercialization of GAVRETO. The Company will not be entitled to receive payment for milestones, if any, achieved during the period between the receipt of the notice of termination and the effective date of termination. The termination of the collaboration agreement does not have an impact on the Company's current accounting treatment related to the Roche pralsetinib collaboration.

In the U.S., the Company and Roche agreed to work together to co-commercialize pralsetinib and 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 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 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.

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 shares of common stock to Roche Holdings at a purchase price of $96.57 per share and received an aggregate of $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 Roche is the Company's customer in those transactions.

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 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.

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 for up to 24 months. Given that Roche is not obligated to purchase any minimum amount or quantities of the development and commercial supply from the Company, the Company concluded that, for the purpose of ASC 606, the provision of manufacturing activities related to development and commercial supply of pralsetinib in Roche Territory was an option but not a performance obligation of the Company at the inception of the Roche collaboration agreement and is accounted for if and when exercised. The Company also concluded that there is no separate material right in connection with the development and commercial supply of pralsetinib, as the expected pricing was not issued at a significant and incremental discount. 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 the revenue is recognized when the related sales occur. Costs that are incurred associated with the Roche Territory activities are reimbursable from Roche and are recognized as revenue.

For the purposes of ASC 606, the transaction price of the Roche collaboration agreement at the outset of the arrangement 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, which was allocated to the performance obligation related to the pralsetinib licenses. Through September 30, 2023, the Company has achieved an aggregate of $105.0 million in specified regulatory and commercialization milestones which were added to the estimated transaction price of the Roche pralsetinib agreement.

The following table summarizes revenue recognized under the Roche pralsetinib collaboration during the three and nine months ended September 30, 2023 and 2022 (in thousands):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2023	2022	2023	2022
Manufacturing and research and development services related to ex-US territory-specific activities	$ 213	$ 3,971	$ 570	$ 4,663
Royalty revenue	300	311	1,102	910
Total Roche pralsetinib collaboration revenue	$ 513	$ 4,282	$ 1,672	$ 5,573

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 are accounted for as an increase to or reduction of research and development expenses.

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. In December 2020, the FDA granted a subsequent accelerated approval for GAVRETO, expanding the labeled indications to include adult and pediatric patients 12 years of age and older with advanced or metastatic RET-mutant medullary thyroid cancer (MTC) who require systemic therapy (which indication was subsequently voluntarily withdrawn by Roche in June 2023, followed by the official FDA withdrawal on July 20, 2023), or with advanced or metastatic RET fusion-positive thyroid cancer who require systemic therapy and who are radioactive iodine-refractory (if radioactive iodine is appropriate). In August 2023, the FDA converted the accelerated approval of GAVRETO to full regular approval for the treatment of adult patients with metastatic RET fusion-positive NSCLC.

Prior to July 1, 2021, the Company was the principal for product sales to customers in the U.S. and recognized revenues on sales to third parties in product revenue, net in its consolidated statements of operations and comprehensive loss. On July 1, 2021, Roche took over certain responsibilities associated with product sales to customers, pricing and distribution matters for GAVRETO in the U.S. and became the principal for recording product sales to customers in the U.S., and the Company recognized its portion of the commercial losses sharing as collaboration loss sharing in its consolidated statements of operations and comprehensive loss.

The following table summarizes the amount recognized from loss sharing from product sales of GAVRETO to customers in the U.S. during the three and nine months ended September 30, 2023 and 2022 (in thousands):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2023	2022	2023	2022
The Company's share of loss in the U.S. for pralsetinib	$ 1,771	$ 1,665	$ 4,301	$ 7,076

The following table summarizes the amounts recognized as reductions to selling, general and administrative expenses related to the commercialization of GAVRETO in the U.S. and increases in research and development expenses related to global development activities for pralsetinib under the Roche pralsetinib collaboration during the three and nine months ended September 30, 2023 and 2022 (in thousands):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2023	2022	2023	2022
Reductions to selling, general and administrative expenses	$ 3,063	$ 3,560	$ 8,618	$ 12,808
Increases in research and development expenses	$ 7,603	$ 6,111	$ 21,226	$ 9,815

The following table summarizes the contract assets and liability associated with the Roche pralsetinib collaboration as of September 30, 2023 and December 31, 2022 (in thousands):

	September 30, 2023	December 31, 2022
Unbilled accounts receivable	$ 304	$ —
Accrued expenses	$ 6,221	$ 6,519

Although the Company sold its right to receive royalty payments from Roche's sales of GAVRETO in Roche Territory to Royalty Pharma in June 2022, given the Company's significant continuing involvement in the generation of future royalties, the Company continues to account for any royalties earned related to the Roche Territory activities under the Roche pralsetinib collaboration agreement as collaboration revenue on its consolidated statements of operations and comprehensive loss. For additional information, see Note 3 – *Financing Arrangements*.

Clementia

In October 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 through September 30, 2023, the Company has received an aggregate of $50.0 million in cash milestone payments. Subject to the terms of the Clementia agreement, in addition to the upfront and milestone payments received through September 30, 2023, the Company is eligible to receive up to $460.0 million in contingent payments, including specified development, regulatory and sales-based milestones 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 upon at least 12 months' prior written notice to the Company. 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 at the outset of the arrangement was $46.5 million, which was allocated to the three performance obligations on a relative stand-alone selling price basis, and was recognized as revenue during 2019 and 2020.

During the three and nine months ended September 30, 2023, and during the three months ended September 30, 2022, no revenue was recognized from the Clementia collaboration. During the nine months ended September 30, 2022, cash consideration associated with an achieved development milestone of $30.0 million was added to the estimated

transaction price for the Clementia agreement and recognized as revenue. The other potential milestone payments that the Company is eligible to receive were excluded from the transaction price, as the amounts were fully constrained based on the probability of achievement. The Company reevaluates 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 adjusts 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.

There was no revenue deferred as a contract liability associated with the Clementia agreement as of September 30, 2023 and December 31, 2022.

CStone Pharmaceuticals

In June 2018, the Company entered into a collaboration and license agreement (the CStone agreement) with CStone Pharmaceuticals (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 through September 30, 2023, the Company has achieved an aggregate of $38.5 million in milestones under this collaboration. Subject to the terms of the CStone agreement, in addition to the upfront payments received and milestones achieved through September 30, 2023, the Company will be eligible to receive up to $307.5 million in contingent payments, including specified development, regulatory and sales-based milestones for licensed products. In addition, CStone is 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 is 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 are shared by the Company and CStone.

Pursuant to the terms of the CStone agreement, CStone is responsible for conducting all development and commercialization activities in the CStone Territory related to the licensed products. Subject to specified exceptions, during the term of the CStone agreement, each party has agreed that neither it nor its affiliates will conduct specified development and commercialization activities in the CStone Territory related to selective inhibitors of FGFR4, KIT, PDGFRA and RET. In addition, under the CStone agreement, each party has granted the other party specified intellectual property licenses to enable the other party to perform its obligations and exercise its rights under the CStone agreement, including license grants to enable each party to conduct research, development and commercialization activities pursuant to the terms of the CStone agreement.

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, 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, net payments received by the Company for global development activities under the CStone agreement, including manufacturing, are accounted for as a reduction of related expenses.

The Company did not have significant manufacturing and research and development services related to the global development activities during the three and nine months ended September 30, 2023. During the three and nine months ended September 30, 2022, the Company recognized a reduction of $0.5 million and $1.6 million, respectively, in expenses related to manufacturing and research and development activities, net of expenses payable to CStone.

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 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 at 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 in 2018.

The Company did not achieve any milestones under the CStone agreement during the three months ended September 30, 2023 and 2022. During the nine months ended September 30, 2023 and 2022, cash considerations associated with the achieved regulatory milestones of $9.0 million and $4.0 million, respectively, were added to the estimated transaction price for the CStone agreement and recognized as revenue. The Company reevaluates 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 adjusts 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.

Subsequent to the CStone agreement, the Company entered into various commercial supply and manufacturing technology transfer agreements for avapritinib and pralsetinib related to supply of drug substance and commercialization activities conducted specifically for the CStone Territory. The manufacturing activities in these agreements were considered as distinct performance obligations from the CStone collaboration agreement and collaboration revenue is recognized upon delivery of the drug substance and drug product to CStone.

A summary of revenue recognized under the CStone agreement during the three and nine months ended September 30, 2023 and 2022 is as follows (in thousands):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2023	2022	2023	2022
License milestone revenue	$ —	$ —	$ 9,000	$ 4,000
Manufacturing services and royalty revenue related to CStone Territory-specific activities	1,820	2,915	7,861	14,209
Total CStone collaboration revenue	$ 1,820	$ 2,915	$ 16,861	$ 18,209

The following table presents the contract assets and contract liability associated with the CStone collaboration as of September 30, 2023 and December 31, 2022 (in thousands):

	September 30, 2023	December 31, 2022
Accounts receivable, net	$ 5,338	$ 4,991
Unbilled accounts receivable	83	1,529
Contract liability	3,010	2,265

The contract liability associated with the CStone collaboration as of September 30, 2023 and December 31, 2022 resulted primarily from advance payments made by CStone in connection with commercial supply of pralsetinib for the CStone Territory.

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 small molecule therapeutics targeting kinases believed to be important in cancer immunotherapy, as single products or possibly in combination with other therapeutics.

Under the Roche immunotherapy agreement, Roche was originally 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. Four of the five development programs were ended in prior reporting periods and on April 30, 2023, the Company and Roche entered into a mutual termination agreement to terminate the Roche immunotherapy agreement, and licenses granted by the Company to Roche related to MAP4K1 (BLU-852) terminated in their entirety. Certain licenses granted by Roche to the Company survived and became exclusive, worldwide, perpetual, royalty-free and irrevocable. The Company retained ownership of the collaboration compounds directed to MAP4K1 and all of the other previously terminated kinase targets developed under the collaboration.

The Roche immunotherapy agreement represented a vendor-customer relationship under ASC 606 as the Company performed its 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.

The aggregate net transaction price of the Roche immunotherapy agreement was $64.7 million, which comprised of an upfront payment of $45.0 million, an aggregate of $25.0 million in research milestones achieved under the collaboration, and a reduction of $5.3 million as a result of the Company's payment to Roche for certain clinical development costs. This payment resulted from a cost sharing under the clinical development plan for IND-enabling activities for BLU-852, which the Company and Roche endorsed in 2022.

The Company recognized revenue associated with the performance obligation as the research and development services were 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 for each respective period. The amounts received that had not yet been recognized as revenue were deferred as a contract liability on the Company's consolidated balance sheet and recognized over the remaining research and development period until the performance obligation was satisfied. The performance obligation was completely satisfied as of June 30, 2023.

During the three months ended September 30, 2023, the Company did not record any revenue under the Roche immunotherapy agreement. During the nine months ended September 30, 2023, the Company recognized research and development services revenue of $25.7 million under the Roche immunotherapy agreement, of which $16.0 million resulted from changes in contract liability balances as of December 31, 2022 and $9.7 million resulted from the catch-up revenue recognized as a result of the collaboration termination effective in April 2023. The collaboration agreement termination caused the reduction in the estimated lifetime cost to satisfy the Company's performance obligation under the Roche immunotherapy collaboration and the estimated cost to be shared with Roche for the IND-enabling activities for BLU-852, and consequently, increased the transaction price and the percentage of completion of revenue to be recognized under the collaboration agreement.

During the three and nine months ended September 30, 2022, the Company recognized $2.5 million and $1.7 million in revenue under the Roche immunotherapy agreement, respectively, of which, $1.4 million and $3.8 million was recognized due to the changes in the contract liability balances at the beginning of the respective periods, respectively.

As of September 30, 2023, the Company did not have any liabilities related to the Roche immunotherapy collaboration. As of December 31, 2022, the Company had revenue deferred as a contract liability related to the Roche immunotherapy agreement of $16.0 million, of which $2.4 million was included in current liabilities, and accrued expenses of $11.2 million, of which $4.0 million was included in current liabilities.

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, performance-based restricted stock units, unrestricted stock, performance-based 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, 2023, the number of shares reserved for issuance under the 2015 Plan was increased by 2,398,356 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, 2023, there were 4,896,334 shares available for future grant under the 2015 Plan.

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. In June 2022, the Company's board of directors approved the reservation of an additional 1,500,000 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, 2023, there were 1,366,923 shares available for future grant under the Inducement Plan.

Stock options

The following table summarizes the stock option activity for the nine months ended September 30, 2023:

	Shares	Weighted-Average Exercise Price
Outstanding at December 31, 2022	6,233,451	$ 69.14
Granted	1,182,245	45.31
Exercised	(154,433)	22.02
Canceled	(277,649)	70.90
Outstanding at September 30, 2023	6,983,614	$ 66.08
Exercisable at September 30, 2023	4,756,302	$ 68.88

As of September 30, 2023, the total unrecognized compensation expense related to unvested stock option awards was $69.2 million, which is expected to be recognized over a weighted-average period of approximately 2.61 years.

Restricted stock units

The following table summarizes the restricted stock units activity for the nine months ended September 30, 2023:

	Shares	Weighted-Average Grant Date Fair Value
Unvested shares at December 31, 2022	1,893,944	$ 73.28
Granted	888,010	44.78
Vested	(569,385)	72.64
Forfeited	(119,829)	64.97
Unvested shares at September 30, 2023	2,092,740	$ 61.85

As of September 30, 2023, the total unrecognized compensation expense related to unvested restricted stock units was $99.0 million, which is expected to be recognized over a weighted-average period of approximately 2.55 years.

Performance-based restricted stock units

During the first quarter of 2023, the Company began granting performance-based restricted stock units (PSUs) that will settle in stock. PSUs awarded to employees have a three-year performance period and vest on the third anniversary of the grant date. The vesting of these awards is subject to the respective employee's continued employment. The number of PSUs granted represents the target number of units that are eligible to be earned based on the achievement of cumulative three-year performance measures established at the beginning of the performance period, which ends on December 31 of the third year of the performance period.

Participants may ultimately earn between zero and 200.0% of the target number of PSUs granted based on the degree of achievement of the performance metric based on a three-year cumulative relative total shareholder return metric. Accordingly, additional PSUs may be issued or currently issued PSUs may be cancelled upon final determination of the number of units earned.

The following table summarizes the PSU activity for the nine months ended September 30, 2023:

	Shares	Weighted-Average Grant Date Grant Date Fair Value
Unvested shares at December 31, 2022	—	$ —
Granted	52,500	59.32
Vested	—	—
Forfeited	—	—
Unvested shares at September 30, 2023	52,500	$ 59.32

As of September 30, 2023, the total unrecognized compensation expense related to unvested PSUs was $2.5 million, which is expected to be recognized over a weighted-average period of approximately 2.42 years.

The Company values PSUs on the grant date using a lattice model with a Monte Carlo simulation. This valuation methodology utilizes several key assumptions, including defined consecutive trading day average closing stock price on the grant date, valuation date stock price, expected volatilities using historical volatilities, correlation coefficients based on the volatility data, risk-free rates of return and expected dividend yield. The probability of actual shares expected to be earned is considered in the grant date valuation and the expense is not adjusted to reflect the actual units earned.

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, 2023, the number of shares reserved for issuance under the 2015 ESPP was increased by 599,589 shares.

Stock-based compensation expense

The Company recognized stock-based compensation expense of $23.1 million and $70.1 million for the three and nine months ended September 30, 2023, respectively, and $24.1 million and $72.9 million for the three and nine months ended September 30, 2022, respectively. Stock-based compensation expense by award type included within the unaudited condensed consolidated statements of operations and comprehensive loss was as follows (in thousands):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2023	2022	2023	2022
Stock options	$ 9,998	$ 12,062	$ 31,195	$ 37,819
Restricted stock units	12,536	11,802	37,389	34,583
Performance-based restricted stock units	261	—	605	—
Employee stock purchase plan	417	404	1,308	1,000
Subtotal	23,212	24,268	70,497	73,402
Capitalized stock-based compensation costs	(141)	(159)	(410)	(547)
Stock-based compensation expense included in total cost and operating expenses	$ 23,071	$ 24,109	$ 70,087	$ 72,855

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

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2023	2022	2023	2022
Research and development	$ 11,169	$ 10,010	$ 31,512	$ 30,548
Selling, general and administrative	11,902	14,099	38,575	42,307
Total	$ 23,071	$ 24,109	$ 70,087	$ 72,855

12. Net Loss per Share

Basic net loss per share is calculated by dividing net loss by the weighted average shares outstanding during the period, without consideration for common stock equivalents. Diluted net loss per share is calculated by adjusting weighted average shares outstanding for the dilutive effect of common stock equivalents outstanding for the period. For purposes of the dilutive net loss per share calculation, stock options, unvested restricted stock units, PSUs and ESPP shares are considered to be common stock equivalents but are excluded from the calculation of diluted net loss per share, as their effect would be anti-dilutive; therefore, basic and diluted net loss per share were the same for all periods presented as a result of the Company's net loss.

The following common stock equivalents were excluded from the calculation of diluted net loss per share for the three and nine months ended September 30, 2023 and 2022 because including them would have had an anti-dilutive effect (in thousands):

	September 30,	
	2023	2022
Stock options	6,984	6,316
Restricted stock units	2,093	1,838
Performance-based restricted stock units	53	—
ESPP shares	47	46
Total	9,177	8,200

13. Income Taxes

The Company utilizes the asset and liability method of accounting for income taxes. Under this method, deferred tax assets and liabilities are determined based on the difference between the financial statement carrying amounts and tax basis of assets and liabilities using enacted tax rates in effect for years in which the temporary differences are expected to reverse. The Company provides a valuation allowance when it is more likely than not that deferred tax assets will not be realized.

The realization of deferred income tax assets is dependent on the generation of sufficient taxable income during future periods in which temporary differences are expected to reverse. Where the realization of such assets does not meet the more likely than not criterion, the Company applies a valuation allowance against the deferred income tax asset under consideration. The valuation allowance is reviewed periodically and if the assessment of the more likely than not criterion changes, the valuation allowance is adjusted accordingly. As of September 30, 2023, the Company has a full valuation allowance applied against its U.S. and foreign deferred tax assets.

Effective January 1, 2022, a provision of the Tax Cuts and Jobs Act (TCJA) has taken effect creating a significant change to the treatment of research and experimental (R&E) expenditures under Section 174 of the IRC (Sec. 174 expenses). Historically, businesses have had the option of deducting Sec. 174 expenses in the year incurred or capitalizing and amortizing the costs over five years. The new TCJA provision, however, eliminates this option and will require Sec. 174 expenses associated with research conducted in the U.S to be capitalized and amortized over a five-year period. For expenses associated with research outside of the United States, Sec. 174 expenses will be capitalized and amortized over a 15-year period. The Company has included the tax impact of capitalizing and amortizing these costs

over the required periods for the nine months ended September 30, 2023.

On June 30, 2022, the Company entered into a Royalty Purchase Agreement with Royalty Pharma and a Future Revenue Purchase Agreement with Sixth Street Partners. Pursuant to the agreements, the Company received gross proceeds of $175.0 million from Royalty Pharma in June 2022 and $250.0 million from Sixth Street Partners in July 2022 upon the transactions closing. The total cash consideration of $425.0 million, in its entirety, was considered taxable income for calendar year ended December 31, 2022. Therefore, the $425.0 million was included in the estimated taxable income calculation when estimating the Company's forecasted 2022 annual effective tax rate. As of September 30, 2022, the Company expected to be in a taxable income position for the calendar year ended December 31, 2022, and recorded an income tax expense of $0.9 million and $4.2 million for the three and nine months ended September 30, 2022, respectively.

On August 16, 2022, President Biden signed the Inflation Reduction Act (IRA) of 2022 (H.R. 5376) into law. It includes income tax incentives designed to encourage investment in renewable and alternative energy sources, adoption of electric vehicles, and improvement in the energy efficiency of buildings and communities. To finance these incentives, the law imposes a 15% corporate alternative minimum tax (CAMT) on adjusted financial statement income of corporations with profits over $1 billion. It also introduces a new excise tax on corporate stock buybacks of public US companies. The CAMT is effective for tax years beginning after December 31, 2022 while the excise tax on corporate stock buybacks is effective for repurchases of stock after December 31, 2022. The Company does not anticipate the IRA having a significant impact on the Company's effective tax rate or income tax payable and deferred income tax positions.

As of September 30, 2023, the Company expects to be in a taxable loss position for the calendar year ended December 31, 2023, and has recorded an income tax expense of $0.2 million and $0.9 million for the three and nine months ended September 30, 2023. The Company recorded an income tax provision despite forecasting a taxable loss due to the impact of recording unfavorable discrete items in the period, and taxable income from the jurisdictions in which the Company is subject to tax.

As of September 30, 2023, the Company had gross unrecognized tax benefit, excluding interest and penalties of approximately $0.2 million. As of December 31, 2022, the Company did not have any gross unrecognized tax benefit. The company recognizes interest and penalties related to unrecognized tax benefits in the provision for income taxes. As of September 30, 2023, the Company recorded an insignificant amount of interest and penalties related to uncertain tax positions.

