Table of Contents

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, DC 20549

Form 10-K

(Mark One)

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

For the fiscal year ended December 31, 2024

OR

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

For the transition period from _____ to _____

Commission File Number: 001-37359

BLUEPRINT MEDICINES CORPORATION

(Exact name of registrant as specified in its charter)

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

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

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

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

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

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

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

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

Indicate by check mark whether the registrant has submitted electronically 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, a 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 has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. Yes ☑ No ☐

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements. ☐

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to §240.10D-1(b). ☐

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

As of June 30, 2024, the aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant, based on the last reported sales price for the registrant's common stock, par value $0.001 per share, on the Nasdaq Global Select Market on such date, was approximately $6,747,459,120.

Number of shares of the registrant's common stock, par value $0.001 per share, outstanding on February 11, 2025: 63,906,011

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive proxy statement for its 2025 Annual Meeting of Stockholders, which the registrant intends to file with the Securities and Exchange Commission pursuant to Regulation 14A within 120 days after the end of the registrant's fiscal year ended December 31, 2024, are incorporated by reference into Part III of this Annual Report on Form 10-K.

Auditor Firm Id: 42 Auditor Name: Ernst & Young LLP Auditor Location: Boston, Massachusetts, United States

TABLE OF CONTENTS

Unless otherwise stated, all references to "us," "our," "Blueprint," "Blueprint Medicines," "we," the "Company" and similar designations in this Annual Report on Form 10-K refer to Blueprint Medicines Corporation and its consolidated subsidiaries. Blueprint Medicines, AYVAKIT®, AYVAKYT® and associated logos are trademarks of Blueprint Medicines Corporation. Other brands, names and trademarks contained in this Annual Report on Form 10-K are the property of their respective owners.

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 under the heading "Risk Factors" and should be carefully considered, together with other information in this Annual Report on Form 10-K 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®) 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) 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, 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 a history of operating losses and may never become and remain profitable.
- 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 use of new and evolving technologies, such as artificial intelligence, in our business may result in spending material resources and presents risks and uncertainties that can impact our business.
- The price of our common stock has been and may in the future be volatile and fluctuate substantially.

FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this Annual Report on Form 10-K are forward-looking statements. In some cases, you can identify forward-looking statements by words such as "aim," "anticipate," "believe," "contemplate," "continue," "could," "estimate," "expect," "intend," "may," "plan," "potential," "opportunity", "predict," "project," "seek," "should," "target," "will," "would" or the variation or the negative of these words or other comparable terminology, although not all forward-looking statements contain these identifying words.

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

- the 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;
- 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 systemic mastocytosis (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 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 (CStone) to develop and commercialize avapritinib and pralsetinib in Greater China, our collaboration with Zai Lab to develop and commercialize BLU-525, BLU-945, and any back-up and other forms thereof, as inhibitors of epidermal growth factor receptor (EGFR) in Greater China, as well as our ability to maintain these collaborations and establish additional strategic collaborations;
- the potential benefits of our exclusive license agreement with Clementia Pharmaceuticals, Inc., a wholly-owned subsidiary of Ipsen S.A. (Clementia), to develop and commercialize BLU-782 for fibrodysplasia ossificans progressiva;

- the potential benefit of our strategic financing transaction with Garnich Adjacent Investments S.a.r.l. and Tao Talents, LLC, both affiliates of Sixth Street Partners and the potential acceleration of our commercial products and pipeline resulting from the non-dilutive growth capital;

- 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), and our expectations regarding an investment gain from the agreement under which GSK plc will acquire IDRx;

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

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

This Annual Report on Form 10-K also contains estimates, projections and other information concerning our industry, our business and the markets for certain diseases, including data regarding the estimated size of those markets, and the incidence and prevalence of certain medical conditions. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances reflected in this information. Unless otherwise expressly stated, we obtained this industry, business, market and other data from reports, research surveys, studies and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data and similar sources.