14. Leases

The Company's building leases are comprised of office and laboratory spaces under non-cancelable operating leases. The lease agreements contain various clauses for renewal at the Company's option and only certain exercised renewal options were included in the calculation of the operating lease assets and the operating lease liabilities, as other renewal options were not reasonably certain of being exercised as of September 30, 2023. The lease agreements do not contain residual value guarantees and the components of lease cost for the three and nine months ended September 30, 2023 and 2022 were as follows (in thousands):

	Three Months Ended September 30,		Nine Months Ended September 30,	
Operating leases:	2023	2022	2023	2022
Lease cost	$ 5,758	$ 5,322	$ 17,301	$ 16,233
Sublease income	—	(600)	—	(2,132)
Net lease cost	$ 5,758	$ 4,722	$ 17,301	$ 14,101

The Company's sublease agreements for the 38 Sidney Street property expired in 2022. The Company has not entered into any material short-term leases or financing leases as of September 30, 2023.

Supplemental cash flow information related to leases for the nine months ended September 30, 2023 and 2022 is as follows (in thousands):

	Nine Months Ended September 30,	
	2023	2022
Cash paid for amounts included in the measurement of lease liabilities:	$ 13,249	$ 11,668
Lease liabilities arising from obtaining right-of-use assets:		
Operating leases	$ 109	$ —

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	6.1
Weighted average discount rate	7.4%

15. Commitments and Contingencies

Purchase Commitments Associated with Commercial Supply Agreements

In connection with the commercialization of AYVAKIT/AYVAKYT, the Company has negotiated manufacturing agreements with certain vendors that require the Company to meet minimum purchase obligations on an annual basis. During the nine months ended September 30, 2023, there was a decrease of $7.3 million in the Company's contractual obligations described in Note 18 to the consolidated financial statements in the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2022.

Legal Proceedings

The Company is not currently a party to any material legal proceedings. At each reporting date, the Company evaluates whether or not a potential loss amount or a potential range of loss is probable and reasonably estimable under the provisions of the authoritative guidance that addresses accounting for contingencies. The Company expenses the costs related to its legal proceedings as they are incurred.

Indemnification Agreements

In the ordinary course of business, the Company may provide indemnification of varying scope and terms to vendors, lessors, business partners, and other parties with respect to certain matters including, but not limited to, losses arising out of breach of such agreements or from intellectual property infringement claims made by third parties. In addition, the Company has entered into indemnification agreements with members of its board of directors and senior management that will require the Company, among other things, to indemnify them against certain liabilities that may arise by reason of their status or service as directors or officers of the Company. The maximum potential amount of future payments the Company could be required to make under these indemnification agreements is, in many cases, unlimited. To date, the Company has not incurred any material costs as a result of such indemnifications. The Company is not aware of any claims under indemnification arrangements, and it has not accrued any liabilities related to such obligations in its condensed consolidated financial statements as of September 30, 2023 or December 31, 2022.

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 condensed consolidated financial statements and related notes appearing elsewhere in this Quarterly Report on Form 10-Q and the audited consolidated financial statements and related notes thereto and management's discussion and analysis of financial condition and results of operations included in our Annual Report on Form 10-K for the year ended December 31, 2022, filed with the Securities and Exchange Commission (the SEC) on February 16, 2023. 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 global precision therapy company that invents life-changing medicines for people with cancer and blood disorders. Applying an approach that is both precise and agile, we create therapies that selectively target genetic drivers, with the goal of staying one step ahead across stages of disease. Since 2011, we have leveraged our research platform, including expertise in molecular targeting and world-class drug design capabilities, to rapidly and reproducibly translate science into a broad pipeline of precision therapies. We have brought our approved medicines, AYVAKIT®/AYVAKYT® (avapritinib) and GAVRETO® (pralsetinib), to patients in the U.S. and Europe, and we are globally advancing multiple programs for mast cell disorders, including SM and chronic urticaria, breast cancer and other cancers vulnerable to CDK2 inhibition, as well as EGFR-mutant lung cancer.

Our drug discovery approach combines our biological insights with our proprietary compound library and chemistry expertise to design highly selective and potent precision therapies, with the goal of delivering significant and durable clinical benefit to patients based on the genetic driver of their disease. This uniquely targeted, scalable approach is designed to empower the rapid design and development of new treatments and increase the likelihood of success. In addition, our business model integrates our research engine with robust clinical development and commercial capabilities in oncology, hematology, and allergy and immunology to create a cycle of innovation.

Systemic Mastocytosis and other Mast Cell Disorders — AYVAKIT® / AYVAKYT® (avapritinib), Elenestinib (BLU-263), and BLU-808

AYVAKIT®/AYVAKYT® (avapritinib)

We are commercializing avapritinib for the treatment of advanced SM and indolent SM. SM is a rare hematologic 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, in advanced forms of the disease, organ dysfunction and failure. Nearly all cases of SM are driven by the KIT D816V mutation, which aberrantly activates mast cells.

The FDA approved avapritinib under the brand name AYVAKIT for the treatment of adult patients with advanced SM, including ASM, SM-AHN, and MCL in June 2021, and for adult patients with indolent SM in May 2023. In March 2022, the European Commission approved the marketing authorization for AYVAKYT for the treatment of adult patients with ASM, SM-AHN, or MCL, after at least one systemic therapy. These approvals in advanced SM were supported by our ongoing Phase 1 clinical trial in advanced SM, which we refer to as our EXPLORER trial, and our ongoing Phase 2 clinical trial in advanced SM, which we refer to as our PATHFINDER trial.

The FDA's approval of AYVAKIT for the treatment of patients with indolent SM, was supported by data from our Phase 2 clinical trial in indolent SM, which we refer to as the PIONEER trial. The European Medicines Agency, or EMA, validated a type II variation marketing authorization application (MAA) for AYVAKYT in indolent SM with a start of procedure date of January 27, 2023. In February 2023, we presented registrational PIONEER trial data for AYVAKIT in indolent SM at the American Academy of Allergy, Asthma and Immunology, or AAAAI, Annual

Meeting. In May 2023, the New England Journal of Medicine Group published detailed results from the PIONEER trial of AYVAKIT in patients with indolent SM.

The FDA has granted breakthrough therapy designation to avapritinib for (i) the treatment of advanced SM, including the subtypes of ASM, SM-AHN and MCL, and (ii) the treatment of moderate to severe indolent SM. In addition, 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.

Elenestinib (BLU-263)

We are developing elenestinib, or BLU-263, an investigational, orally available, potent and highly selective KIT inhibitor, for the treatment of indolent SM and other mast cell disorders. Elenestinib is designed to have equivalent potency as avapritinib, with low off-target activity and lower penetration of the central nervous system (CNS) relative to avapritinib based on preclinical data.

We are evaluating elenestinib in an ongoing Phase 2/3 clinical trial in indolent SM, which we refer to as our HARBOR trial. In December 2022, we announced top-line, 12-week data from the dose-finding Part 1 of the HARBOR trial. Elenestinib showed improved measures of mast cell burden and patient-reported symptoms, and safety data were consistent with the preclinical profile of elenestinib and a completed Phase 1 healthy volunteer trial. We plan to present HARBOR Part 1 trial data for elenestinib in indolent SM at the American Society of Hematology Annual Meeting in December 2023.

Wild-Type KIT Inhibition (BLU-808)

Mast cells are the primary effector cells in several allergic-inflammatory diseases, including both inducible and spontaneous chronic urticaria, and wild-type KIT plays a central role in mast cell survival, proliferation, and activation. In the first half of 2023, we nominated the development candidate BLU-808 from our discovery programs, an oral, highly potent and selective wild-type KIT inhibitor. We plan to develop BLU-808 as a potential first- and best-in-class treatment for mast cell disorders, including chronic urticaria, a debilitating inflammatory skin disorder characterized by wheals (hives), and sleep disruption, stress and anxiety due to severe itching are major contributors to disease burden, as well as other potential related allergic-inflammatory indications.

PDGFRA-Driven Gastrointestinal Stromal Tumors — AYVAKIT® / AYVAKYT® (avapritinib)

We are commercializing avapritinib for the treatment of patients with PDGFRA exon 18 mutant gastrointestinal stromal tumors (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 AYVAKIT for the treatment of adults with unresectable or metastatic GIST harboring a PDGFRA exon 18 mutation, including PDGFRA D842V mutations, and is approved in Europe with conditional marketing authorization under the brand name AYVAKYT as a monotherapy for the treatment of adult patients with unresectable or metastatic GIST harboring a PDGFRA D842V mutation.

Through our collaboration with CStone, China’s National Medicinal Products Administration (NMPA) approved AYVAKIT for the treatment of adults with unresectable or metastatic GIST harboring a PDGFRA exon 18 mutation, including PDGFRA D842V mutations. AYVAKIT also received accelerated approval from the Taiwan Food and Drug Administration (TFDA) and approval in Hong Kong, both for adults with unresectable or metastatic GIST

harboring PDGFRA D842V mutations.

The FDA has granted breakthrough therapy designation for avapritinib for the treatment of unresectable or metastatic GIST harboring the PDGFRA D842V mutation. In addition, the FDA has granted orphan drug designation to avapritinib for the treatment of GIST, and the European Commission has granted orphan medicinal product designation to avapritinib for the treatment of GIST.

RET-altered Cancers — GAVRETO® (pralsetinib)

We are developing and commercializing pralsetinib for the treatment of RET fusion-positive non-small cell lung cancer (NSCLC), and for the treatment of RET-altered thyroid carcinoma. We are also developing pralsetinib for the treatment of other RET-altered solid tumors. We granted exclusive licenses to F. Hoffmann-La Roche Ltd and Genentech, Inc., a member of the Roche Group (which we refer to together as Roche), and CStone Pharmaceuticals (CStone) to develop and commercialize pralsetinib in their respective territories. In February 2023, we received written notice from Roche of their election to terminate for convenience the Roche pralsetinib collaboration agreement. The termination will become effective in February 2024, at which time we will regain commercialization and development rights for GAVRETO from Roche in the U.S. and Roche Territory. In conjunction with the termination, we have initiated the process of re-partnering GAVRETO for future development and commercialization. See "—Collaborations and Licenses Summary" below.

The FDA granted accelerated approval of pralsetinib in the U.S. under the brand name GAVRETO for the treatment of (i) adult patients with metastatic RET fusion-positive NSCLC as detected by an FDA approved test, (ii) adult and pediatric patients 12 years of age and older with advanced or metastatic RET-mutant medullary thyroid cancer (MTC) who require systemic therapy, and (iii) adult and pediatric patients 12 years of age and older with advanced or metastatic RET fusion-positive thyroid cancer who require systemic therapy and who are radioactive iodine-refractory (if radioactive iodine is appropriate). In June 2023, Roche voluntarily withdrew the indication of GAVRETO for the treatment of adult and pediatric patients 12 years of age and older with advanced or metastatic RET-mutant MTC. The decision to withdraw the indication was made in consultation with the FDA, in accordance with the requirements of the FDA's Accelerated Approval Program, with the official FDA withdrawal of the indication occurring on July 20, 2023. Specifically, AcceleRET-MTC, a Phase 3 clinical trial required by the FDA to convert the accelerated approval of GAVRETO for MTC to a full approval, will no longer be pursued due to lack of feasibility. The decision to withdraw the indication was not due to any new safety or efficacy data for GAVRETO or a product safety or quality issue, and other approved indications for GAVRETO in the U.S. are unaffected. In August 2023, the FDA converted the accelerated approval of GAVRETO to full regular approval for the treatment of adult patients with metastatic RET fusion-positive NSCLC. The confirmatory studies to meet the commitments required to convert RET fusion-positive thyroid cancer for GAVRETO, also approved under accelerated approval, to full approval, are ongoing.

Through our collaboration with Roche, the European Commission granted conditional marketing authorization for GAVRETO as a monotherapy for the treatment of adults with RET fusion-positive advanced NSCLC not previously treated with a RET inhibitor. In November 2022, Roche withdrew its type II variation MAA to the EMA for pralsetinib for RET-altered thyroid cancers in the second-line. Roche stated a change in strategy as the reason for the withdrawal, and that it was unrelated to product quality, efficacy or safety.

In March 2021, through our collaboration with CStone, China's NMPA approved GAVRETO for the treatment of patients with RET fusion-positive NSCLC patients previously treated with platinum-based chemotherapy. In March 2022, China's NMPA approved GAVRETO for the treatment of RET-mutant MTC and RET fusion-positive thyroid cancer. GAVRETO was approved in Hong Kong in July 2022 for the treatment of RET fusion-positive NSCLC. In January 2023, the TFDA approved GAVRETO for the treatment of patients with RET fusion-positive locally advanced or metastatic NSCLC, RET-mutant MTC and RET fusion-positive thyroid cancer. In June 2023, China's NMPA approved GAVRETO for the first-line treatment of adults with locally advanced or metastatic RET fusion-positive NSCLC.

The FDA has granted breakthrough therapy designation to pralsetinib for (i) the treatment of patients with RET fusion-positive NSCLC that has progressed following platinum-based chemotherapy, and (ii) the treatment of patients with RET mutation-positive MTC that requires systemic treatment and for which there are no acceptable alternative

treatments. In addition, the FDA has granted orphan drug designation to pralsetinib for the treatment of RET-rearranged NSCLC, JAK1/2-positive NSCLC or TRKC-positive NSCLC.

EGFR-Mutated NSCLC — BLU-945, BLU-525 and BLU-451

We are developing a portfolio of investigational epidermal growth factor receptor (EGFR) inhibitors with the potential to address a spectrum of common and uncommon EGFR activating mutations, including exon 19 deletions, the L858R mutation, and exon 20 insertions. Patients with EGFR-driven NSCLC have high medical needs despite current standards of care. First, osimertinib has demonstrated shorter overall survival and progression-free survival in patients whose tumors have activating L858R mutations, and there are limited treatment options for exon 20 insertion-driven NSCLC. Second, the majority of patients will ultimately progress due to tumor resistance, and preventing mutations from emerging is an important treatment goal. Third, the brain is a common site of disease progression that has proven difficult to treat. We are working to address these challenges and prolong patient benefit by advancing development of rational combinations with our investigational EGFR therapies. Ultimately, we are seeking to address the significant medical needs in EGFR-mutant NSCLC that affect approximately 60,000 patients in major markets, including the U.S., European Union (EU), the UK, and Japan.

EGFR-Positive NSCLC — BLU-945

BLU-945 is a selective and potent investigational inhibitor of the activating EGFR L858R mutation and on-target T790M and C797X resistance mutations. We are currently evaluating BLU-945 in the Phase 1/2 SYMPHONY trial in patients with EGFR-driven NSCLC. In June 2023, we presented updated monotherapy dose escalation data from the SYMPHONY trial at the American Society of Clinical Oncology (ASCO) Annual Meeting, and initial combination therapy data evaluating BLU-945 in combination with osimertinib in patients with late-line, osimertinib-refractory, EGFR-mutant NSCLC. BLU-945 monotherapy and in combination with osimertinib showed evidence of clinical activity and was generally well tolerated, with infrequent adverse events (AEs) associated with wildtype EGFR inhibition. Dose escalation studies are ongoing to reach the recommended Phase 2 dose (RP2D) and progress to dose expansion with BLU-945 in combination with osimertinib for first-line treatment of patients with EGFR L858R-positive NSCLC.

EGFR-Positive NSCLC — BLU-525

BLU-525 is a next-generation EGFR inhibitor that, based on preclinical data, has a distinct chemical structure with improved kinome selectivity and differentiated metabolism, and equivalent EGFR mutation coverage, wild-type EGFR selectivity, and CNS penetration compared to BLU-701, which was previously in development for EGFR-positive NSCLC. Data supporting the preclinical profile of BLU-525 were reported at the EORTC-NCI-AACR Molecular Targets and Cancer Therapeutics Symposium in October 2022. In March 2023, the FDA accepted our investigational new drug application, or IND, for BLU-525.

EGFR Exon 20 Insertion-Positive NSCLC — BLU-451

BLU-451 is a selective and potent investigational inhibitor under development for the treatment of EGFR exon 20 insertion-positive NSCLC and atypical EGFR mutations that we acquired in December 2021, through our acquisition of Lengo Therapeutics, Inc. In April 2022, we presented the first preclinical data for BLU-451 at the AACR Annual Meeting demonstrating that BLU-451 is a wild-type EGFR-sparing, CNS penetrant molecule which potently inhibited a broad range of exon 20 insertions and uncommon oncogenic point mutations. In addition, BLU-451 led to measurable tumor regression in a preclinical intracranial tumor model. Based on these foundational preclinical data, in March 2022 we initiated the Phase 1/2 trial of BLU-451 in patients with EGFR-driven NSCLC harboring exon 20 insertion mutations, which we refer to as our CONCERTO trial. In June 2023, we presented initial dose escalation data from the CONCERTO trial of BLU-451 at the ASCO Annual Meeting, demonstrating evidence of safety and clinical benefit, including CNS activity, in patients with exon 20 insertion-positive NSCLC, and emerging dose-dependent ctDNA clearance and tumor shrinkage in patients with atypical EGFR mutations. Dose escalation is ongoing to determine a RP2D.

Cancers Vulnerable to CDK2 Inhibition — BLU-222

We are developing an investigational inhibitor, BLU-222, targeting CDK2 for the treatment of patients with cancers vulnerable to CDK2 inhibition. CDK2 is a cell cycle regulator and an important cancer target, with relevance across multiple malignancies, including hormone-receptor-positive breast cancer and other cancers, such as subsets of ovarian and endometrial cancer. Across multiple cancer types, aberrant CCNE1 hyperactivates CDK2, resulting in cell cycle dysregulation and tumor proliferation. Aberrant CCNE1 has been observed as a primary driver of disease, as well as a mechanism of resistance to CDK4/6 inhibitors and other therapies.

At the AACR Annual Meeting in April 2022, we presented preclinical data showing BLU-222 demonstrated significant antitumor activity in a CCNE1-amplified ovarian cancer model. BLU-222 in combination with standard of care agents, including chemotherapy and the PARP inhibitor olaparib, led to sustained tumor regression even after treatment cessation. At the San Antonio Breast Cancer Symposium, in December 2022, we reported preclinical results showing BLU-222 in combination with ribociclib led to sustained antitumor activity, in preclinical models of CDK4/6 inhibitor-naïve and resistant HR+/HER2 breast cancer, supporting the clinical development of this combination regimen.

In the first quarter of 2022, we initiated the Phase 1/2 trial of BLU-222 in cancers vulnerable to CDK2 inhibition, which we refer to as our VELA trial. BLU-222 is being developed as monotherapy and in combination with other agents, including CDK4/6 inhibitors and estrogen receptors, antagonists, in hormone-receptor-positive, HER2-negative breast cancer (HR+/HER- BC), and as a single agent and in combination in CCNE1-amplified tumor types. In June 2023, we presented initial clinical data from the VELA trial at the ASCO Annual Meeting, showing that BLU-222 was generally well-tolerated with evidence of cell cycle pathway modulation and a confirmed partial response in a monotherapy-treated patient with HR+/HER2- metastatic breast cancer who previously received five lines of therapy, including the CDK4/6 inhibitors palbociclib and abemaciclib. We are continuing monotherapy dose escalation to identify a maximum tolerated dose and have initiated dose escalation of BLU-222 in combination with the CDK4/6 inhibitor, ribociclib, and the estrogen receptor antagonist, fulvestrant, in patients with HR+/HER2- metastatic breast cancer.

Advanced Cancers — BLU-852

BLU-852 is a selective and potent investigational inhibitor of MAP4K1, a well-characterized immunokinase that is believed to play a role in T cell regulation, developed under our cancer immunotherapy collaboration with Roche. Following the termination of our collaboration agreement with Roche, we have deprioritized advancement of BLU-852 and are exploring opportunities to re-partner the asset for future development.

Discovery Platform

We 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. In addition, we are expanding our discovery platform by building capabilities, supported by external collaborations, for targeted protein degradation of both kinase and non-kinase targets in precision oncology, with the goal of advancing transformative therapies to patients and further broadening the significant productivity of our research engine. Beyond the discovery programs described above, we have multiple pre-development candidate programs for undisclosed kinase targets.

In 2022, we started several degrader research programs, including three internal programs and two programs under our targeted protein degradation collaboration with Proteovant. Through the Proteovant collaboration, we plan to research and advance up to two novel protein degrader programs into development, with the option to expand to two additional programs. See "*—Collaborations and Licenses*" Summary below.

Development and Commercialization Rights

We currently have worldwide development and commercialization rights to avapritinib, other than the rights licensed to CStone in Mainland China, Hong Kong, Macau and Taiwan (the CStone Territory). We have entered into

distribution agreements for certain countries in which we do not have our own infrastructure, and we plan to pursue additional regulatory approvals and commercialization of avapritinib in additional countries, including through additional distribution agreements. We have granted CStone an exclusive license to develop and commercialize pralsetinib and BLU-554 in the CStone Territory.

We 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. In February 2023, we received written notice from Roche of their election to terminate for convenience the Roche pralsetinib collaboration agreement. The termination will become effective in February 2024, at which time we will regain commercialization and development rights for GAVRETO from Roche in the U.S. and Roche Territory and have initiated the process of re-partnering GAVRETO for future development and commercialization. We will not be entitled to receive payment for milestones, if any, achieved after the receipt of the notice of termination but before the effective date of termination.

We currently have worldwide development and commercialization rights to BLU-945 and BLU-525, and any back-up forms thereof, other than the rights licensed to Zai Lab for these drug candidates in Mainland China, Hong Kong, Macau, and Taiwan (collectively, the Zai Lab Territory).

We have worldwide development and commercialization rights to all of our development and discovery programs, including elenestinib (BLU-263), BLU-451, BLU-222, BLU-852 and BLU-808.

We have granted an exclusive worldwide license to Clementia to develop and commercialize BLU-782.

We have granted an exclusive worldwide license to IDRx for a development candidate-stage KIT exon 13 inhibitor, IDRX-73.

Collaborations and Licenses

Roche—Immunotherapy Collaboration. In March 2016, we entered into a collaboration with Roche to discover, develop and commercialize small molecule therapeutics targeting kinases believed to be important in cancer immunotherapy, including the kinase target MAP4K1, as single products or possibly in combination with other therapeutics. In 2022, Roche endorsed a clinical development plan for IND-enabling activities for BLU-852, as a single agent and in combination with atezolizumab, in advanced cancers. On April 30, 2023, we entered into a mutual termination agreement with Roche, which we refer to as the Termination Agreement, pursuant to which the parties mutually agreed to terminate the Roche immunotherapy agreement such that the rights and licenses granted to Roche related to MAP4K1 have terminated in their entirety and we retained the rights to any and all compounds developed under the collaboration. Further, we retain the flexibility to research, develop, manufacture, commercialize and otherwise exploit the assets developed under the collaboration. We have deprioritized advancement of the program and are exploring opportunities to re-partner the asset for future development.

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 was granted exclusive commercialization rights for pralsetinib outside of the U.S., excluding the CStone Territory, which consists of Mainland China, Hong Kong, Macau and Taiwan. In February 2023, we received written notice from Roche of their election to terminate for convenience the Roche pralsetinib collaboration agreement. The termination will become effective in February 2024, at which time we will regain commercialization and development rights for GAVRETO from Roche in the U.S. and Roche Territory. Until the termination of the collaboration agreement is effective, the parties will continue to perform their respective obligations under the collaboration agreement, including with respect to the development and commercialization of GAVRETO. The parties will enter into a transition plan to facilitate the reversion of the product, including reasonable allocation of costs and expenses. We will not be entitled to receive payment for milestones, if any, achieved after the receipt of the notice of termination but before the effective date of termination. Upon the termination becoming effective, our exclusivity obligations under the collaboration agreement will terminate and we have initiated the process of re-

partnering GAVRETO for future development and commercialization.

CStone. In June 2018, we entered into a collaboration with CStone to develop and commercialize avapritinib, pralsetinib and fisogatinib, as well as 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. Under the collaboration, we 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 (ALK2) in development for the treatment of fibrodysplasia ossificans progressiva (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. Clementia initiated patient dosing in a Phase 2 clinical trial of BLU-782, now referred to as fidrisertib, in the first quarter of 2022.

Zai Lab. In November 2021, we entered into a collaboration with Zai Lab to develop and commercialize certain licensed products for the treatment of EGFR-driven NSCLC in Greater China, including Mainland China, Hong Kong, Macau and Taiwan. The collaboration aims to accelerate and expand global development of the licensed products, which currently includes BLU-945 and BLU-525 (which served as a back-up candidate for BLU-701).

Proteovant. In February 2022, we entered into an exclusive collaboration with Proteovant to jointly research and advance up to two novel targeted protein degrader therapies as well as up to two additional novel protein degrader target programs as we may mutually agree with Proteovant (each such program is referred to as a target program). On a target program-by-target program basis, we will have an exclusive option to obtain a worldwide, exclusive license to develop and commercialize any licensed compound and licensed product under each target program. Proteovant will have the right to opt into the global development and U.S. commercialization of certain licensed compounds and licensed products under the second target program that we option, and, if we expand to additional target programs, Proteovant will have the same opt-in right for the fourth target program that we option.

IDRx. In August 2022, we entered into a license agreement with IDRx, Inc., or IDRx, which we refer to as the IDRx License Agreement. Pursuant to the IDRx License Agreement, we granted IDRx an exclusive, worldwide, royalty-bearing license to exploit our internally discovered development candidate-stage KIT exon 13 inhibitor, IDRX-73.

In connection with the IDRx License Agreement, we also entered into a stock purchase agreement with IDRx, which we refer to as the IDRx Stock Purchase Agreement, pursuant to which we received 4,509,105 shares of IDRx's Series A preferred stock and the right to receive additional shares of IDRx's Series A preferred stock through an anti-dilution provision subject to a defined financing cap and the eligibility to receive up to $217.5 million in contingent cash payments, including specified development, regulatory and sales-based milestone payments and tiered royalty payments. In July 2023, we received an additional 192,282 shares pursuant to the anti-dilution provision in the IDRx Stock Purchase Agreement.

Mergers & Acquisitions Summary

Lengo Therapeutics. In December 2021, we completed our acquisition of Lengo Therapeutics, Inc., along with its lead compound LNG-451, now known as BLU-451, which is in development for the treatment of NSCLC in patients with EGFR exon 20 insertion mutations. The acquisition also included additional undisclosed preclinical precision oncology programs and research tools, including a catalog of covalent, highly brain penetrant kinase inhibitors that we plan to add to our proprietary compound library to further enable future drug discovery efforts.

We will continue to evaluate additional collaborations, acquisitions, 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, acquisitions, partnerships and license agreements to capitalize on or expand our discovery platform.

Financing Arrangements Summary

Royalty Purchase Agreement. In June 2022, we entered into a purchase and sale agreement, which we refer to as the Royalty Purchase Agreement, with Royalty Pharma. Pursuant to this Royalty Purchase Agreement, we received an upfront cash payment of $175.0 million and the right to receive up to $165.0 million in certain milestone payments, subject to the achievement of specified net sales milestones by Roche, in exchange for all of our existing rights to receive royalty payments on the net sales of GAVRETO worldwide excluding the CStone Territory and U.S. territory under the terms of the Roche pralsetinib collaboration agreement. However, in February 2023, Roche provided written notice of its election to terminate the Roche pralsetinib collaboration agreement for convenience. Following the termination of the Roche pralsetinib collaboration agreement, if the specified net sales milestone thresholds under the Royalty Purchase Agreement with Royalty Pharma are not otherwise met, we may no longer be eligible to receive any of the contingent milestone payments under the Royalty Purchase Agreement.

Synthetic Royalty Facility. In June 2022, we entered into a purchase and sale agreement, which we refer to as the Future Revenue Purchase Agreement with Sixth Street Partners. In July 2022, upon the closing of the transaction pursuant to the Future Revenue Purchase Agreement, we received gross proceeds of $250.0 million in exchange for future royalty payments at a rate of 9.75% on up to $900 million each year of (i) aggregate worldwide annual net product sales of AYVAKIT/AYVAKYT (avapritinib) and (ii) if it is approved, aggregate worldwide annual net product sales of elenestinib, but excluding sales in Greater China, subject to a cumulative cap of 1.45 times the upfront invested capital or a total of $362.5 million. In the event that certain revenue targets are not achieved by specified dates, the royalty rate and cumulative cap shall be increased to 15% and 1.85 times the invested capital (or $462.5 million), respectively.

Debt Facility. In June 2022, we entered into a Financing Agreement for up to $660.0 million with Sixth Street Partners. The Financing Agreement, as amended, provides for (i) a senior secured term loan facility of up to $150.0 million and (ii) a senior secured delayed draw term loan facility of up to $250.0 million to be funded in two tranches at our choice, subject to certain terms and conditions. The loans will mature on June 30, 2028 and bear interest at a variable rate equal to either the Secured Overnight Financing Rate (SOFR) plus 6.50% or the base rate plus 5.50%, subject to a floor of 1% and 2% with respect to the SOFR and base rate, respectively. The initial gross proceeds of $150.0 million was funded in July 2022. In addition, we may at any time request an incremental term loan in an amount not to exceed $260.0 million on terms to be agreed and subject to the consent of the lenders providing such incremental term loan. In August 2023, we received the first tranche of the senior secured delayed draw term loan facility in the amount of $100.0 million in gross proceeds.

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, collaboration and license agreements, future royalty and revenue monetization, and a term loan. Through September 30, 2023, we have received an aggregate of $3.7 billion from such transactions, including $1.9 billion in aggregate gross proceeds from the sale of common stock in our initial public offering, or IPO, follow-on public offerings, through our “at the market” stock offering program and the equity investment by Roche, $115.1 million in gross proceeds from the issuance of convertible preferred stock, $175.0 million in gross proceeds from our Royalty Purchase Agreement with Royalty Pharma, $250.0 million in gross proceeds from our Future Revenue Purchase Agreement with Sixth Street Partners, $1.0 billion in upfront and milestone payments under our collaborations with Roche, CStone and Zai Lab, our license agreement with Clementia and our former collaboration with Alexion Pharma Holding, or Alexion, and $250.0 million in gross proceeds from a term loan from Sixth Street Partners. In addition, since January 2020, we have also generated revenue through the sales of our approved drug products.

Since inception, we have incurred significant operating losses. Our net loss was $396.1 million for the nine months ended September 30, 2023. Our net losses were $557.5 million and $644.1 million for the years ended December 31, 2022 and 2021, respectively. As of September 30, 2023, we had an accumulated deficit of $2,229.0 million. We expect to continue to incur significant expenses and operating losses over the next few years. We anticipate variability in

our expenses in future periods in connection with our ongoing activities, particularly as we:

- maintain and expand our sales, marketing and distribution infrastructure to continue to commercialize our drug and any current or future drug candidates for which we may obtain marketing approval;
- seek marketing approval for avapritinib in additional geographies, particularly for indolent SM in geographies outside of the U.S.;
- initiate or advance clinical development activities for other current or future drug candidates as monotherapies or in combination with other agents;
- continue to discover, validate and develop additional drug candidates or development candidates, including elenestinib (BLU-263), BLU-945, BLU-525, BLU-451, BLU-222 and BLU-808;
- continue to manufacture increasing quantities of drug substance and drug product material for use in preclinical studies, clinical trials and commercialization and to purchase quantities of other agents for use in our clinical trial as we develop our drugs and drug candidates as potential combination therapies or for use as comparator agents;
- conduct research and development activities under our collaborations with Zai Lab and Proteovant;
- 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; and
- hire additional research, clinical, quality, manufacturing, regulatory, commercial and general and administrative personnel.

Revenue

In January 2020, the FDA granted approval of avapritinib under the brand name AYVAKIT for the treatment of adults with unresectable or metastatic GIST harboring a PDGFRA exon 18 mutation, including PDGFRA D842V mutations. In September 2020, 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. In June 2021, the FDA granted a subsequent approval for AYVAKIT, expanding the labeled indications to include adult patients with advanced SM, including ASM, SM-AHN and MCL. In March 2022, the European Commission expanded the marketing authorization for AYVAKYT to include the treatment of adult patients with ASM, SM-AHN, or MCL, after at least one systemic therapy. In May 2023, the FDA approved AYVAKIT for the treatment of adult patients with indolent SM.

For the three and nine months ended September 30, 2023, our revenue primarily consisted of product sales of AYVAKIT/AYVAKYT as well as some collaboration and license revenue under our collaboration agreements with our collaboration partners. During the nine months ended September 30, 2023, our collaboration and license revenue primarily included amounts that were recognized related to an achieved milestone payment under our collaboration with CStone and research and development services under our immunotherapy collaboration with Roche.

In the future, we expect to generate revenue from a combination of sources, including sales of our current drug product and any current or future drug candidates for which we receive marketing approval, royalties on drug sales, upfront, milestone, profit sharing and other payments, if any, under any current or future collaboration and license agreements, including revenues related to the supply of our drug candidates or approved drugs to our various collaboration partners. We anticipate variability in revenue in the future as a result of the timing and amount of product sales, license fees, manufacturing services, and achievement of milestones or other payments under our collaboration or license agreements, if any.

During 2023, we expect net product revenues to increase, as compared to 2022, as we continue to add new patients onto AYVAKIT/AYVAKYT, including advanced SM and indolent SM with the recent label expansion.

Cost of Sales

Our cost of sales includes the cost of producing and distributing inventories that are related to product revenue as well as the sales of drug substance and drug product to our collaboration partners during the respective period, including salary related expenses 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.

Prior to receiving the initial FDA approval for AYVAKIT in January 2020, and subsequent approval in June 2021, we manufactured inventory to be sold upon commercialization and recorded approximately $31.0 million related to this inventory as research and development expense. As a result, the manufacturing costs related to the inventory build-up incurred before FDA approval were expensed in prior periods and are therefore excluded from the cost of goods sold for the three and nine months ended September 30, 2023 and 2022, respectively. We estimate our cost of goods sold related to product revenue as a percentage of net product revenue will continue to be positively impacted as we sell through certain inventory that was previously expensed prior to FDA approval. We expect to sell through our pre-launch inventory in the near term. Once the low-cost inventory balances are sold through, we estimate our costs of goods sold related to product sales to remain in the mid-single digit percentage range. Cost of goods sold related to sales of drug products to our collaboration partners are at lower margins and partially offset the positive impact of the previously expensed inventory.

Expenses

Collaboration Loss Sharing

On July 1, 2021, Roche took over certain responsibilities associated with product sales to customers, pricing and distribution matters related to GAVRETO in the U.S. and became the principal for recording product sales to customers in the U.S. Collaboration loss sharing consists of our share of the losses incurred from sales of GAVRETO to customers in the U.S. under our collaboration for pralsetinib with Roche. For additional information, see Note 10, *Collaboration and License Agreements*, to our unaudited condensed consolidated financial statements. We anticipate variability in collaboration loss sharing from period to period as a result of the timing and amount of GAVRETO sales.

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:

- expenses incurred to acquire in-process research and development asset with no alternative future use;
- employee-related expenses including salaries, benefits, and stock-based compensation expense;
- expenses incurred under agreements with third parties that conduct research and development, preclinical activities, clinical activities and manufacturing on our behalf;
- expenses incurred in connection with development activities under our collaboration for pralsetinib with Roche and research and development activities under our collaboration with Proteovant;
- the cost of consultants in connection with our research and development activities;
- the cost associated with regulatory quality assurance and quality control operations;

- the cost of lab supplies and acquiring, developing and manufacturing preclinical 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 material net cash inflows will commence from the sale of our current or future drug candidates for which we received marketing approval. 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 manufacturing capabilities or making arrangements with third-party manufacturers to ensure adequate clinical and commercial supply;

- obtaining and maintaining patent and trade secret protection and regulatory exclusivity for AYVAKIT/AYVAKYT, GAVRETO and our drug candidates;

- commercializing AYVAKIT/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.

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 tables summarize our research and development expenses by program for the three and nine months ended September 30, 2023 and 2022. Other development and pre-development candidate expenses, unallocated expenses and internal research and development expenses have been classified separately.

	Three Months Ended September 30,			
	2023	2022	Dollar change	% Change
Avapritinib external expenses	$ 5,618	$ 17,240	$ (11,622)	(67)%
Pralsetinib external expenses	7,602	3,028	4,574	151
BLU-263 external expenses	6,092	10,574	(4,482)	(42)
EGFR franchise (BLU-451/525/701/945) external expenses	11,917	22,864	(10,947)	(48)
BLU-222 external expenses	11,951	11,454	497	4
BLU-808 external expenses	3,278	820	2,458	300
Other development and pre-development candidate expenses and unallocated expenses	25,385	28,111	(2,726)	(10)
Internal research and development expenses	38,409	33,890	4,519	13
Total research and development expenses	$ 110,252	$ 127,981	$ (17,729)	(14)%

	Nine Months Ended September 30,			
	2023	2022	Dollar change	% Change
Avapritinib external expenses	$ 26,059	$ 41,174	$ (15,115)	(37)%
Pralsetinib external expenses	17,066	22,658	(5,592)	(25)
BLU-263 external expenses	19,822	28,595	(8,773)	(31)
EGFR franchise (BLU-451/525/701/945) external expenses	45,061	66,304	(21,243)	(32)
BLU-222 external expenses	33,819	32,173	1,646	5
BLU-808 external expenses	6,501	1,456	5,045	346
Other development and pre-development candidate expenses and unallocated expenses	69,864	67,884	1,980	3
Internal research and development expenses	111,992	99,335	12,657	13
Total research and development expenses	$ 330,184	$ 359,579	$ (29,395)	(8)%

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

We expect variability in our research and development expenses in future periods as our drug candidate development programs progress. 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 will vary depending on clinical data results and our resources allocation priorities. In addition, our research and development expenses may increase with potential new collaborations and future acquisitions. 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 approved drugs or drug candidates for which we may receive marketing approval, 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.

During 2023, we expect our research and development expenses will decline, as compared to 2022, due to our focused approach towards optimizing operational efficiency across our portfolio while executing across our top priority programs.

Selling, General and Administrative Expenses

Selling, general and administrative expenses consist primarily of compensation and benefits, including stock-based compensation expense, for commercial operations and 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, insurance fees, 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 globally. 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 expenses associated with operating as a public company and expanding the scope of our operations.

During 2023, we expect that selling, general and administrative expenses will increase, as compared to 2022, as we continue to build out our global commercial and compliance infrastructure and field team to support the launch of indolent SM.

Interest Income (Expense), net

Interest income (expense), net consists primarily of interest expense related to our financing arrangements with Royalty Pharma and Sixth Street Partners. Interest expense on liabilities related to the sale of future royalties and revenues consists of the periodic interest calculated using the effective interest rate method over the future estimated royalty payments due to Royalty Pharma and Sixth Street Partners over the life of the agreements. Interest expense on the term loan with Sixth Street Partners results from the amortization of the debt liability using the effective interest method over the maturity of the term loan. We anticipate variability in interest expense from period to period as a result of the timing and amount of the sales of the underlying products and the changes in interest rates. For additional information, see Note 3, *Financing Arrangements*, to our unaudited condensed consolidated financial statements.

Interest income (expense), net also includes income earned on cash equivalents and marketable securities. Our interest income may fluctuate depending on the movement of interest rates and our total amount of cash equivalents and marketable securities.

Other Income (Expense), net

Other income (expense), net consists of miscellaneous income and expenses unrelated to our core operations, including the impacts of foreign currency exchange differences.

Income Tax Expense

Income tax expense consists of federal, state and foreign income taxes incurred.

Critical Accounting Policies and Estimates

For a description of our critical accounting policies and estimates, 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, 2022. There have been no significant changes to our critical accounting policies and estimates since December 31, 2022 with the exception of the below new policy and estimate.

Performance-Based Restricted Stock Unit Awards

Fair value of performance-based restricted stock unit awards (PSUs) at the grant date are estimated using a lattice model with a Monte Carlo simulation. This valuation methodology utilizes several key assumptions, the defined consecutive trading day average closing stock price on the grant date, expected volatility of our stock price, risk-free rates of return and expected dividend yield. The probability of actual shares expected to be earned is considered in the grant date valuation and the expense is not adjusted to reflect the actual units earned. The PSUs cliff vest at the end of the service period and therefore the compensation expense for PSUs is recognized straight-line over the applicable service period.

Results of Operations

Comparison of Three Months Ended September 30, 2023 and 2022

The following table summarizes our results of operations for the three months ended September 30, 2023 and 2022, together with the changes in those items in dollars and as a percentage (in thousands):

	Three Months Ended September 30,			
	2023	2022	Dollar Change	% Change
Total revenues	$ 56,566	$ 65,977	$ (9,411)	(14)%
Total cost and operating expenses	185,546	190,254	(4,708)	(2)
Total other expense, net	(4,536)	(8,000)	3,464	43
Loss before income taxes	(133,516)	(132,277)	(1,239)	(1)
Income tax expense	197	886	(689)	(78)
Net loss	$ (133,713)	$ (133,163)	$ (550)	(0)%

Total Revenues

Total revenues consist of the following (in thousands):

	Three Months Ended September 30,			
	2023	2022	Dollar Change	% Change
Product revenue, net	$ 54,228	$ 28,634	$ 25,594	89 %
Collaboration and license revenue	2,338	9,843	(7,505)	(76)
License revenue - related party	—	27,500	(27,500)	(100)
Total revenues	$ 56,566	$ 65,977	$ (9,411)	(14)%

Product Revenue, Net

The following table summarizes revenue recognized from sales of AYVAKIT/AYVAKYT during the three months ended September 30, 2023 and 2022 (in thousands):

	Three Months Ended September 30,			
	2023	2022	Dollar Change	% Change
United States	$ 49,121	$ 25,054	$ 24,067	96 %
Rest of World	5,107	3,580	1,527	43
Total	$ 54,228	$ 28,634	$ 25,594	89 %

Product revenue, net increased during the three months ended September 30, 2023 as compared to the three months ended September 30, 2022 primarily driven by growth in the number of SM patients on therapy, including advanced SM and indolent SM with the recent label expansion.