For purposes of this Annual Report on Form 10-K, including the footnotes to our consolidated financial statements, (i) with respect to our now terminated 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

Item 1. Business.

Overview

We are a global, fully-integrated biopharmaceutical company that invents life-changing medicines. We seek to alleviate human suffering by solving important medical problems in two core focus areas: allergy/inflammation and oncology/hematology. Our approach targets the root causes of disease, using deep scientific knowledge in our core focus areas and drug discovery expertise across multiple therapeutic modalities. We have a track record of success with two approved medicines, including AYVAKIT®/AYVAKYT® (avapritinib), which we are bringing to patients with systemic mastocytosis (SM) and PDGFRA Exon 18 mutant GIST in the U.S. and Europe. Leveraging our established research, development, and commercial capability and infrastructure, we now aim to significantly scale our impact by advancing a broad pipeline of programs ranging from early science to advanced clinical trials in mast cell diseases including SM and chronic urticaria, breast cancer and other solid tumors.

Since 2011, we have advanced a drug discovery approach that combines evolving biological insights with our proprietary research platform and drug design capabilities, which currently focuses on small molecule inhibitors and targeted protein degraders. We aim to rapidly and reproducibly translate science into durable clinical benefit for broad populations of patients with significant medical needs, including patients with mast cell diseases, breast cancer and other solid tumors. Our focused business model integrates our research engine with robust clinical development and commercial capabilities in allergy/inflammation and solid tumors to create a sustainable cycle of innovation.

Mast Cell Diseases — AYVAKIT®/AYVAKYT® (avapritinib), Elenestinib (BLU-263), and BLU-808

Mast cells are core drivers of biology in a range of inflammatory diseases. KIT-mediated signaling plays a central role in survival, proliferation, and activation of mast cells and KIT is a clinically validated mast cell target. The KIT receptor regulates growth, proliferation, and activation of mast cells – characterized by the release of inflammatory molecules like cytokines, histamine, tryptase, and heparin in a process called degranulation. Under normal conditions, these molecules mediate the normal physiological response to an inflammatory stimulus – leading to symptoms like sneezing, swelling, itching, and gastrointestinal effects.

There are many disease states caused by increased activation of mast cells. In addition to diseases caused by a KIT receptor mutation, there are also diseases that may be treated by dialing down mast cell activation. SM is a disorder of mast cells driven by the KIT D816V mutation in nearly all cases. Other mast cell disorders, including chronic urticaria, asthma and other skin, respiratory, and gastrointestinal disorders are characterized by generalized mast cell dysregulation, which has been shown to be modifiable with inhibition of wild-type KIT.

We continue to build a mast cell disease franchise, based on our deep understanding of mast cell biology and the KIT pathway. We are commercializing our first KIT D816V inhibitor, AYVAKIT/AYVAKYT globally for the treatment of advanced SM and indolent SM. We are developing elenestinib, or BLU-263, an investigational, orally available, potent and highly selective KIT D816V inhibitor, for the treatment of indolent SM. Additionally, we are advancing BLU-808, a potent and selective wild-type KIT inhibitor, for mast cell diseases, including chronic urticaria allergic rhinitis/allergic conjunctivitis, allergic asthma, and mast cell activation syndrome (MCAS). With AYVAKIT, we were able to demonstrate that successful inhibition of mutated KIT with a highly potent and specific molecule can result in the first and only approved disease modifying therapy for SM. Through AYVAKIT development, we have amassed considerable data on mast cell biology and a strong clinical understanding of disease areas connected to mast cell activation, which is helping to drive our efforts to extend our position in SM and expand into other mast cell disorders. We are doing this by leveraging our deep understanding of mast cell biology to drive scientific innovation; bringing that innovation to patients with our clinical and regulatory know-how; and driving compelling top-line revenue growth through commercial execution.