Collaboration and License Revenue

The following table summarizes the revenue recognized from our collaboration and license agreements during the three months ended September 30, 2023 and 2022 (in thousands):

	Three Months Ended September 30,			
	2023	2022	Dollar change	% Change
CStone collaboration	$ 1,820	$ 2,915	$ (1,095)	(38)%
Collaboration with Roche for pralsetinib	513	4,282	(3,769)	(88)
Roche immunotherapy collaboration	—	2,475	(2,475)	(100)
Other	5	171	(166)	(97)
Total collaboration and license revenue	$ 2,338	$ 9,843	$ (7,505)	(76)%

Revenue recognized from our collaboration and license agreements decreased during the three months ended September 30, 2023 as compared to the three months ended September 30, 2022 primarily due to:

- Decreased revenue from our collaboration with Roche for pralsetinib during the three months ended September 30, 2023 as compared to the three months ended September 30, 2022 primarily due to a decrease in manufacturing services related to Roche Territory-specific activities.

- Decreased revenue from our CStone collaboration during the three months ended September 30, 2023 as compared to the three months ended September 30, 2022 primarily due to a decrease in manufacturing services and royalty revenue related to CStone Territory-specific activities.

- No revenue was recognized under the Roche immunotherapy agreement during the three months ended September 30, 2023 as a result of the collaboration agreement termination effective in April 2023.

License revenue – related party

License revenue – related party decreased by $27.5 million during the three months ended September 30, 2023 as compared to the three months ended September 30, 2022. The decrease resulted from the license revenue recorded under the IDRx License Agreement that was executed during the three months ended September 30, 2022.

Cost of Product Sales

The following table summarizes the cost of product sales during the three months ended September 30, 2023 and 2022 (in thousands):

	Three Months Ended September 30,			
	2023	2022	Dollar change	% Change
Cost of product sales	$ 1,685	$ 710	$ 975	137 %
Cost of collaboration sales	1,097	2,290	(1,193)	(52)
Total cost of sales	$ 2,782	$ 3,000	$ (218)	(7)%

Cost of sales decreased during the three months ended September 30, 2023 as compared to the three months ended September 30, 2022 primarily due to a decrease in the cost of collaboration related sales which was primarily driven by a decrease in manufacturing services related to our collaboration partners. The increase in cost of product sales was primarily driven by an increase in product sales.

Collaboration Loss Sharing

The following table summarizes the collaboration loss sharing expense during the three months ended September 30, 2023 and 2022 (in thousands):

	Three Months Ended September 30,			
	2023	2022	Dollar Change	% Change
Collaboration loss sharing	$ 1,771	$ 1,665	$ 106	6 %

Collaboration loss sharing under the collaboration with Roche for pralsetinib increased for the three months ended September 30, 2023 as compared to the three months ended September 30, 2022 primarily due to a decrease in GAVRETO product sales in the U.S. during the three months ended September 30, 2023 as compared to the three months ended September 30, 2022.

Research and Development Expense

The following table summarizes the research and development expenses during the three months ended September 30, 2023 and 2022 (in thousands):

	Three Months Ended September 30,			
	2023	2022	Dollar change	% Change
Clinical and manufacturing related activities	$ 35,790	$ 54,531	$ (18,741)	(34)%
Compensation and related expenses	28,112	24,719	3,393	14
Early drug discovery and platform	17,515	20,787	(3,272)	(16)
Stock-based compensation	11,169	10,010	1,159	12
Consulting and professional services	7,731	9,561	(1,830)	(19)
Facilities and IT	8,764	7,086	1,678	24
Other	1,171	1,287	(116)	(9)
Total research and development expenses	$ 110,252	$ 127,981	$ (17,729)	(14)%

Research and development expense decreased for the three months ended September 30, 2023 as compared to the three months ended September 30, 2022 primarily due to a decrease of $18.7 million in clinical and manufacturing related activities primarily due to our focused approach towards optimizing operational efficiency across our portfolio while executing across our top priority programs as well as the timing of manufacturing of clinical trial materials.

Selling, General and Administrative Expense

The following table summarizes the sales, general and administrative expenses during the three months ended September 30, 2023 and 2022 (in thousands):

	Three Months Ended September 30,			
	2023	2022	Dollar change	% Change
Compensation and related expenses	$ 29,669	21,661	$ 8,008	37 %
Stock-based compensation	11,901	14,099	(2,198)	(16)
Commercial and related expenses	13,071	7,719	5,352	69
Consulting and professional services	9,787	8,131	1,656	20
Facilities and IT	3,226	2,537	689	27
Other	3,087	3,461	(374)	(11)
Total sales, general and administrative expenses	$ 70,741	$ 57,608	$ 13,133	23 %

Selling, general and administrative expense increased for the three months ended September 30, 2023 as compared to the three months ended September 30, 2022 primarily due to:

- An increase of $8.0 million in compensation and related expenses driven by increased headcount in our field team to support our commercial activities related to indolent SM launch; and
- An increase of $5.4 million in commercial and related activities primarily related to the expansion of our commercial infrastructure for commercialization of AYVAKIT/AYVAKYT.

Interest Expense, Net

The following table summarizes the interest expense, net, during the three months ended September 30, 2023 and 2022 (in thousands):

	Three Months Ended September 30,			
	2023	2022	Dollar Change	% Change
Interest income	$ 9,329	$ 2,950	$ 6,379	216 %
Interest expense	(13,137)	(11,346)	(1,791)	16
Interest expense, net	$ (3,808)	$ (8,396)	$ 4,588	(55)%

Interest expense, net, decreased for the three months ended September 30, 2023 as compared to the three months ended September 30, 2022 primarily due to higher interest income earned on our investments, partially offset by higher interest charges on the liability related to the sale of future revenues and the term loan with Sixth Street Partners during the three months ended September 30, 2023 as compared to the three months ended September 30, 2022.

Other Income (Expense), Net

The following table summarizes the other income (expense), net, during the three months ended September 30, 2023 and 2022 (in thousands):

	Three Months Ended September 30,			
	2023	2022	Dollar Change	% Change
Other income (expense), net	$ (728)	$ 396	$ (1,124)	(284)%

Other expense, net, increased for the three months ended September 30, 2023 as compared to the three months ended September 30, 2022 primarily due to a decrease in other income. During the three months ended September 30, 2022, we recorded other income from a transfer of pre-launch inventory to a third party whereas no such other income was recorded during the three months ended September 30, 2023.

Income Tax Expense

The following table summarizes the income tax expense during the three months ended September 30, 2023 and 2022 (in thousands):

	Three Months Ended September 30,			
	2023	2022	Dollar Change	% Change
Income tax expense	$ 197	$ 886	$ (689)	(78)%

Income tax expense decreased for the three months ended September 30, 2023 as compared to the three months ended September 30, 2022 primarily due to the Company's estimated taxable loss position for the year ended December 31, 2023, whereas, during the three months ended September 30, 2022, the Company was in estimated taxable income position for the calendar year ended December 31, 2022 due to the cash considerations received under the royalty purchase agreement and the purchase and sale agreement entered into with Royalty Pharma and Sixth Street Partners in June 2022.

Comparison of Nine Months Ended September 30, 2023 and 2022

The following table summarizes our results of operations for the nine months ended September 30, 2023 and 2022, together with the changes in those items in dollars and as a percentage (in thousands):

	Nine Months Ended September 30,			
	2023	2022	Dollar Change	% Change
Total revenues	$ 177,423	$ 165,255	$ 12,168	7 %
Total cost and operating expenses	558,591	552,974	5,617	1
Total other expense, net	(13,993)	(6,952)	(7,041)	(101)
Loss before income taxes	(395,161)	(394,671)	(490)	0
Income tax expense	907	4,200	(3,293)	(78)
Net loss	$ (396,068)	$ (398,871)	$ 2,803	1 %

Total Revenues

Total revenues consist of the following (in thousands):

	Nine Months Ended September 30,			
	2023	2022	Dollar Change	% Change
Product revenue, net	$ 133,173	$ 80,929	$ 52,244	65 %
Collaboration and license revenue	44,250	56,826	(12,576)	(22)
License revenue - related party	—	27,500	(27,500)	(100)
Total revenues	$ 177,423	$ 165,255	$ 12,168	7 %

Product Revenue, Net

The following table summarizes revenue recognized from sales of AYVAKIT/AYVAKYT during the nine months ended September 30, 2023 and 2022 (in thousands):

	Nine Months Ended September 30,			
	2023	2022	Dollar Change	% Change
United States	$ 118,355	$ 70,888	$ 47,467	67 %
Rest of World	14,818	10,041	4,777	48
Total	$ 133,173	$ 80,929	$ 52,244	65 %

Product revenue, net increased during the nine months ended September 30, 2023 as compared to the nine months ended September 30, 2022 primarily driven by growth in the number of SM patients on therapy, including advanced SM and indolent SM with the recent label expansion.

Collaboration and License Revenue

The following table summarizes the revenue recognized from our collaboration and license agreements during the nine months ended September 30, 2023 and 2022 (in thousands):

	Nine Months Ended September 30,			
	2023	2022	Dollar change	% Change
Roche immunotherapy collaboration	$ 25,706	$ 1,710	$ 23,996	n/a %
CStone collaboration	16,861	18,209	(1,348)	(7)
Collaboration with Roche for pralsetinib	1,672	5,573	(3,901)	(70)
Clementia license agreement	—	30,000	(30,000)	(100)
Other	11	1,334	(1,323)	(99)
Total collaboration and license revenue	$ 44,250	$ 56,826	$ (12,576)	(22)%

Revenue recognized from our collaboration and license agreements decreased during the nine months ended September 30, 2023 as compared to nine months ended September 30, 2022 primarily due to:

- Decreased revenue from our license agreement with Clementia due to revenue from a $30.0 million milestone payment related to a specified development milestone achieved during the nine months ended September 30, 2022.

- Decreased revenue from our collaboration with Roche for pralsetinib during the nine months ended September 30, 2023 as compared to the nine months ended September 30, 2022 primarily due to a decrease in manufacturing services related to Roche Territory-specific activities.

The decreases was partially offset by increased revenue under our Roche immunotherapy collaboration during the nine months ended September 30, 2023 due to the collaboration agreement termination which resulted in the reduction in the costs incurred to satisfy our performance obligation under the Roche immunotherapy collaboration, and consequently, increased the transaction price and the percentage of completion of revenue to be recognized under the collaboration agreement.

License revenue – related party

License revenue – related party decreased by $27.5 million during the nine months ended September 30, 2023 as compared to the nine months ended September 30, 2022. The decrease resulted from the license revenue recorded under the IDRx License Agreement that was executed during the nine months ended September 30, 2022.

Cost of Product Sales

The following table summarizes the cost of product sales during the nine months ended September 30, 2023 and 2022 (in thousands):

	Nine Months Ended September 30,			
	2023	2022	Dollar change	% Change
Cost of product sales	$ 4,671	$ 2,139	$ 2,532	118 %
Cost of collaboration sales	3,609	10,826	(7,217)	(67)
Total cost of sales	$ 8,280	$ 12,965	$ (4,685)	(36)%

Cost of sales decreased during the nine months ended September 30, 2023 as compared to the nine months ended September 30, 2022 primarily due to a decrease in the cost of collaboration related sales which was driven primarily by a decrease in manufacturing services related to our collaboration partners. The increase in cost of product sales was primarily driven by an increase in product sales.

Collaboration Loss Sharing

The following table summarizes the collaboration loss sharing expense during the nine months ended September 30, 2023 and 2022 (in thousands):

	Nine Months Ended September 30,			
	2023	2022	Dollar Change	% Change
Collaboration loss sharing	$ 4,301	$ 7,076	$ (2,775)	(39)%

Collaboration loss sharing under the collaboration with Roche for pralsetinib decreased for the nine months ended September 30, 2023 as compared to the nine months ended September 30, 2022 primarily due to higher GAVRETO product sales in the U.S. during the nine months ended September 30, 2023 as compared to the nine months ended September 30, 2022.

Research and Development Expense

The following table summarizes the research and development expenses during the nine months ended September 30, 2023 and 2022 (in thousands):

	Nine Months Ended September 30,			
	2023	2022	Dollar change	% Change
Clinical and manufacturing related activities	$ 109,540	$ 149,193	$ (39,653)	(27)%
Compensation and related expenses	83,384	71,307	12,077	17
Early drug discovery and platform	55,551	58,609	(3,058)	(5)
Stock-based compensation	31,513	30,548	965	3
Consulting and professional services	22,255	25,320	(3,065)	(12)
Facilities and IT	25,454	21,037	4,417	21
Other	2,487	3,565	(1,078)	(30)
Total research and development expenses	$ 330,184	$ 359,579	$ (29,395)	(8)%

Research and development expense decreased for the nine months ended September 30, 2023 as compared to the nine months ended September 30, 2022 primarily due to:

- A decrease of $39.7 million in clinical and manufacturing related activities primarily due to our focused approach towards optimizing operational efficiency across our portfolio while executing across our top priority programs, the timing of manufacturing of clinical trial materials and decreased activities related to pralsetinib clinical studies; offset by

- An increase of $12.1 million in compensation and related expenses driven by increased headcount to support the progression of our pipeline.

Selling, General and Administrative Expense

The following table summarizes the sales, general and administrative expenses during the nine months ended September 30, 2023 and 2022 (in thousands):

	Nine Months Ended September 30,			
	2023	2022	Dollar change	% Change
Compensation and related expenses	$ 90,872	$ 63,601	$ 27,271	43 %
Stock-based compensation	38,575	42,307	(3,732)	(9)
Commercial and related expenses	34,489	24,299	10,190	42
Consulting and professional services	30,067	25,118	4,949	20
Facilities and IT	10,184	8,453	1,731	20
Other	11,639	9,576	2,063	22
Total sales, general and administrative expenses	$ 215,826	$ 173,354	$ 42,472	25 %

Selling, general and administrative expense increased for the nine months ended September 30, 2023 as compared to the nine months ended September 30, 2022 primarily due to:

- An increase of $27.3 million in compensation and related expenses driven by increased headcount in our sales force to support our commercial activities related to indolent SM launch; and
- An increase of $10.2 million in commercial and related activities primarily related to the expansion of our commercial infrastructure for commercialization of AYVAKIT/AYVAKYT.

Interest Expense, Net

The following table summarizes the interest expense, net, during the nine months ended September 30, 2023 and 2022 (in thousands):

	Nine Months Ended September 30,			
	2023	2022	Dollar Change	% Change
Interest income	$ 22,978	$ 3,824	$ 19,154	501 %
Interest expense	(36,602)	(11,351)	(25,251)	222
Interest expense, net	$ (13,624)	$ (7,527)	$ (6,097)	81 %

Interest expense, net, increased for the nine months ended September 30, 2023 as compared to the nine months ended September 30, 2022 primarily due to the interest charges on the liability related to the sale of future revenues and the term loan with Sixth Street Partners. The increase in interest expense was partially offset by higher interest income earned on the Company's investments during the nine months ended September 30, 2023 as compared to the nine months ended September 30, 2022.

Other Income (Expense), Net

The following table summarizes the other income (expense), net, during the nine months ended September 30, 2023 and 2022 (in thousands):

	Nine Months Ended September 30,			
	2023	2022	Dollar Change	% Change
Other income (expense), net	$ (369)	$ 575	$ (944)	(164)%

Other expense, net, increased for the nine months ended September 30, 2023 as compared to the nine months ended September 30, 2022 primarily due to a decrease in other income and an increase in foreign exchange losses.

During the nine months ended September 30, 2022, we recorded other income from a transfer of pre-launch inventory to a third party, whereas no such other income was recorded during the nine months ended September 30, 2023.

Income Tax Expense

The following table summarizes the income tax expense during the nine months ended September 30, 2023 and 2022 (in thousands):

	Nine Months Ended September 30,			
	2023	2022	Dollar Change	% Change
Income tax expense	$ 907	$ 4,200	$ (3,293)	(78)%

Income tax expense decreased for the nine months ended September 30, 2023 as compared to the nine months ended September 30, 2022 primarily due to the Company's estimated taxable loss position for the year ended December 31, 2023, whereas, during the nine months ended September 30, 2022, the Company was in estimated taxable income position for the calendar year ended December 31, 2022 due to the cash considerations received under the royalty purchase agreement and the purchase and sale agreement entered into with Royalty Pharma and Sixth Street Partners in June 2022.

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 and license agreements, future royalty and revenue monetization, and a term loan. Through September 30, 2023, we have received an aggregate of $3.7 billion from such transactions, including $1.9 billion in aggregate gross proceeds from the sale of common stock in our IPO, follow-on public offerings, through our "at the market" stock offering program and the equity investment by Roche, $115.1 million in gross proceeds from the issuance of convertible preferred stock, $175.0 million in gross proceeds from our Royalty Purchase Agreement with Royalty Pharma, $250.0 million in gross proceeds from our Future Revenue Purchase Agreement with Sixth Street Partners, $1.0 billion in upfront payments and milestone payments under our collaborations with Roche, CStone and Zai Lab, our license agreement with Clementia and our former collaboration with Alexion, and $250.0 million in gross proceeds from a term loan from Sixth Street Partners. In addition, since January 2020, we have also generated revenue through the sales of our approved drug products.

As of September 30, 2023, we had cash, cash equivalents and marketable securities of $827.2 million.

Cash Flows

The following table provides information regarding our cash flows for the nine months ended September 30, 2023 and 2022:

	Nine Months Ended September 30,	
(in thousands)	2023	2022
Net cash used in operating activities	$ (357,919)	$ (380,872)
Net cash provided by (used in) investing activities	195,271	(96,258)
Net cash provided by financing activities	103,697	559,319
Net increase (decrease) in cash, cash equivalents, and restricted cash	$ (58,951)	$ 82,189

Net Cash Used in Operating Activities. For the nine months ended September 30, 2023, compared to the same period in 2022, the $23.0 million decrease in net cash used in operating activities was primarily due to an increase in non-cash adjustments of $24.2 million and a decrease in net loss of $2.8 million, partially offset by the changes in our operating assets and liabilities of $4.1 million. The changes in non-cash adjustments were primarily due to the $27.5 million non-cash customer consideration related to our IDRx License Agreement that was executed during the nine months ended September 30, 2022, partially offset by the increase of $12.4 million in the net accretion of discounts

related to our investments in marketable securities. The changes in net cash flows related to changes in our operating assets and liabilities were generally due to timing of vendor invoices and payments.

Net Cash Provided by (Used in) Investing Activities. For the nine months ended September 30, 2023, compared to the same period in 2022, the $291.5 million increase in net cash provided by investing activities was primarily due to the $295.2 million increase in net proceeds received from maturities of our investments in marketable securities.

Net Cash Provided by Financing Activities. For the nine months ended September 30, 2023, compared to the same period in 2022, the $455.6 million decrease in net cash provided by financing activities was primarily due to the $415.8 million in net proceeds provided by the sale of future royalties and future revenues during the nine months ended September 30, 2022 and the $39.8 million decrease in net proceeds provided by the term loan facility.

Debt Financing

In June 2022, we entered into a Royalty Purchase Agreement with Royalty Pharma. Pursuant to the Royalty Purchase Agreement, we received an upfront payment of $175.0 million in consideration for our rights to receive royalty payments on the net sales of GAVRETO worldwide excluding the CStone Territory and U.S. territory under the terms of the Roche pralsetinib collaboration agreement. Net proceeds from the transaction were recorded as liabilities related to sale of future royalties and revenues on the consolidated balance sheet and as of September 30, 2023, the net carrying value of the liability related to this arrangement was $175.3 million.

In July 2022, we closed a Future Revenue Purchase Agreement with Sixth Street Partners and received gross proceeds of $250.0 million in exchange for future royalty payments at a rate of 9.75% on up to $900 million each year of (i) aggregate worldwide annual net product sales of AYVAKIT/AYVAKYT (avapritinib) and (ii) if it is approved, aggregate worldwide annual net product sales of elenestinib (BLU-263), but excluding sales in Greater China, subject to a cumulative cap of 1.45 times the upfront invested capital or a total of $362.5 million. In the event that certain revenue targets are not achieved by specified dates, the royalty rate and cumulative cap shall be increased to 15% and 1.85 times the invested capital (or $462.5 million), respectively. Net proceeds from the transaction were recorded as liabilities related to sale of future royalties and revenues on the consolidated balance sheet and as of September 30, 2023, the net carrying value of the liability related to this arrangement was $264.9 million.

In July 2022, we closed a Financing Agreement for up to $660.0 million with Sixth Street Partners. The Financing Agreement, entered into by the parties in connection with the transaction provides for (i) a senior secured term loan facility of up to $150.0 million and (ii) a senior secured delayed draw term loan facility of up to $250.0 million to be funded in two tranches at our choice subject to certain terms and conditions. The loans will mature on June 30, 2028 and bear interest at a variable rate equal to either the Secured Overnight Financing Rate (SOFR) plus 6.50% or the base rate plus 5.50%, subject to a floor of 1% and 2% with respect to the SOFR and base rate, respectively. The initial gross proceeds of $150.0 million was funded in July 2022. In August 2023, we received the first tranche of the senior secured delayed draw term loan facility in the amount of $100.0 million in gross proceeds. In addition, we may at any time request an incremental term loan in an amount not to exceed $260.0 million on terms to be agreed and subject to the consent of the lenders providing such incremental term loan. As of September 30, 2023, the net carrying value of the term loan was $238.4 million.

Our obligations under the Financing Agreement are secured, subject to certain exceptions, by security interests in the substantially all of our assets and our certain subsidiaries. The Financing Agreement contains negative covenants that, among other things and subject to certain exceptions, could restrict our ability to incur additional liens, incur additional indebtedness, make investments, including acquisitions, engage in fundamental changes, sell or dispose of assets that constitute collateral, including certain intellectual property, pay dividends or make any distribution or payment on or redeem, retire or purchase any equity interests, amend, modify or waive certain material agreements or organizational documents and make payments of certain subordinated indebtedness. The Financing Agreement also requires us to have consolidated liquidity of at least (i) $50.0 million during the period commencing from the date on which the term loans are funded to the date which is the day before the next term loans are funded and (ii) $80.0 million for each day thereafter. For additional information, see Note 3, *Financing Arrangements*, to our unaudited condensed consolidated financial statements.

Funding Requirements

We expect variability in our expenses in connection with our ongoing activities, particularly as we continue the research and development of, initiate or continue clinical trials of, and seek marketing approval for our drug candidates. In addition, 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 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 or business objectives. 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, 2023, we had cash, cash equivalents and marketable securities of $827.2 million. Based on our current operating plans, we anticipate our existing cash, cash equivalents and marketable securities, 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 and may increase as a result of many factors, including:

- the success of our commercialization efforts and market acceptance for AYVAKIT/AYVAKYT 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 and any of our current or future drug candidates for which we receive marketing approval;
- the costs of securing manufacturing, packaging and labeling arrangements to ensure adequate supply for development activities and commercial production, including API, drug substance and drug product material for use in preclinical studies, clinical trials, our compassionate use program and for use as commercial supply, as applicable;
- the cost of purchasing quantities of agents for use in our clinical trials in connection with our efforts to develop our drugs and drug candidates, including for development as combination therapies;
- the scope, progress, results and costs of drug discovery, preclinical 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, to the extent these expenses are not the responsibility of our collaboration partners;
- the success of our collaborations with CStone, Zai Lab and Proteovant and our license agreements with Clementia and IDRx, 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, our financing arrangements, or any collaboration, partnership, financing 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 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 preclinical 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 and achieve substantial revenues for any of our drugs or drug candidates that receive marketing approval. In addition, our drugs and any current or future drug candidates that receive marketing approvals 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 we can generate material net cash inflows from our operations, we may choose to finance our cash needs primarily through a combination of public and private equity offerings, debt financings, future revenue monetizations, collaborations, strategic alliances and licensing arrangements. We do not have any committed external sources of funds, other than our collaborations with CStone and Zai Lab, the license agreements with Clementia and IDRx, the Royalty Purchase Agreement with Royalty Pharma, and the Financing Agreement with Sixth Street Partners, 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. Additional debt financing, if available, would increase our fixed payment obligations and may involve agreements that include additional 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, licensing arrangements or future revenue monetizations 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 related to certain commercial manufacturing agreements.

During the nine months ended September 30, 2023, there was a decrease of $7.3 million in our contractual obligations 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, 2022.

Item 3. Quantitative and Qualitative Disclosures About Market Risk

As of September 30, 2023 and December 31, 2022, we had cash, cash equivalents and marketable securities of $827.2 million and $1,078.5 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 resulting from the Federal Reserve’s raising of interest rates. 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 monetary policy from the U.S. and international central banks, inflationary pressures, and geopolitical developments, or instability or volatility in the global markets. 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, 2023 and December 31, 2022, we held limited funds and future obligations denominated in foreign currencies.

Inflation generally affects us by increasing our cost of labor, clinical trial and manufacturing costs and indirectly increasing interest rates. Inflation rates, particularly in the U.S., have increased recently to levels not seen in years. We have not seen a significant impact from inflation on our business, financial condition or results of operations during the three and nine months ended September 30, 2023. However, if inflation remains at current levels for an extended period of time, or increases, our costs are likely to increase, which may negatively impact our margins and cash flows.

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, 2023. Based upon such evaluation, our Chief Executive Officer and Chief Financial Officer have concluded that, as of September 30, 2023, 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, nor are we aware of any governmental proceedings involving potential monetary sanctions of $300,000 or more.

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.

Risk Factor Summary

Below is a summary of the material risks to our business, operations and the investment in our common stock. This summary does not address all of the risks that we face. Risks and uncertainties not presently known to us or that we presently deem less significant may also impair our business operations. Additional discussion of the risks summarized in this risk factor summary, and other risks that we face, can be found below and should be carefully considered, together with other information in this Quarterly Report on Form 10-Q in its entirety before making investment decisions regarding our common stock.

- We are in the process of growing as a commercial company and the marketing and sale of AYVAKIT® (avapritinib) (marketed in Europe under the brand name AYVAKYT®), GAVRETO® (pralsetinib) or any future approved drugs may be unsuccessful or less successful than anticipated.
- 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.
- 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 may be adversely affected.
- We face substantial competition, which may result in our commercial opportunity being reduced or limited by others commercializing, developing or discovering drugs before or more successfully than we do.
- 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.
- If we are unable to obtain regulatory approval for our drug candidates (including for avapritinib in additional geographies, particularly for indolent SM in geographies outside of the U.S.) and ultimately commercialize them, or experience significant delays in doing so, our business may be materially harmed.
- 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.
- If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals for our drug candidates and, if applicable, for any related companion diagnostic tests, we will not be able to commercialize, or may be delayed in commercializing, such drug candidates, and our ability to generate revenue 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, result in restrictive distribution or result in other negative consequences following marketing approval, if any.
- Positive preclinical data, individual case report presentations, and interim or early or clinical results for our drug candidates may not be indicative of future results and may not evolve into final clinical data that supports continued clinical development or into registration-enabling data.
- We may not be successful in our efforts to expand our pipeline of drug candidates.
- We are required to comply with comprehensive and ongoing regulatory requirements for any of our

current or future approved drugs, including conducting confirmatory clinical trials for any drug that receives accelerated approval. In addition, our current or future approved drugs 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.

- We have incurred operating losses since our inception and anticipate that we will incur continued losses for the foreseeable future.

- We have entered into collaborations and licenses with our partners for the development and commercialization of several of our drugs and drug candidates. If our collaborations are not successful, we may not be able to capitalize on the market potential of these drugs and drug candidates.

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

- We contract with third parties for the manufacture of our approved drugs and drug candidates, including for preclinical, clinical and commercial supply. This reliance on third parties increases the risk that we will not have sufficient quantities of our approved drugs or drug candidates or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.

- 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.

- 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.

- We may acquire or in-license businesses, technologies or platforms, approved drugs, drug candidates or discovery-stage programs, or form strategic alliances, collaborations or partnerships, in the future, and we may not realize the benefits of such acquisitions, in-licenses, alliances, collaborations or partnerships.

- The price of our common stock has been and may in the future be volatile and fluctuate substantially.

Risks Related to Commercialization

We are in the process of growing as a commercial company and the marketing and sale of AYVAKIT/AYVAKYT, GAVRETO or any future approved drugs may be unsuccessful or less successful than anticipated.

We have two approved precision therapies, AYVAKIT/AYVAKYT and GAVRETO. While we have been commercializing AYVAKIT in the U.S. and AYVAKYT in Europe and co-commercializing GAVRETO with Roche in the U.S., we only have several years' experience as a commercial company, and we have a limited track record demonstrating our ability to successfully overcome the many of the risks and uncertainties encountered by companies commercializing drugs in the biopharmaceutical industry. Marketing applications for avapritinib and pralsetinib are currently under review or planned in the U.S. or globally. 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 patients who may receive our drugs and any future drugs;

- obtain and maintain adequate pricing and reimbursement for AYVAKIT/AYVAKYT and any future drugs;
- gain regulatory acceptance for the development and commercialization of current or future drug candidates in our pipeline, including for additional indications or in additional geographies for marketed drugs in our portfolio;
- maintain our existing collaborations with CStone Pharmaceuticals, or CStone, and Zai Lab;
- expand our global operations or enter into collaboration, partnerships or distribution arrangements in geographies where we may not have current operations or expertise; 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 commercialize our current or future approved drugs, develop current or future drug candidates, expand our business or continue our operations.

The commercial success of AYVAKIT/AYVAKYT and GAVRETO, as well as any other drugs that we may bring to the market, will depend upon the degree of market acceptance by physicians, patients, third-party payors and others in the medical community.

AYVAKIT/AYVAKYT and GAVRETO, as well 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 revenues and may not become profitable. The degree of market acceptance for AYVAKIT/AYVAKYT and GAVRETO, as well as 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 the drug's approved labeling;
- the relative convenience and ease of administration;
- the willingness of eligible patients 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 drug candidate displays a favorable efficacy and safety profile in preclinical and clinical studies and the drug candidate receives marketing approval, 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, including more resources than those required for treatments marketed by competitors, and may never be successful. Any of these factors may cause our approved drugs, as well as 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.

We continue to build out our commercial capabilities and infrastructures and have been growing our sales and distribution experience and 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 continue 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 or can successfully compete with other companies 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.

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.

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 drugs could be delayed which would negatively impact our ability to generate product revenues.

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.

The precise incidence and/or prevalence for SM, chronic urticaria and other mast cell disorders, RET-altered cancers, EGFR-mutated NSCLC, CDK2-vulnerable cancers and GIST are unknown. Our projections of the number of people who have these diseases, the frequency of the genetic alterations targeted by our drugs and drug candidates and the subset of patients who have the potential to benefit from our treatment options are based on estimates. These estimates have been derived from a variety of sources, including scientific literature, surveys of clinics, patient foundations or third-party market research, and may prove to be incorrect. Further, new studies may change the estimated incidence or prevalence of these cancers and the number of patients may turn out to be lower than expected. Additionally, the potentially addressable patient population for our approved drugs and drug candidates may be limited or may not be amenable to treatment with our precision therapies.

Accordingly, the incidence and/or prevalence of the diseases we aim to address 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 commercializing, developing or discovering 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.

AYVAKIT/AYVAKYT and elenestinib (BLU-263) face competition for advanced SM from Novartis AG's midostaurin and imatinib, and may face competition from drug candidates in development, including that being developed by Cogent Biosciences, Inc. Avapritinib and elenestinib may face non-advanced SM competition from drug candidates in development, including those being developed by AB Science S.A., Allakos Inc., Celldex Therapeutics, Inc., Cogent Biosciences, Inc. and Invea Therapeutics Inc.

AYVAKIT/AYVAKYT may face competition from drug candidates in development for PDGFRA-driven 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 and RET fusion-positive thyroid cancer, from Eli Lilly and Company's selpercatinib. If pralsetinib receives marketing approval for patients with 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 for RET-altered cancers, including those being developed by AstraZeneca plc, Boston Pharmaceuticals, Inc., Eisai Inc., Exelixis, Inc., GlaxoSmithKline plc, Mirati Therapeutics, Inc., Novartis AG, Pfizer Inc., and Stemline 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.

We are developing BLU-525 and BLU-945 for treatment-resistant EGFR-mutated NSCLC, which, if approved, will face competition from AstraZeneca plc's osimertinib and aumolertinib, which is under collaboration between Jiangsu Hansoh Pharmaceutical Group Co., Ltd. and EQRx, Inc. and approved in China. In addition, BLU-525 and BLU-945 may face competition from drug candidates in development for EGFR-mutated NSCLC, including those being developed by Abbisko Therapeutics Co. Ltd, Shanghai Allist Pharmaceuticals Co. Ltd. (Allist), Arrivent Biopharma, Inc., Betta Pharmaceuticals Co. Ltd., Black Diamond Therapeutics, Inc., Boehringer Ingelheim RCV GmbH & Co KG, Bridge Biotherapeutics, Inc., C4 Therapeutics, Inc., Daiichi Sankyo Company, Limited, Janssen Pharmaceuticals, Inc., J INTS Bio, Kanaph Therapeutics Inc., Qilu Pharmaceutical Co., Ltd., RedCloud Bio, Scorpion Therapeutics, Inc., Suzhou Junjing Biosciences, Suzhou Puhe Biopharma Co. Limited, Systimmune, Taiho Oncology, Therapex, Theseus Pharmaceuticals, Inc.

We are developing BLU-451 for NSCLC driven by EGFR exon 20 insertions or other rare, atypical mutations, which, if approved, will face competition from AstraZeneca plc's osimertinib, Boehringer Ingelheim Pharmaceuticals' afatinib, and Janssen Pharmaceuticals's amivantamab. In addition, BLU-451 may face competition from drug candidates in development for NSCLC driven by EGFR exon 20 insertions or other rare, atypical mutations, including those being developed by Abbisko Therapeutics Co., Ltd., Allist Pharmaceuticals Co. Ltd., Arrivent Biopharma, Inc., Avistone, Bayer AG, Black Diamond Therapeutics, Cullinan Oncology, Inc., Daiichi Sankyo Company, Limited, Dizal Pharmaceutical Co. Ltd., Shenzhen Forward Pharmaceutical Co., Ltd., Huadong Medicine Co., Ltd., Shanghai Junshi Biosciences Co., Ltd., Oric Pharmaceuticals, Inc., Scorpion Therapeutics, Inc., Suzhou Puhe Biopharma Co. Limited, Taiho Oncology, and TYK Medicines, Inc.

We are developing BLU-222 for cancers vulnerable to CDK2 inhibition, including CCNE1-aberrant cancers, which, if approved, will face competition from indication-specific therapies such as AstraZeneca and Daiichi Sankyo's Enhertu, AstraZeneca and Merck's olaparib, Clovis Oncology's rucaparib, Eisai's lenvatinib, Genentech's bevacizumab, GSK's niraparib, GSK's dostarlimab, Menarini Group & Stemline Therapeutics' elacestrant, Merck's pembrolizumab, and Novartis' alpelisib. In addition, BLU-222 may face competition from drug candidates in development, including those being developed by Acrivon Therapeutics, Allorion Therapeutics, Inc., Anrui Biomedical Technology, Arvinas, AstraZeneca plc, Aucentra Therapeutics, BioTheryX, Inc., Cedilla Therapeutics, Inc., Cyclacel Pharmaceuticals Inc., Eli Lilly and Company, Exelixis, Gilead Sciences, Inc., IMPACT Therapeutics, Inc., Incyclix Bio, LLC, Incyte Corporation, Monte Rosa Therapeutics, Inc., Pfizer Inc., Plexium, Inc., Regor Therapeutics Inc., Relay Therapeutics, Inc., Repare Therapeutics, Inc., Satya Pharma Innovations Pvt. Ltd., and Zentalis Pharmaceuticals, Inc.

We are developing BLU-852 for advanced cancers susceptible to MAP4K1 inhibition, which, if approved, will face competition from immuno-oncology products, including those developed by Bristol-Myers Squibb Company, Merck & Co., Inc., Regeneron Pharmaceuticals, Inc., Sanofi S.A., and AstraZeneca plc. In addition, BLU-852 may face competition from drug candidates in development for advanced cancers susceptible to MAP4K1 inhibition, including those being developed by 1st Biotherapeutics, Inc., BeiGene Ltd., Glenmark Pharmaceuticals Limited, MingMed Biotechnology Co., Ltd., Nimbus Therapeutics, LLC, Pfizer Inc., Regor Pharmaceuticals Inc., and Treadwell Therapeutics, Inc.

We are developing BLU-808 for chronic urticaria, which if approved, will face competition from other therapies, including omalizumab developed by Genentech and Novartis. In addition, BLU-808 may face competition from drug candidates in development for chronic urticaria, including those developed by Allakos Inc., Amgen Inc., AstraZeneca plc, Celldex Therapeutics, Inc., Escient Pharmaceuticals, Inc., Evommune, Inc, Incyte Corporation, Inmagene Biopharmaceuticals Co. Ltd., Jasper Therapeutics, Inc., Modulus Discovery Inc., Novartis AG, Regeneron Pharmaceuticals, Inc., Sanofi S.A., and Third Harmonic Bio, Inc.

Many of the companies against which we are competing or against which we may compete in the future have significantly greater financial resources and expertise in research and development, manufacturing, preclinical 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.

Increasing demand for compassionate use of our drug candidates could negatively affect our reputation and harm our business.

We are developing drug candidates for the treatment of indications for which there are currently limited or no available therapeutic options. It is possible for individuals or groups to target companies with disruptive social media campaigns related to a request for access to unapproved drugs for patients with significant unmet medical need. If we experience a similar social media campaign regarding our decision to provide or not provide access to any of our current or future drug candidates under an expanded access policy, our reputation may be negatively affected and our business may be harmed.

Media attention to individual patients' expanded access requests has resulted in the introduction and enactment of legislation at the local and national level referred to as "Right to Try" laws, such as the federal Right to Try Act of 2017, which are intended to allow patients access to unapproved therapies earlier than traditional expanded access programs. A possible consequence of both activism and legislation in this area may be the need for us to initiate an unanticipated expanded access program or to make our drug candidates more widely available sooner than anticipated.

In addition, some patients who receive access to drugs prior to their commercial approval through compassionate use, expanded access programs or right to try access, collectively referred to as compassionate use programs, have life-threatening illnesses and have exhausted all other available therapies. The risk for serious adverse events in this patient population is high, which, if those adverse events are determined to be drug-related, could have a negative impact on the safety profile of our drug candidates if we were to provide them to these patients, which could cause significant delays or an inability to successfully commercialize our drug candidates and materially harm our business. If we were to provide patients with any of our drug candidates under a compassionate use program, our supply capabilities may limit the number of patients who are able to enroll in the program and we may in the future need to restructure or pause any compassionate use program in order to enroll sufficient numbers of patients in our controlled clinical trials required for regulatory approval and successful commercialization of our drug candidates, which could prompt adverse publicity or other disruptions related to current or potential participants in such programs.

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 industry-wide in developing and commercializing these types of companion diagnostic tests. To be successful, we need to address a number of scientific, technical and logistical challenges. We have entered into agreements to develop and/or commercialize companion diagnostic tests with third parties, including for avapritinib in order to identify GIST patients with the

PDGFRA D842V mutation, and pralsetinib in order to identify NSCLC patients with RET fusions. We have limited experience in the development and commercialization of companion diagnostic tests with third parties and may not be successful in developing and commercializing appropriate companion diagnostic tests with third parties 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. We are relying on third parties to design, manufacture, obtain regulatory clearance or approval for and commercialize the companion diagnostic tests, including for avapritinib and pralsetinib, 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 current and future 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, prevent or revoke 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 may be materially harmed.

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.

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

If we are unable to establish, maintain and, if necessary, expand 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.

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 or a new indication for a drug product for which we establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses, which may be costly.

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. 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. 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.

If we do not establish, maintain and, if necessary, expand 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.

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 in additional geographies, particularly for indolent SM in geographies outside of the U.S., and ultimately commercialize them, or experience significant delays in doing so, our business will be materially harmed.

Our ability to generate material net cash inflows from our operations will depend heavily on the successful development and commercialization of our drugs and drug candidates. Each of our drug candidates will require additional preclinical or clinical development, management of clinical, preclinical and manufacturing activities, regulatory approval in multiple jurisdictions, obtaining manufacturing supply, substantial investment and significant marketing efforts before we generate substantial revenues from sales for those drug candidates, if approved. 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 our drugs or 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. 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 our drugs and drug candidates as monotherapies and in combination with other agents;
- successful initiation and completion of preclinical studies for our other drug candidates;
- successful development of any companion diagnostic tests for use with our drugs and drug candidates;
- receipt of regulatory approvals from applicable regulatory authorities and transitioning any conditional marketing authorizations to full approvals;
- in-house commercial manufacturing capabilities or 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 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 drugs and 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, 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. Because the target patient populations for our drug candidates and approved drugs in clinical development for additional indications are relatively small, it may be difficult to successfully identify patients. Although we have entered into or plan to enter into agreements with third parties to develop companion diagnostic tests for use in some of our other current or future clinical trials in order to help identify eligible patients, we may experience delays in reaching, or fail to reach, agreement on acceptable terms to develop such companion diagnostic tests. 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.

In addition, we experienced some delays or disruptions in enrollment in our ongoing clinical trials due to the COVID-19 pandemic, and we may experience additional delays or disruptions in the future due to the changes in local site or IRB policies, availabilities of site staff, and reprioritization of hospital resources. Furthermore, some of our competitors have ongoing clinical trials for drug candidates that treat the same indications as our drug candidates and approved drugs in clinical development for additional indications, 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.

Our inability to identify patients appropriate for enrollment in our clinical trials, or to enroll a sufficient number of patients in our clinical trials, would result in significant delays and could require us to abandon one or more clinical trials altogether. Enrollment delays in our clinical trials may result in increased development costs for our drug candidates, which would cause the value of our company to decline and limit our ability to obtain additional financing. If we are unable to include patients with the driver of the disease, including the applicable genomic alteration for diseases in genomically defined patient populations, this could compromise our ability to seek participation in the FDA's expedited review and approval programs, including breakthrough therapy designation and fast track designation, or otherwise to seek to accelerate clinical development and regulatory timelines.

If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals for our drug candidates and, if applicable, for any related companion diagnostic tests, we will not be able to commercialize, or may 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 avapritinib in order to identify GIST patients with the PDGFRA D842V mutation, and pralsetinib in order to identify NSCLC patients with RET fusions, and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale, distribution, import and export, are subject to comprehensive regulation by the FDA and other regulatory agencies in the 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 pralsetinib.

We expect to rely on third-party CROs and/or regulatory consultants to assist us in filing and supporting the applications necessary to gain regulatory approvals. Securing regulatory approval requires the submission of extensive preclinical 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. Should FDA determine that an inspection is necessary for approval of a marketing application and an inspection cannot be completed during the review cycle due to restrictions on travel, 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, FDA may defer action on the application until an inspection can be completed. 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 preclinical, clinical or other studies. We currently have multiple marketing applications for our drug candidates under review across the world.

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 preclinical 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; and
- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval;

In addition, even if we were to obtain approval, regulatory authorities may approve any of our drug candidates for fewer or more limited indications than we request, may not approve the price we intend to charge for our drugs and related companion diagnostic tests, may grant approval contingent on the performance of costly post-marketing clinical trials or 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. Additionally, the receipt of regulatory approval for one indication does not ensure the likelihood of success for regulatory approval of expanded indications for a marketed product. 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.

Inadequate funding for the FDA, the SEC and other government agencies, including from government shutdowns, or other disruptions to these agencies' operations, could hinder their ability to hire and retain key leadership and other personnel, prevent new products and services from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, the ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory and policy changes. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of the SEC and other government agencies on which our operations may rely, including those that fund research and development activities, is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA and other agencies may also slow the time necessary for new drug candidates to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, future government shutdowns could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

Results from earlier stage trials may not be predictive of the results of later stage trials and interim and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available or as additional analyses are conducted and as the data are subject to audit and verification procedures that could result in material changes in the final data.

The results of preclinical studies and early clinical trials of our drug candidates may not be predictive of the results of later-stage clinical trials. In addition, initial success in clinical trials may not be indicative of results obtained when such trials are completed. There is typically an extremely high rate of attrition from the failure of drug candidates proceeding through clinical trials. Drug candidates in later stages of clinical trials may fail to show the desired safety and efficacy profile despite having progressed through preclinical studies and initial clinical trials. A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or emergence of unacceptable safety issues, notwithstanding promising results in earlier trials. Most drug candidates that commence clinical trials are never approved as products and there can be no assurance that any of our future clinical trials will ultimately be successful or support further clinical development of any of our drug candidates. Drug candidates that appear promising in the early phases of development may fail to reach the market for several reasons, including:

- preclinical studies or clinical trials may show the drug candidates to be less effective than expected (e.g., a clinical trial could fail to meet its primary endpoint(s)) or to have unacceptable side effects or toxicities;
- failure to establish clinical endpoints that applicable regulatory authorities would consider clinically meaningful;
- failure to receive the necessary regulatory approvals;
- manufacturing issues, formulation issues, pricing or reimbursement issues or other factors that make a drug candidate uneconomical; and

- the proprietary rights of others and their competing products and technologies that may prevent one of our drug candidates from being commercialized.

In addition, differences in trial design between early-stage clinical trials and later-stage clinical trials make it difficult to extrapolate the results of earlier clinical trials to later clinical trials. Moreover, clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their drug candidates performed satisfactorily in clinical trials have nonetheless failed to obtain marketing approval of their products.

Additionally, from time to time, we may publish interim or preliminary data from our clinical studies. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Preliminary data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, interim and preliminary data should be viewed with caution until the final data are available. Material adverse changes between preliminary or interim data and final data could significantly harm our business prospects.

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, result in restrictive distribution 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 preclinical 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 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 preclinical studies or clinical trials related to on-target toxicity. If on-target toxicity is observed, or if our 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.

We may seek designation for our discovery platform as a designated platform technology, but we might not receive such designation, and even if we do, such designation may not lead to faster drug development or a faster regulatory review or approval process.

We may seek designation for our discovery platform as a designated platform technology. Under the Food and Drug Omnibus Reform Act of 2022 (FDORA), a platform technology incorporated within or utilized by a drug product is eligible for designation as a designated platform technology if (1) the platform technology is incorporated in, or utilized by, a drug approved under an NDA; (2) preliminary evidence submitted by the sponsor of the approved or licensed drug, or a sponsor that has been granted a right of reference to data submitted in the application for such drug, demonstrates that the platform technology has the potential to be incorporated in, or utilized by, more than one drug without an adverse effect on quality, manufacturing, or safety; and (3) data or information submitted by the applicable person indicates that incorporation or utilization of the platform technology has a reasonable likelihood to bring significant efficiencies to the drug development or manufacturing process and to the review process. A sponsor may request the FDA to designate a platform technology as a designated platform technology concurrently with, or at any time after, submission of an investigational new drug (IND) application for a drug that incorporates or utilizes the platform technology that is the subject of the request. If so designated, the FDA may expedite the development and review of any subsequent original NDA for a drug that uses or incorporates the platform technology. Even if we believe our discovery platform meets the criteria for such designation, the FDA may disagree and instead determine not to grant such designation. In addition, the receipt of such designation for a platform technology does not ensure that a drug will be developed or reviewed more quickly or receive FDA approval. Moreover, the FDA may revoke a designation if the FDA determines that a designated platform technology no longer meets the criteria for such designation.

A fast track or breakthrough therapy designation by the FDA for our drug candidates may not lead to a faster development or regulatory review or approval process, and it does not increase the likelihood that our drug candidates will receive marketing approval.

We may seek fast track or breakthrough therapy designation for some of our current or future drug candidates. Fast track designation is designed for drug candidates intended for the treatment of a serious or life-threatening disease or condition, where nonclinical or clinical data demonstrate the potential to address an unmet medical need for this disease or condition. 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 fast track or 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. The FDA has granted fast track designation to BLU-782 for the treatment of

FOP. The FDA has granted breakthrough therapy designation to avapritinib for the treatment of moderate to severe indolent SM. In addition, the FDA previously granted breakthrough designation to our drugs, AYVAKIT and GAVRETO, for the treatment of certain patients with GIST, advanced SM, moderate to severe indolent SM and RET-altered cancers, respectively.

Designation as a fast track or 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 fast track or breakthrough therapy, the FDA may disagree and instead determine not to make such designation. In any event, the receipt of a fast track or 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 fast track or breakthrough therapies, the FDA may later decide that the drugs no longer meet the conditions for qualification.

We may seek approval of our drug candidates, where applicable, under the FDA's accelerated approval pathway. A product may be eligible for accelerated approval if it is designed to treat a serious or life-threatening disease or condition and generally provides a meaningful advantage over available therapies. In addition, it demonstrates an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality (IMM), that is reasonably likely to predict an effect on IMM or other clinical benefit. As a condition of accelerated approval, the FDA likely would require that we perform adequate and well-controlled post-marketing clinical trials, and under FDORA the FDA is now permitted to require, as appropriate, that such trials be underway prior to approval or within a specific time period after the date of approval for a product granted accelerated approval. FDORA also gives the FDA increased authority to withdraw approval of a drug or biologic granted accelerated approval on an expedited basis if the sponsor fails to conduct such studies in a timely manner, send the necessary updates to the FDA, or if such post-approval studies fail to verify the product's predicted clinical benefit. Under FDORA, the FDA is empowered to take action, such as issuing fines, against companies that fail to conduct with due diligence any post-approval confirmatory study or submit timely reports to the agency on their progress. These confirmatory trials must be completed with due diligence. In addition, the FDA currently requires, unless otherwise informed by the agency, pre-approval of promotional materials for products receiving accelerated approval, which could adversely impact the timing of the commercial launch of the product. Thus, even if we seek to utilize the accelerated approval pathway, we may not be able to obtain accelerated approval and, even if we do, we may not experience a faster development, regulatory review or approval process for that product. In addition, receiving accelerated approval does not assure that the product's accelerated approval will eventually be converted to a traditional approval. Additionally, if we are not able to obtain full approval of any accelerated approval product, including through the completion of post-marketing studies, we or our partners may decide to withdraw marketing of such products. Specifically, in June 2023, Roche voluntarily withdrew the indication of GAVRETO for the treatment of adult and pediatric patients 12 years of age and older with advanced or metastatic RET-mutant MTC. The decision to withdraw the indication was made in consultation with the FDA, in accordance with the requirements of the FDA's Accelerated Approval Program, with the official FDA withdrawal of the indication occurring on July 20, 2023.

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 for the treatment of HCC. In addition, the European Commission, or EC, has granted orphan 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 EU, 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 EU, the European Commission grants orphan medicinal product designation after receiving the opinion of the European Medicines Agency's, 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 medicinal products that are intended for the diagnosis, prevention or treatment of life threatening or chronically debilitating conditions affecting not more than five (5) in ten thousand (10,000) persons in the EU or for products intended for the diagnosis, prevention, or treatment of a life threatening, seriously debilitating or serious and chronic condition when, without incentives, it is unlikely that sales of the product in the EU would generate sufficient return to justify the necessary investment in developing the product. In each case, there must be no satisfactory method of diagnosis, prevention, or treatment authorized for marketing in the EU (or, if such a method exists, the product would be of significant benefit to those affected by the condition). In the EU, 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 EC 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 EU. The EU exclusivity period can be reduced to six years if a drug no longer meets the criteria for orphan medicinal product 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.

On August 3, 2017, Congress passed the FDA Reauthorization Act of 2017, or FDARA. FDARA, among other things, codified the FDA's preexisting regulatory interpretation, to require that a drug Sponsor demonstrate the clinical superiority of an orphan drug that is otherwise the same as a previously approved drug for the same rare disease in order to receive orphan drug exclusivity. The law reverses prior precedent holding that the Orphan Drug Act unambiguously requires that the FDA recognize the orphan exclusivity period regardless of a showing of clinical superiority. Moreover, in the Consolidated Appropriations Act of 2021, Congress did not further change this interpretation when it clarified that the interpretation codified in FDARA would apply in cases where FDA issued an orphan designation before the enactment of FDARA but where product approval came after the enactment of FDARA. The FDA may further reevaluate the Orphan Drug Act and its regulations and policies. We do not know if, when, or how the FDA may change the orphan drug regulations and policies in the future, and it is uncertain how any changes might affect our business. Depending on what changes the FDA may make to its orphan drug regulations and policies, our business could be adversely impacted. 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.

The FDA may further reevaluate the Orphan Drug Act and its regulations and policies. We do not know if, when, or how the FDA may change the orphan drug regulations and policies in the future, and it is uncertain how any changes might affect our business. Depending on what changes the FDA may make to its orphan drug regulations and policies, our business could be adversely impacted.

We may not be successful in our efforts to expand our 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. We may also pursue opportunities to acquire or in-license additional businesses, technologies or drugs, form strategic alliances or create joint ventures with third parties to complement or augment our existing business. For example, in February 2022 we entered into a collaboration with Proteovant to research and advance novel targeted protein degrader therapies leveraging Proteovant's artificial intelligence-enhanced targeted protein degradation platform and our small molecule precision medicine capabilities. However, we may not be able to identify any drug candidates for our pipeline through such acquisitions or in-licenses.

Even if we are successful in continuing to build and expand 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, 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 human capital and financial 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.

At any time and for any reason, we may determine that one or more of our discovery programs or preclinical 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 preclinical 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.

We intend to develop drug candidates in combination with other therapies, which exposes us to additional risks.

We intend to develop, launch and commercialize BLU-945, BLU-525, BLU-222 and potentially other drug candidates in combination with one or more approved or unapproved therapies. Even if any drug candidate we develop were to receive marketing approval for use in combination with other approved therapies, the FDA, the EMA or other regulatory authorities could still revoke approval of the therapy used in combination with our drug candidate. If the therapies used in combination with our drug candidates are replaced as the standard of care for the indications we choose for any of our drug candidates, the FDA, EMA or regulatory authorities may require us to conduct additional clinical trials which may experience complications surrounding trial execution, such as complexities surrounding trial design, establishing trial protocols and interpretability of results, clinical site access and initiation, patient recruitment and enrollment, quality and supply of clinical doses, safety issues or a lack of clinically relevant activity. The uncertainty resulting for the use of our drug candidates in combination with other approved or unapproved therapies may make it difficult to accurately predict side effects in the future clinical trials. The occurrence of any of these risks could result in our own drug candidates, if approved, being removed from the market if they are not also approved as monotherapies or being less successful commercially.

Further, we will not be able to market and sell any drug candidate we develop in combination with an unapproved therapy for a combination indication if that unapproved therapy does not ultimately obtain marketing approval either alone or in combination with our drug candidate. In addition, unapproved therapies face the same risks

described with respect to our drug candidates currently in development and clinical trials, including the potential for serious adverse effects, delay in their clinical trials and lack of FDA approval.

If the FDA, EMA or other regulatory authorities do not approve these other products or revoke their approval of, or if safety, efficacy, quality, manufacturing or supply issues arise with, the agents we choose to evaluate in combination with our drug candidates we may be unable to obtain approval of or market such combination therapy.

Risks Related to Government Legislations and Regulations

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

We have in the past and may in the future seek approval of current or future drug candidates, where applicable, under the FDA's accelerated approval pathway. 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 AYVAKYT, or comparable regulatory authorities in other jurisdictions may be required to undergo one or more confirmatory clinical trials, as a condition of accelerated approval, be required to perform adequate and well-controlled post-marketing clinical trials to confirm the product's clinical benefit. These post-market confirmatory trials must be completed according to timelines agreed upon with the FDA, and if they are not completed in accordance with these timelines than it could result in withdrawal of the indication. For example, the voluntary withdrawal AcceleRET-MTC, a Phase 3 clinical trial required by the FDA to convert the accelerated approval of GAVRETO for MTC to a full approval, is no longer being pursued due to lack of feasibility. 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. In addition, under FDORA the FDA is now permitted to require, as appropriate, that post-marketing trials be underway prior to approval or within a specific time period after the date of approval for a product granted accelerated approval. FDORA also gives the FDA increased authority to withdraw approval of a drug or biologic granted accelerated approval on an expedited basis if the sponsor fails to conduct such studies in a timely manner, send the necessary updates to the FDA, or if such post-approval studies fail to verify the product's predicted clinical benefit. Under FDORA, the FDA is empowered to take action, such as issuing fines, against companies that fail to conduct with due diligence any post-approval confirmatory study or submit timely reports to the agency on their progress.

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 requirements, as well as continued compliance with current Good Manufacturing Practices (cGMPs) and Good Clinical Practices (GCPs) for any clinical trials that we conduct post-approval. In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are subject to periodic unannounced inspections by the FDA and state agencies for compliance with cGMP requirements. For certain commercial prescription drug products, manufacturers and other parties involved in the supply chain must also meet chain of distribution requirements and build electronic, interoperable systems for product tracking and tracing and for notifying the FDA of counterfeit, diverted, stolen and intentionally adulterated products or other products that are otherwise unfit for distribution in the United States. 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. Additionally, under FDORA, sponsors of approved drugs and biologics must provide 6 months' notice to the FDA of any changes in marketing status, such as the withdrawal of a drug, and failure to do so could result in the FDA placing the product on a list of discontinued products, which would revoke the product's ability to be marketed. The FDA closely regulates the post-approval marketing and promotion of pharmaceutical and biological products to ensure such

products are marketed only for the approved indications and in accordance with the provisions of the approved labeling. 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.

Regulatory agencies may also impose requirements for costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of a product. The FDA and other agencies, including the Department of Justice (DOJ), closely regulate and monitor the post-approval marketing and promotion of products to ensure that they are manufactured, marketed and distributed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA imposes stringent restrictions on manufacturers' communications regarding off-label use, and if we, or any future collaborators, do not market any of our products for which we, or they, receive marketing approval for only their approved indications, we, or they, may be subject to warnings or enforcement action for off-label marketing, government investigations, or litigation. Violation of the Federal Food, Drug, and Cosmetic Act and other statutes, including the False Claims Act, relating to the promotion and advertising of prescription drugs may lead to investigations or allegations of violations of federal and state healthcare fraud and abuse laws and state consumer protection laws and could expose our company to substantial civil or criminal penalties.

Even though we may have obtained approvals for certain of our products, 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. See section entitled "*Business – Coverage and Reimbursement*" included in our Annual Report on Form 10-K for the year ended December 31, 2022.

Our ability to commercialize any drugs and drug candidates successfully also will depend in part on the extent to which coverage and reimbursement for these drugs and 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 additional 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 (CMS), an agency within the U.S. Department of Health and Human Services (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 other 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.

The United States has enacted or proposed legislative and regulatory changes affecting the healthcare system that could prevent or delay marketing approval of our current drug candidates or any future drug candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any product for which we obtain marketing approval. Changes in regulations, statutes or the interpretation of existing regulations could impact our business in the future by requiring, for example: (i) changes to our manufacturing arrangements; (ii) additions or modifications to product labeling; (iii) the recall or discontinuation of our products; or (iv) additional record-keeping requirements. If any such changes were to be imposed, they could adversely affect the operation of our business.

In the United States, there have been and continue to be a number of legislative initiatives to contain healthcare costs. For example, in March 2010, the ACA was passed, which substantially changes the way healthcare is financed by

both governmental and private insurers, and significantly impacts the U.S. pharmaceutical industry. In August 2022, the Inflation Reduction Act of 2022, or IRA, was signed into law. The IRA includes several provisions that will impact our business to varying degrees, including provisions that reduce the out-of-pocket spending cap for Medicare Part D beneficiaries from $7,050 to $2,000 starting in 2025, thereby effectively eliminating the coverage gap, impose new manufacturer financial liability on all drugs in Medicare Part D, allow the U.S. government to negotiate Medicare Part B and Part D pricing for certain high-cost drugs and biologics without generic or biosimilar competition, require companies to pay rebates to Medicare for drug prices that increase faster than inflation, and delay the rebate rule that would require pass through of pharmacy benefit manager rebates to beneficiaries. Further, under the IRA, orphan drugs are exempted from the Medicare drug price negotiation program, but only if they have one orphan designation and for which the only approved indication is for that disease or condition. If a product receives multiple rare disease designations or has multiple approved indications, it may not qualify for the orphan drug exemption. The implementation of the IRA is currently subject to ongoing litigation challenging the constitutionality of the IRA's Medicare drug price negotiation program. The effect of IRA on our business and the healthcare industry in general is not yet known.

At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological 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, designed to encourage importation from other countries and bulk purchasing.

We may face competition in the U.S. for our development candidates and investigational medicines, if approved, from therapies sourced from foreign countries that have placed price controls on pharmaceutical products. 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. For example, President Biden has issued multiple executive orders that have sought to reduce prescription drug costs. In February 2023, HHS also issued a proposal, in response to an October 2022 executive order from President Biden, that includes a proposed prescription drug pricing model that will test whether targeted Medicare payment adjustments will sufficiently incentivize manufacturers to complete confirmatory trials for drugs approved through FDA's accelerated approval pathway. Although a number of these and other proposed measures may require authorization through additional legislation to become effective, and the Biden administration may reverse or otherwise change these measures, both the Biden administration and Congress have indicated that they will continue to seek new legislative measures to control drug costs. The Creating and Restoring Equal Access to Equivalent Samples Act (the CREATES Act) was enacted in 2019 requiring sponsors of approved new drug applications and biologics license applications to provide sufficient quantities of product samples on commercially reasonable, market-based terms to entities developing generic drugs and biosimilar biological products. The law establishes a private right of action allowing developers to sue application holders that refuse to sell them product samples needed to support their applications. If we are required to provide product samples or allocate additional resources to respond to such requests or any legal challenges under this law, our business could be adversely impacted.

Other legislative measures have also been enacted that may impose additional pricing and product development pressures on our business, and 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 health care industry may be enacted in the future or what effect recently enacted federal legislation or any such additional legislation or regulation would have on our business. The pendency or approval of such proposals or reforms could result in a decrease in our stock price or limit our ability to raise capital or to enter into collaboration agreements for the further development and commercialization of our approved drugs and drug candidates.

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.

Our arrangements with third-party payors and customers expose us to broadly applicable fraud and abuse and other healthcare laws and regulations, including but not limited to, the federal healthcare Anti-Kickback Statute, the False Claims Act, the federal Health Insurance Portability and Accountability Act of 1996 (HIPAA) the Physician Payment Sunshine Act, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 (HITECH), the federal false statements statute, federal consumer protection and unfair competition laws and similar state and foreign laws and regulations that may regulate the business or financial arrangements and relationships through which we market, sell and distribute our drugs. The number and complexity of federal, state, and foreign laws continue to increase, and additional governmental resources are being used to enforce these laws and to prosecute companies and individuals who are believed to be violating them. See section entitled "*Business – Other Healthcare Laws*" included in our Annual Report on Form 10-K for the year ended December 31, 2022.

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 current or future 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. 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 EU, 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.

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 Financial Position and Need for Additional Capital

We are a precision therapy company in the process of growing our operations. We have incurred significant operating losses since our inception and anticipate that we will incur continued losses for the foreseeable future.

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 preclinical 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 preclinical studies and clinical trials for our drug candidates and commercial sale of our approved drugs.

To date, we have financed our operations primarily through public offerings of our common stock, private placements of our convertible preferred and common stock, collaboration and license agreements, future royalty and revenue monetization, and a term loan. Through September 30, 2023, we have received an aggregate of $3.7 billion from such transactions, including $1.9 billion in aggregate gross proceeds from the sale of common stock in our initial public offering, follow on public offerings, through our “at the market” stock offering program and the equity investment by Roche, $115.1 million in gross proceeds from the issuance of convertible preferred stock, $175.0 million in gross proceeds from our Royalty Purchase Agreement with Royalty Pharma, $250.0 million in gross proceeds from our Future Revenue Purchase Agreement with Sixth Street Partners, $1.0 billion in upfront payments and milestone payments under our collaborations with Roche, CStone and Zai Lab, our license agreement with Clementia and our former collaboration with Alexion Pharma Holding, or Alexion and $250.0 million in gross proceeds from a term loan from Sixth Street Partners. In addition, since January 2020, we also have generated revenue through sales of our drug products.

Since inception, we have incurred significant operating losses. Our net loss was $396.1 million for the nine months ended September 30, 2023. Our net losses were $557.5 million and $644.1 million for the years ended December 31, 2022 and 2021, respectively. As of September 30, 2023, we had an accumulated deficit of $2,229.0 million.

Substantially all of our operating losses have resulted from costs incurred in connection with our research and development programs and from selling, 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 may 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 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 drugs or any drug candidates for which we may receive marketing approval. 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.

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, including for avapritinib in additional geographies, particularly for indolent SM in geographies outside of the U.S.;
- continue to maintain and expand commercial manufacturing capabilities or make arrangements with third-party manufacturers to ensure clinical supply and commercial manufacturing;
- maintain and, if necessary, expand a sales, marketing and distribution infrastructure to commercialize AYVAKIT/AYVAKYT and any current or future drug candidates for which we obtain marketing approval;

- achieve market acceptance in the medical community and with third-party payors for AYVAKIT/AYVAKYT, GAVRETO and any current or future drug candidates for which we receive marketing approval; and

- compete with companies that may have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved drugs.

We expect to incur significant sales and marketing costs as we commercialize AYVAKIT/AYVAKYT, 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 material net cash inflows from our operations, we will not become profitable and may be unable to continue operations without continued funding.

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 and commercialization of pharmaceuticals is capital intensive. We are currently advancing multiple drug candidates and development programs through clinical and preclinical development. Our expenses may 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 in additional geographies, particularly for indolent SM in geographies outside of the U.S. In addition, we expect to incur additional significant commercialization expenses for AYVAKIT/AYVAKYT 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.

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

- the success of our commercialization efforts and market acceptance for AYVAKIT/AYVAKYT 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 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 preclinical studies, clinical trials, our compassionate use program and for use as commercial supply, as applicable;

- the cost of purchasing quantities of agents for use in our clinical trials in connection with our efforts to develop our drugs and drug candidates, including for development as combination therapies;

- the scope, progress, results and costs of drug discovery, preclinical 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 in additional geographies, particularly for indolent SM in geographies outside of the U.S.;

- the success of our collaborations with CStone and Zai Lab and our license agreements with Clementia and IDRx, 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, our financing agreements, or any collaboration, partnership, financing 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 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.

Accordingly, we may seek additional funding in connection with our continuing operations or business objectives. Any additional fundraising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize any of our approved drugs or drug candidates. 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. 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 or on attractive terms, 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 as we can generate material net cash inflows from our operations, we expect to finance our cash needs primarily through a combination of public and private equity offerings, debt financings, collaborations, strategic alliances, licensing arrangements and future revenue monetizations. We do not have any committed external source of funds, other than our collaborations with CStone and Zai Lab and the license agreements with Clementia and IDRx, the Royalty Purchase Agreement with Royalty Pharma, and the Financing Agreement with Sixth Street Partners, 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 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.

If we raise funds through additional collaborations, strategic alliances, licensing arrangements or future revenue monetizations 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. Further, due to the uncertainty of pharmaceutical development, the high historical failure rates generally associated with drug development and uncertainty of successful commercialization, we may not receive any regulatory, development, sales-based milestones or royalty payments under any such collaborations, strategic alliances, licensing arrangements or future revenue monetizations.

In June 2022, we entered into a Royalty Purchase Agreement with Royalty Pharma, pursuant to which, we sold our right to receive all of the royalties payable to the Company with respect to net sales by Roche, in all countries besides China, Hong Kong, Macau, Taiwan (collectively, Greater China) and the U.S., of GAVRETO under the collaboration agreement, dated July 13, 2020, by and between the Company and Roche, as amended, which we refer to as the Roche pralsetinib collaboration agreement. As consideration for the arrangement, we received $175.0 million upfront in cash and may receive up to $165.0 million in contingent milestone payments. However, in February 2023, Roche provided written notice of its election to terminate the Roche pralsetinib collaboration agreement for convenience. Following the termination of the Roche pralsetinib collaboration agreement, if the specified net sales milestone thresholds under the Royalty Purchase Agreement with Royalty Pharma are not otherwise met, we may no longer be eligible to receive any of the contingent milestone payments under the Royalty Purchase Agreement.

In June 2022, we entered into a Future Revenue Purchase Agreement with Sixth Street Partners, the other purchasers from time to time party thereto, and Sixth Street Partners as representative for the purchasers, pursuant to which, we sold our right to receive future royalty payments at a rate of 9.75% on up to $900 million each year of (i) aggregate worldwide annual net product sales of AYVAKIT/AYVAKYT (avapritinib) and (ii) if it is approved, aggregate worldwide annual net product sales of elenestinib, but excluding sales in Greater China, subject to a cumulative cap of 1.45 times the upfront invested capital or a total of $362.5 million. In the event that certain revenue targets are not achieved by specified dates, the royalty rate and cumulative cap shall be increased to 15% and 1.85 times the invested capital (or $462.5 million), respectively. As consideration for the arrangement, we received $250.0 million in cash in July 2022 upon the transactions closing.

Our level of indebtedness and the terms of the Financing Agreement with Sixth Street Partners could adversely affect our operations and limit our ability to plan for or respond to changes in our business. If we are unable to comply with restrictions in the Financing Agreement, the repayment of our existing indebtedness could be accelerated.

Under the Financing Agreement with Sixth Street Partners we have incurred a substantial amount of debt, which could adversely affect our business. In July 2022, we drew down the senior secured term loan of $150.0 million. The facility also includes a senior secured delayed draw term loan of up to $250.0 million to be funded in two tranches: (i) a tranche A delayed draw loan in an aggregate principal amount of $100.0 million and (ii) a tranche B delayed draw term loan in an aggregate principal amount of up to $150.0 million. We may also at any time request an incremental term loan in an amount not to exceed $260.0 million on terms to be agreed and subject to the consent of the lenders providing such incremental term loan. In August 2023, we received the first tranche of the senior secured delayed draw term loan facility in the amount of $100.0 million in gross proceeds.

Our level of indebtedness could affect our business in the following ways, among other things: make it more difficult for us to satisfy our contractual and commercial commitments; require us to use a substantial portion of our cash flow from operations to pay interest and principal, which would reduce funds available for working capital, capital expenditures and other general corporate purposes; limit our ability to obtain additional financing for working capital, capital expenditures, acquisitions and other investments or general corporate purposes; heighten our vulnerability to downturns in our business, our industry or in the general economy; place us at a disadvantage compared to those of our competitors that may have proportionately less debt; limit management’s discretion in operating our business; and limit our flexibility in planning for, or reacting to, changes in our business, the industry in which we operate or the general economy.

The Financing Agreement requires us to make certain payments of principal and interest over time and contains several other restrictive covenants. Among other requirements of the Financing Agreement, we and our subsidiaries party to the Financing Agreement must maintain a minimum consolidated liquidity of $80.0 million. These and other terms in the Financing Agreement could restrict our ability to grow our business or enter into transactions that we believe would be beneficial to our business.

Our business may not generate cash flows from operations in the future that are sufficient to service our debt and support our growth strategies. If we are unable to generate such cash flows, we may be required to adopt one or more alternatives, such as obtaining additional equity capital on terms that may be onerous or highly dilutive, selling assets, or restructuring debt. Our ability to refinance our indebtedness will depend on the capital markets and our financial condition at such time. We may not be able to engage in any of these activities or engage in these activities on desirable terms, which could result in a default on our debt obligations.

Risks Related to Our Dependence on Third Parties

We have entered into collaborations and licenses with our partners for the development and commercialization of several of our drugs and drug candidates. If our collaborations are not successful, we may not be able to capitalize on the market potential of these drugs and drug candidates.

We have entered into collaborations and licenses with CStone, Zai Lab, Proteovant, Clementia and IDRx for the development and commercialization of several of our drugs and drug candidates, and may enter into additional collaborations and licenses with other third parties in the future. 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. In some situations, we may not be able to influence our collaboration partners' decisions regarding the development and collaboration of our partnered drugs and drug candidates, and as a result, our collaboration partners may not pursue or prioritize the development and commercialization of those partnered drugs and drug candidates in a manner that is in our best interest. 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 or result in litigation or arbitration, which would be time-consuming and expensive. 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. Any termination or expiration of our collaboration or license agreements with CStone, Zai Lab, Proteovant, Clementia or IDRx, or of any future collaboration or license agreement, could adversely affect us financially or harm our business reputation. For example, in February 2023, Roche provided written notice of its election to terminate for convenience our collaboration agreement for the development and commercialization of GAVRETO worldwide, excluding the CStone Territory. While we will regain rights to the development and commercialization of GAVRETO following the effective date of such termination, there can be no assurance that we will be able to successfully enter into a new arrangement with a third party to collaborate on the development and commercialization or GAVRETO, or that we will be able to successfully commercialize GAVRETO through our own organization. Further, following the termination of such collaboration agreement, if the specified net sales milestone thresholds under the Royalty Purchase Agreement with Royalty Pharma are not otherwise met, we may no longer be eligible to receive any of the contingent milestone payments under the Royalty Purchase Agreement.

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

We do not have the ability to independently conduct clinical trials. We rely on medical institutions, clinical investigators, CROs, contract laboratories and other third parties to conduct or otherwise support clinical trials for our 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 and sponsor the clinical trials for our approved drugs and drug candidates, CROs will conduct all of our 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. 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 approved drugs and drug candidates, including for preclinical, clinical and commercial supply. This reliance on third parties increases the risk that we will not have sufficient quantities of our approved 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, primarily on third parties for the manufacture of our drug candidates for preclinical 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 manufacturing organizations (CMOs) 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 CMOs for compliance with cGMPs in connection with the manufacture of our drugs and drug candidates. Manufacturers and manufacturers' facilities are required to comply with extensive FDA, and comparable foreign regulatory authority requirements, including ensuring that quality control and manufacturing procedures conform to cGMP regulations and applicable product tracking and tracing requirements. If our CMOs 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 CMOs 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 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, and could require comparability studies for the setup of manufacturing operations at alternative facilities. If any CMO with whom we contract fails to perform its obligations, we may be forced to manufacture the materials ourselves, for which we may not have the capabilities or resources, or enter into an agreement with a different CMO, which we may not be able to do on reasonable terms, if at all. In either scenario, our clinical trials supply or commercial distribution could be delayed significantly as we establish alternative supply sources. In some cases, the technical skills required to manufacture our products or drug candidates may be unique or proprietary to the original CMO and we may have difficulty, or there may be contractual restrictions prohibiting us from, transferring such skills to a back-up or alternate supplier, or we may be unable to transfer such skills at all. In addition, if we are required to change CMOs for any reason, we will be required to verify that the new CMO maintains facilities and procedures that comply with quality standards and with all applicable regulations. We will also need to verify, such as through a manufacturing comparability study, that any new manufacturing process will produce our drug candidate according to the specifications previously submitted to or approved by the FDA or another regulatory authority. The delays associated with the verification of a new CMO could negatively affect our ability to develop drug candidates or commercialize our products in a timely manner or within budget. Furthermore, a CMO may possess technology related to the manufacture of our drug candidate that such CMO owns independently. This would increase our reliance on such CMO or require us to obtain a license from such CMO in order to have another CMO manufacture our drug products or drug candidates. In addition, in the case of the CMOs that supply our drug candidates, changes in manufacturers often involve changes in manufacturing procedures and processes, which could require that we conduct bridging studies between our prior clinical supply used in our clinical trials and that of any new manufacturer. We may be unsuccessful in demonstrating the comparability of clinical supplies which could require the conduct of additional clinical trials. 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.

We do not have long-term supply agreements with all of our CMOs, and may purchase our required drug supply, including the API, drug product and drug substance used in our drugs and drug candidates, on a purchase order basis with certain CMOs. 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 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. In March 2020, the U.S. enacted the CARES Act in response to the U.S. COVID-19 pandemic. Throughout the COVID-19 pandemic, there was public concern over the availability and accessibility of critical medical products, and the CARES Act enhanced 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. If we experience shortages in the supply of our marketed products, our results could be materially impacted.

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 CMOs 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 our drug and drug candidates are supplied to us primarily 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, if any of our suppliers ceases its operations for any reason or is unable or unwilling to supply API, drug product or drug substance in sufficient quantities or on the timelines necessary to meet our needs, it could significantly and adversely affect our business, the supply of our drug candidates or approved drugs and our financial condition.

For all of our drug candidates, we may from time to time explore opportunities 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 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 our approved drugs and clinical-stage drug candidates through 2023.

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, 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 and our core technologies, including our novel target discovery engine, our proprietary compound library, targeted protein degrader platform 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, as well as the use of these compounds in the treatment of diseases, formulations, solid forms, and manufacturing processes and other 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.

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 our drugs and drug candidates. 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 and licensed patent portfolio may not provide us with adequate and continuing patent protection sufficient to exclude others from commercializing drugs similar or identical to our 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 a patent owned by third parties that has generic method of treatment claims that may cover pralsetinib. If the claims of this third-party patent are asserted against us, we do not believe pralsetinib or our proposed activities related to such compound would be found to infringe any valid claim of this patent. 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, there may be circumstances, when 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, and if our patents are successfully challenged, we may face generic competition prior to the expiration dates of our U.S. Orange Book listed 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 small molecule therapeutics. Some of these patent applications have already been allowed or issued, and others may issue in the future. For example, we are aware of a patent owned by a third party that has generic method of treatment claims that may cover pralsetinib. If the claims of this third-party patent are asserted against us, we do not believe pralsetinib or our proposed activities related to such compound would be found to infringe any valid claim of this patent. 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, including against ANDA filers, we may be required to resort to litigation, that includes 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.

If we are not able to obtain, or in applicable cases maintain, patent term extension or non-patent exclusivity in the United States under the Hatch-Waxman Act and in foreign countries under similar legislation, thereby potentially

extending the marketing exclusivity term of our products or product candidates, our business may be materially harmed.

Depending upon the timing, duration and specifics of FDA marketing approval of our products or product candidates, one of the U.S. patents covering each of such products or product candidates or the use thereof may be eligible for up to five years of patent term extension under the Hatch-Waxman Act. The Hatch-Waxman Act allows a maximum of one patent to be extended per FDA approved product as compensation for the patent term lost during the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval and only those claims covering such approved drug product, a method for using it or a method for manufacturing it may be extended. Patent term extension also may be available in certain foreign countries upon regulatory approval of our product candidates. Nevertheless, we may not be granted patent term extension either in the United States or in any foreign country because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. Moreover, the term of extension, as well as the scope of patent protection during any such extension, afforded by the governmental authority could be less than we request.

If we are unable to obtain patent term extension, or the term of any such extension is less than we request, the period during which we will have the right to exclusively market our product may be shortened and our competitors may obtain approval of competing products following our patent expiration sooner, and our revenue could be reduced, possibly materially.

It is possible that we will not obtain patent term extension under the Hatch-Waxman Act for a U.S. patent covering a product candidate even where that patent is eligible for patent term extension, or if we obtain such an extension, it may be for a shorter period than we had sought. Further, for certain of our licensed patents, we do not have the right to control prosecution, including filing with the USPTO, an application for patent term extension under the Hatch-Waxman Act. Thus, if one of our licensed patents is eligible for patent term extension under the Hatch-Waxman Act, we may not be able to control whether an application to obtain a patent term extension is filed, or an extension obtained, from the USPTO.

Also, there are detailed rules and requirements regarding the patents that may be submitted to the FDA for listing in the Approved Drug Products with Therapeutic Equivalence Evaluations, or the Orange Book. We may be unable to obtain patents covering our product candidates that contain one or more claims that satisfy the requirements for listing in the Orange Book. Even if we submit a patent for listing in the Orange Book, the FDA may decline to list the patent, or a manufacturer of generic drugs may challenge the listing. If a patent covering one of our approved products is not listed in the Orange Book, a manufacturer of generic drugs would not have to provide advance notice to us of any abbreviated new drug application, or ANDA, filed with the FDA to obtain permission to sell a generic version of such product.

Depending upon the timing and specifics of marketing approval of our products, the FDA and other applicable regulatory authorities may grant certain non-patent exclusivities. However, we may be unable to secure or maintain additional non-patent exclusivity for our products or maintain any non-patent exclusivity. Similarly, although we intend to seek new chemical entity exclusivity, and potentially other exclusivities, for product candidates we are developing, we may not be successful in doing so. Moreover, these non-patent exclusivities, if granted, are limited and other companies may be able to submit marketing applications and receive approval earlier than we anticipate.

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, drug candidates 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 drugs, drug candidates and 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.

We depend on intellectual property licensed from third parties and termination of any of these licenses could result in the loss of significant rights, which would harm our business.

Under our current license agreements, we may not have the final or sole decision on whether we are able to opt out certain of our in-licensed European patents and patent applications from the recently created Unified Patent Court (UPC) for the European Union, that was ratified on June 1, 2023. Our licensors may decide to not opt out the of the UPC, which would subject our in-licensed European patents and patent applications to the jurisdiction of the UPC. Furthermore, even if our licensors decide to opt out of the UPC, we cannot guarantee that our licensors will comply with the legal formalities and requirements for properly opting out of the UPC. Thus, we cannot be certain that our in-licensed European patents and patent applications will not fall under the jurisdiction of the UPC. Under the UPC, a single European patent would be valid and enforceable in numerous European countries. A challenge to the validity of a European patent under the UPC, if successful, could result in a loss of patent protection in numerous European countries which could have a material adverse impact on our business and our ability to commercialize or license our technology and product candidates.

Issued patents covering our product candidates could be found invalid or unenforceable if challenged in court or the USPTO.

Our European patents and patent applications could be challenged in the recently created UPC for the European Union, that was ratified on June 1, 2023. We may decide to opt out our European patents and patent applications from the UPC. However, if certain formalities and requirements are not met, our European patents and patent applications could be challenged for non-compliance and brought under the jurisdiction of the UPC. We cannot be certain that our European patents and patent applications will avoid falling under the jurisdiction of the UPC, if we decide to opt out of the UPC. Under the UPC, a granted European patent would be valid and enforceable in numerous European countries. Although such patent rights would apply to numerous European countries, a successful challenge to a European patent under the UPC could result in loss of patent protection in numerous European countries. Accordingly, a single proceeding under the UPC addressing the validity and infringement of the European patent could result in loss of patent

protection in numerous European countries rather than in each validated country separately as such patents always have been adjudicated. Such a loss of patent protection could have a material adverse impact on our business and our ability to commercialize or license our technology and product candidates.

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 the 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 and targeted degrader platform, 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, drugs, and drug candidates 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 drugs or 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 Our Business, including Employee Matters, Managing Growth and Others

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, commercial, business development, financial and legal expertise of our executive officers, 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 (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, 2023, we had 661 full-time and part-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 or political 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 caused extreme volatility and disruptions in the capital and credit markets. In addition, geopolitical developments, such as the Israeli-Palestinian conflict, Russian invasion of Ukraine or deterioration in the bilateral relationship between the U.S. and China could contribute to disruption, instability and volatility in the global markets, as well as an increased inflation, which in turn could adversely impact our operations and those of third parties upon which we rely. Geopolitical conflicts could also have an adverse impact on third parties located in the involved jurisdictions, which could in turn have an adverse impact on our business. For example, certain of our distributors are located in Israel, and may be adversely impacted by the Israeli-Palestinian conflict. Related sanctions, export controls or other actions that may be initiated by nations including the U.S., the EU, Israel or Russia (e.g., potential cyberattacks, disruption of energy flows) could adversely affect our business, our supply chain, CROs, CMOs, clinical trial sites, collaborative partners, distributors or other third parties with which we conduct business. There can be no assurance that further deterioration in credit and financial markets and confidence in economic conditions will not occur. 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.

Political developments can also lead to uncertainty around regulations and rules that may materially affect our business. For example, as the UK regulatory system is now independent from the EU, a long-term effect of Brexit could be that the UK significantly alters its regulations affecting the clearance or approval of our drug or drug candidates that are developed in the UK. 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 UK, as compared to the EU and elsewhere.

Rising inflation rates could negatively impact our revenues and profitability if increases in the prices of our products or a decrease in spending on products in the biopharmaceutical industry in general results in lower sales by us or those who we collaborate with. In addition, if our costs increase and we are not able to correspondingly adjust our commercial relationships to account for this increase, our net income would be adversely affected, and the adverse impact may be material.

Inflation rates, particularly in the U.S., have increased recently to levels not seen in years. Increased inflation may result in decreased demand for our products, increased operating costs (including our labor costs), reduced liquidity, and limitations on our ability to access credit or otherwise raise debt and equity capital. In addition, the United States Federal Reserve has raised, and may again raise, interest rates in response to concerns about inflation. Increases in

interest rates, especially if coupled with reduced government spending and volatility in financial markets, may have the effect of further increasing economic uncertainty and heightening these risks. In an inflationary environment, we may be unable to raise the sales prices of our products at or above the rate at which our costs increase, which could reduce our profit margins and have a material adverse effect on our financial results and net income. We also may experience lower than expected sales and potential adverse impacts on our competitive position if there is a decrease in spending on products in the biopharmaceutical industry in general or a negative reaction to our pricing or the pricing of those we do, or will collaborate with. A reduction in our revenue would be detrimental to our profitability and financial condition and could also have an adverse impact on our future growth.

Foreign currency exchange rates fluctuations could have an adverse impact on our operating results.

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. If the U.S. dollar weakens against a specific foreign currency, our revenues will increase, having a positive impact on net income, but our overall expenses will increase, having a negative impact. Conversely, if the U.S. dollar strengthens against a specific foreign currency, our revenues will decrease, having a negative impact on net income, but our overall expenses will decrease, having a positive impact. Continued fluctuations in foreign exchange rates can impact our operating results 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 CMOs, 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. Cyber-attacks also could include phishing attempts or e-mail fraud to cause payments or information to be transmitted to an unintended recipient and could include the use of artificial intelligence, or AI, and machine learning to launch more automated, targeted and coordinated attacks on targets. 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.

Similarly, the increasing use of AI, and machine learning technology in the biopharmaceutical industry presents new risks and challenges. The use of AI based software may lead to the inadvertent release of confidential or proprietary information, which may adversely impact our ability to realize the benefit of our intellectual property, cause us to incur liabilities as the result of any breaches of confidentiality or impact our ability to comply with data security and privacy laws. Further, as the regulatory framework for these technologies evolves, it is possible that new laws and regulations will be adopted, or that existing laws and regulations may be interpreted in ways that would affect our business, including as a result of the cost to comply with such laws or regulations.

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. Notably, for example, 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 Economic Area, or EEA, as well as any company outside the EEA that collects or otherwise processes personal data in connection with the offering goods or services to individuals in the EEA 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, ensuring we have a valid legal basis to process personal data, maintaining records of our processing activities and to document data protection impact assessments where there is high risk processing, limitations on retention of information, mandatory data breach notification requirements, ensuring appropriate technical and organizational measures to be put in place to safeguard personal data 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. Further to the UK's exit from the European Union on January 31, 2020, the GDPR ceased to apply in the UK at the end of the transition period on December 31, 2020. However, as of January 1, 2021, the UK's European Union (Withdrawal) Act 2018 incorporated the GDPR (as it existed on December 31, 2020 but subject to certain UK specific amendments) into UK law (referred to as the UK GDPR). The UK GDPR and the UK Data Protection Act 2018 set out the UK's data protection regime, which is independent from but aligned to the EU's data protection regime. Non-compliance with the UK GDPR may result in monetary penalties of up to £17.5 million or 4% of worldwide revenue, whichever is higher. In this document, "GDPR" refers to both the EU and the UK GDPR, unless specified otherwise. 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 EEA.

EEA Member States have adopted national laws to implement the GDPR which may partially deviate from the GDPR. Further, competent authorities in the EEA Member States may interpret GDPR obligations slightly differently from country to country. For these reasons, we do not expect to operate in a uniform legal landscape in the EEA. In addition, the UK has announced plans to reform the country's data protection legal framework in its Data Reform Bill, but these plans have been put on hold.

Further, European data protection laws also regulates the transfer of personal data from the EEA and Switzerland to third countries that are not considered to provide adequate protections are provided for personal data. With regard to transfers of personal data from the EEA, transfers to third countries that have not been approved as "adequate" are prohibited unless an appropriate safeguard specified by the GDPR is implemented, such as the Standard Contractual Clauses, or SCCs, approved by the European Commission, or EC, or binding corporate rules, or a derogation applies. In the past, companies in the U.S. were able to rely upon the Privacy Shield framework to legitimize data transfers from the EEA to the U.S. In July 2020, the Court of Justice of the European Union, or CJEU, in Case C-311/18 (Data Protection Commissioner v Facebook Ireland and Maximillian Schrems, or Schrems II) invalidated the EU-U.S. Privacy Shield on the grounds that the Privacy Shield failed to offer adequate protections to EU personal data transferred to the U.S. The CJEU, in the same decision, deemed that the Standard Contractual Clauses, or SCCs, published by the EC are valid. However, the CJEU ruled that transfers made pursuant to the SCCs need to be assessed on a case-by-case basis to ensure the law in the recipient country provides "essentially equivalent" protections to safeguard the transferred personal data as the EEA, and required businesses to adopt supplementary measures if such standard is not met.

On June 4, 2021, the European Commission issued new SCCs that account for the CJEU's decision and other developments, which need to be put in place for new contracts involving the transfer of personal data from the EEA to a third country since September 27, 2021, and incorporated into existing contracts since December 27, 2022. The New SCCs do not apply to the UK, but the UK Information Commissioner's Office has published its own transfer mechanism, the International Data Transfer Agreement, or UK IDTA, which entered into force on 21 March 2022, and enables data transfers originating from the UK. It requires a similar assessment of the data protection provided in the importer's country. The UK IDTA needs to be concluded in new contracts involving the transfer of personal data from the UK as of 22 September 2022. Organizations have until 21 March 2024 to update existing agreements. On July 10, 2023, the EU adopted an adequacy decision for a new "Data Privacy Framework," which replaces the invalidated Privacy Shield, for personal data transferred from the EU to the U.S. On July 17, 2023 the U.S. Department of Commerce released registration means and requirements for U.S. companies to register. The Framework provides additional certification mechanisms to provide for UK and Swiss data transfers. We will be required to implement these new safeguards when conducting restricted cross-border data transfers and doing so will require significant effort and cost. These and other future developments regarding the flow of data across borders could increase the cost and complexity of delivering our services in some markets and may lead to governmental enforcement actions, litigation, fines, and penalties or adverse publicity, which could adversely affect our business and financial position.

Although the UK is regarded as a third country under the EU's GDPR, the EC has issued a decision recognizing the UK as providing adequate protection under the EU GDPR and, therefore, transfers of personal data originating in the EEA to the UK remain unrestricted. Like the EU GDPR, the UK GDPR restricts personal data transfers outside the UK to countries not regarded by the UK as providing adequate protection. The UK government has confirmed that personal data transfers from the UK to the EEA remain free flowing.

While we have taken steps to mitigate the impact on us with respect to transfers of data, such as implementing the SCCs in new contracts with our service providers, customers, subsidiaries, and are updating existing contracts with the new SCCs in anticipation of the December 2022 deadline, the validity of these transfer mechanisms remains uncertain. Complying with this guidance as it exists today and evolves will be expensive and time consuming and may ultimately prevent us from transferring personal data outside the EEA, which would cause significant business disruption for ourselves and our customers and potentially require the changes in the way our products are configured, hosted and supported.

In addition, we are subject to Swiss data protection laws, including the Federal Act on Data Protection, or FADP. While the FADP provides broad protections to personal data, on September 25, 2020, the Swiss federal Parliament enacted a revised version of the FADP, which is anticipated to become effective in September 2023. The new version of the FADP aligns Swiss data protection law with the GDPR.

Further, in addition to existing European data protection law, the European Union also is considering another draft data protection regulation. The proposed regulation, known as the Regulation on Privacy and Electronic Communications (ePrivacy Regulation), would replace the current ePrivacy Directive. The Draft Regulation is still the subject of negotiations between the Council of the European Union and the European Parliament. It is unclear when the Draft Regulation will enter into force. New rules related to the ePrivacy Regulation are likely to include enhanced consent requirements in order to use communications content and communications metadata, as well as obligations and restrictions on the processing of data from an end-user's terminal equipment, which may negatively impact our product offerings and our relationships with our customers.

Preparing for and complying with the evolving application of the GDPR, national laws in Switzerland and the UK, as well as ePrivacy Regulation (if and when it becomes effective) has required and will continue to require us to incur substantial operational costs and may require us to change our business practices. Despite our efforts to bring practices into compliance with the GDPR, appliable national data protection laws and before the effective date of the ePrivacy Regulation, we may not be successful either due to internal or external factors such as resource allocation limitations. Non-compliance could result in proceedings, fines or penalties against us by governmental entities, customers, data subjects, consumer associations or others.

In addition to European data protection requirements, 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.

Additionally, a new California ballot initiative, the California Privacy Rights Act (CPRA) was passed in November 2020 and became effective on January 1, 2023. The CPRA imposes additional obligations on companies covered by the legislation and will significantly modify the CCPA, including by expanding consumers' rights with respect to certain sensitive personal information. The CPRA also creates a new state agency that will be vested with authority to implement and enforce the CCPA and the CPRA. The effects of the CCPA and the CPRA are potentially significant and may require us to modify our data collection or processing practices and policies and to incur substantial costs and expenses in an effort to comply and increase our potential exposure to regulatory enforcement and/or litigation.

Also, on March 2, 2021, Virginia enacted the Consumer Data Protection Act, or CDPA. The CDPA became effective on January 1, 2023. The CDPA regulates how businesses, which the CDPA refers to as "controllers", collect

and share personal information. The law applies to companies that conduct business in Virginia or product products or services that are targeted to residents of Virginia and either: (1) annually control or process personal data of at least 100,000 Virginia residents; or (2) control or process the personal data of at least 25,000 Virginia residents and derive over 50% of gross revenue from the sale of personal data. While the CDPA incorporates many similar concepts of the CCPA and CPRA, there are also several key differences in the scope, application, and enforcement of the law that will change the operational practices of controllers. The CDPA regulates impact how controllers collect and process personal sensitive data, conduct data protection assessments, transfer personal data to affiliates, and respond to consumer rights requests. In addition, on July 8, 2021, Colorado's governor signed the Colorado Privacy Act, or CPA, into law. The CPA is rather similar to the Virginia's CPDA but also contains additional requirements. The new measure applies to companies conducting business in Colorado or who produce or deliver commercial products or services intentionally targeted to its residents of the state and that either: (1) control or process the personal data of at least 100,000 Colorado residents during a calendar year; or (2) derive revenue or receive a discount on the price of goods or services from the sale of personal data and process or control the personal data of at least 25,000 Colorado residents.

Moreover, on March 24, 2022, Utah's governor signed the Utah Consumer Privacy Act, or UCPA, into law. The UCPA will take effect on December 31, 2023. Also, in 2022, Connecticut Governor Lamont signed the Connecticut Data Privacy Act, or CTDPA, into laws. The UCPA and CTDPA draw heavily upon their predecessors in Virginia and Colorado. With Oregon's governor signing of the Oregon Consumer Privacy Act on July 18, 2023, there are eleven states with signed comprehensive privacy laws that are either effective or will be effective in the next three years. Furthermore, on April 27, 2023 Washington state signed the My Health My Data Act (MHMDA) a consumer health privacy law aimed at expanding protections to health data historically not covered by existing laws. The MHMDA requires sweeping changes to how impacted organizations obtain consent and authorization to collect and share consumer health information. New privacy and data security laws have been proposed in more than half of the states in the U.S. and in the U.S. Congress. With bills proposed in many other jurisdictions, it remains quite possible that other states will follow suit. Such proposed legislation, if enacted, may add additional complexity, variation in requirements, restrictions and potential legal risk, require additional investment of resources in compliance programs, impact strategies and the availability of previously useful data and could result in increased compliance costs and/or changes in business practices and policies. The existence of comprehensive privacy laws in different states in the country will make our compliance obligations more complex and costly and may increase the likelihood that we may be subject to enforcement actions or otherwise incur liability for noncompliance.

The increasing number and complexity of regional, country and U.S. state data protection laws, and other changes in laws or regulations across the globe, especially those 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 preclinical 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 platforms, approved drugs, drug candidates or discovery-stage programs, or form strategic alliances, collaborations or partnerships, in the future, and we may not realize the benefits of such acquisitions, in-licenses, alliances, collaborations or partnerships.

We may acquire or in-license additional businesses, technologies or platforms, approved drugs, drug candidates or discovery-stage programs, or form strategic alliances, collaborations or partnerships 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 or drug candidates resulting from a strategic alliance, collaboration, partnership or acquisition that delay or prevent us from realizing their expected benefits or enhancing our business. In addition, we cannot assure you that, following any such transaction, 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. We assess the impact of various tax reform proposals and modifications to existing tax treaties in all jurisdictions where we have operations to determine the potential effect on our business and any assumptions we have made about our future taxable income. We cannot predict whether any specific proposals will be enacted, the terms of any such proposals or what effect, if any, such proposals would have on our business if they were to be enacted. For tax years beginning after December 31, 2021, the Tax Cuts and Jobs Act of 2017 eliminates the once available option to deduct research and development expenditures currently and requires taxpayers to amortize specified research expenditures attributable to domestic research over a period of five years and fifteen years for research activities attributable to foreign research. As of September 30, 2023, the U.S. Congress has not passed legislation that would defer the amortization requirement to future periods and as such the inability to deduct research and development expenditures in their entirety in 2022 and 2023 will have a material impact on the carryover of taxable losses used to offset future taxable income, and in turn will impact our cash flows in future years.

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 $125.61 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 23, 2023. 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. 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, 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 February 2022, we entered into a new sales agreement with Cowen and Company, LLC through which we may, from time to time, issue and sell shares of our common stock having an aggregate offering price of up to $300.0 million, subject to the terms and conditions of the sales agreement. We did not sell any shares of common stock under this sales agreement as of September 30, 2023. If we seek authorization to sell shares of common stock under the new sales agreement, enter into new “at the market” stock offering programs, or conduct a public offering or private offering 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. 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.

We have in the past relied in part on sales of our common shares through our at-the-market (ATM) offering program to raise capital. Increased volatility and decreases in market prices of equity securities generally and of our common shares in particular may have an adverse impact on our willingness and/or ability to continue to sell our common shares through our ATM offering. Decreases in these sales could affect the cost or availability of equity capital, which could in turn have an adverse effect on our business, including current operations, future growth, revenues, net income and the market prices of our common shares.

In February 2022, we commenced a new at-the-market, or ATM, program to raise capital. Under our ATM program, we have entered into a sales agreement to sell common shares, up to a maximum aggregate market value of

$300.0 million, through one or more at-the-market offerings. Given volatility in the capital markets, we may not be willing or able to continue to raise equity capital through our ATM program. We may, therefore, need to turn to other sources of funding that may have terms that are not favorable to us, or reduce our business operations given capital constraints.

Alternative financing arrangements, if we pursue any, could involve issuances of one or more types of securities, including common stock, preferred stock, convertible debt, warrants to acquire common stock or other securities. These securities could be issued at or below the then prevailing market price for our common shares. In addition, if we issue debt securities, the holders of the debt would have a claim to our assets that would be superior to the rights of stockholders until the principal, accrued and unpaid interest and any premium or make-whole has been paid. In addition, if we borrow funds and/or issue debt securities through a subsidiary, the lenders and/or holders of those debt securities would have a right to payment that would be effectively senior to the company's equity ownership in the subsidiary, which would adversely affect the rights of holders of both the company's equity securities and its debt and debt securities.

Interest on any newly-issued debt securities and/or newly-incurred borrowings would increase our operating costs and increase our net loss, and these impacts may be material. If the issuance of new securities results in diminished rights to holders of our common stock, the market price of our common shares could be materially and adversely affected. Should the financing we require to sustain our working capital needs be unavailable or prohibitively expensive when we require it, the consequences could result in a material adverse effect on our business, operating results, financial condition and prospects.

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, enhanced procedural mechanics and disclosure requirements in connection with stockholder nominations and submissions of stockholder proposals, 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, 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 federal district courts of the United States 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 federal district courts of the United States as the exclusive forum for such Securities Act causes of action. 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.

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 bringing a claim that is covered by the Delaware forum provision do not reside in or near the State of Delaware. 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 federal district courts of the United States 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 substantial 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 (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 (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.

Repurchases of our capital stock may be subject to additional tax.

Congress recently enacted a new 1% excise tax on certain stock repurchases (or similar transactions) effected by publicly traded domestic corporations such as ours. This tax could make stock repurchases less desirable (and therefore less likely) as compared with other possible uses of our funds, and could reduce the amount of cash available if we do determine to pursue a stock repurchase.

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 (the Code), 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, 2022, we had federal net operating loss carryforwards of approximately $647.9 million, and our ability to utilize those net operating loss carryforwards could be limited by an "ownership change" as described above, which could result in increased tax liability to us. In addition, pursuant to the TCJA, we may not use net operating loss carry-forwards 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 to prior years. These rules apply regardless of the occurrence of an ownership change.

With respect to the net operating losses and research and development tax credit carryforwards acquired from the acquisition of Lengo Therapeutics, Inc. (Lengo), the Company has completed a study to assess whether an ownership change under Section 382 of the Code has occurred, or whether there have been multiple ownership changes since Lengo's formation. Based on the study all the net operating losses and research and development credits acquired will be available for utilization within their applicable carryforward periods.

In April 2022, the Company completed an update to the prior Section 382 study dated February 25, 2021. Since the Section 382 owner shifts are tested on a cumulative basis, the current update incorporates the period from February 7, 2017, the day of the last identified ownership change, through December 31, 2021. The analysis concluded that it is more likely than not that an additional ownership change did not occur during the update analysis period. This is assuming that no further significant shifts in stock ownership have occurred by virtue of equity events that have not yet been reported in publicly available SEC filings. The Company engaged its external tax advisor to determine if the Company had equity activity through December 31, 2022 that would give rise to a greater than 50% ownership change. The previous Section 382 model, through December 31, 2021, was updated for reported transactions among the Company's 5% owners. The analysis concluded that there was no additional Company equity activity through December 31, 2022 that would rise to the level of a >50% ownership change.

As part of this update, the Company also analyzed the shifts in the stock ownership of Lengo, which was acquired by the Company on December 29, 2021, for purposes of determining (1) whether and when Lengo experienced an "ownership change," as defined in Section 382(g)(1) of the Code, during the period beginning March 6, 2019, the date of the first reported issuance of Lengo stock, and ending on December 29, 2021 (Owner Shift Analysis), and (2) the extent to which Lengo's net operating loss and tax credit carryforwards may be subject to limitation under Sections 382 and 383 as a result of any such ownership changes (Limitation Analysis) (collectively, the Analysis). The analysis concluded that it is more likely than not that ownership changes occurred on (1) March 26, 2020 in connection with the issuance of Series A Preferred stock and (2) on December 29, 2021 in connection with the Company's acquisition of Lengo. An analysis of Lengo was not required as it was merged into the Company effective June 24, 2022.

Item 5. Other Information

During the three months ended September 30, 2023, one of the Company's officers adopted a "Rule 10b5-1 trading arrangement," as the term is defined in Item 408(a) of Regulation S-K. We describe the material terms of this Rule 10b5-1 trading arrangement below.

Name and Title	Action Taken	Type of Trading Arrangement	Nature of Trading Arrangement	Duration of Trading Arrangement	Aggregate Number of Securities
Ariel Hurley *(Senior Vice President, Finance and Principal Accounting Officer)*	Adoption *(9/13/23)*	Trading plan intended to satisfy the affirmative defense conditions of Securities Exchange Act Rule 10b5-1(c)	Sale of the Company's common stock pursuant to the terms of the trading plan	9/13/23 – 9/23/24	16,867

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	Inline 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*	Inline XBRL Taxonomy Extension Schema Document
101.CAL*	Inline XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF*	Inline XBRL Taxonomy Extension Definition Linkbase Document
101.LAB*	Inline XBRL Taxonomy Extension Label Linkbase Document
101.PRE*	Inline 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.

\# Indicates management contract or compensatory plan or arrangement.

† Certain portions of the exhibit have been omitted pursuant to Regulation S-K Item 601(b) because it is both (i) not material to investors and (ii) information that the Company treats as private or confidential.

+ 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 26, 2023

By: /s/ Kathryn Haviland
Kathryn Haviland
President, Chief Executive Officer and Director
(Principal Executive Officer)

Date: October 26, 2023

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

Exhibit 31.1

CERTIFICATIONS

I, Kathryn Haviland, 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 26, 2023

By:/s/ Kathryn Haviland
Kathryn Haviland
President, Chief Executive Officer and Director
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATIONS

I, Michael Landsittel, certify that:

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

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

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

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

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

(b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

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

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

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

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

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

Date: October 26, 2023

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

Exhibit 32.1

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

In connection with the Quarterly Report on Form 10-Q of Blueprint Medicines Corporation (the "Company") for the period ended September 30, 2023 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 26, 2023

By: /s/ Kathryn Haviland
Kathryn Haviland
President, Chief Executive Officer and Director
(Principal Executive Officer)

Date: October 26, 2023

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