Systemic Mastocytosis (SM)

SM is a disorder of the mast cells, the key effector cells of allergic inflammation, which have several physiologic roles including wound healing, regulation of vascular and epithelial permeability and immune cell recruitment. The signature of SM is the overproduction of mast cells and the accumulation of mast cells in the bone marrow and other organs, including the liver, spleen, gastrointestinal tract and bones. Mast cell activation and histamine release can lead to severe allergic symptoms ranging from a skin rash to hives, fever and anaphylaxis, while mast cell accumulation in advanced cases of SM can eventually lead to organ dysfunction and failure.

SM comprises a spectrum of disease, including indolent and advanced subtypes, with nearly all patients (approximately 95 percent) having a KIT D816V mutation as the underlying driver of the disease. Indolent SM, which is the most common form of SM, is characterized by often severe, unpredictable and debilitating symptoms due to mast cell activation. Symptoms may include unpredictable hypersensitivity reactions, including anaphylaxis, gastrointestinal distress including severe nausea, vomiting and diarrhea, and extensive skin rashes that cause pain, discomfort and social isolation. Advanced SM is a rarer form of SM associated with mast cell infiltration of organ systems resulting in an increasingly severe impact on life expectancy, and includes three subsets: aggressive SM (ASM), SM with an associated hematological neoplasm (SM-AHN) and mast cell leukemia (MCL). These advanced forms of SM have historically had a median overall survival (OS) of less than six months to 3.5 years and are characterized by prominent organopathy and dysfunction, as well as the debilitating symptoms of mast cell activation.

Advanced SM accounts for approximately 10 percent of SM patients, whereas non-advanced SM accounts for about 90 percent of patients. Population studies suggest that SM prevalence could range from 1 in 10,000 up to 1 in 5,000 adults. This prevalence translates to about 30,000-60,000 patients in the US. Adding the United Kingdom, Germany, France, Spain, and Italy to the estimate for the US, the prevalence is about 60,000-120,000 patients.

The current treatment paradigm for SM varies by disease subtype. Currently, there are no approved therapies other than AYVAKIT designed to potently and selectively inhibit the KIT D816V mutation. There are two approved therapies for advanced SM: midostaurin and imatinib. Midostaurin is a multi-kinase inhibitor with limited KIT D816V inhibitory activity. Imatinib is approved only for patients with the ASM subtype who do not harbor the KIT D816V mutation, or who have an unknown mutation status. Other treatments used in advanced SM include interferon alpha or cytoreductive agents to reduce mast cell burden, or treatments aimed at addressing the associated blood disorder.

For patients with indolent SM, AYVAKIT/AYVAKYT is the only approved therapy in the U.S. and EU. Beyond AYVAKIT, management is symptom-directed and includes avoidance of triggers of mast cell activation (such as insect stings). Common off-label treatments for indolent SM include histamine blockers, cromolyn, epinephrine, corticosteroids, and, in cases of refractory patients, cytoreductive agents. Patients often take multiple symptom-directed treatments to manage their disease, and a reduction in polypharmacy burden is an important treatment goal.

AYVAKIT®/AYVAKYT® (avapritinib)

We are commercializing avapritinib for the treatment of advanced SM and indolent SM. 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. In December 2023, the European Commission approved AYVAKYT for the treatment of adult patients with indolent SM with moderate to severe symptoms inadequately controlled on symptomatic treatment. These approvals in advanced SM were supported by our Phase 1 clinical trial in advanced SM, which we refer to as our EXPLORER trial, and our ongoing registrational clinical trial in advanced SM, which we refer to as our PATHFINDER trial. The approvals of AYVAKIT for the treatment of patients with indolent SM, were supported by data from our ongoing Phase 2/3 clinical trial in indolent SM, which we refer to as the PIONEER trial. At the European Academy of Allergy and Clinical Immunology (EAACI) Congress May/June 2024, we presented long-term data from PIONEER, demonstrating that with a median follow-up of more than two years, AYVAKIT showed durable efficacy and a favorable safety profile in patients with indolent SM, and that safety data were consistent for the small number of patients who doses escalated to 50 mg once daily.

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.

Avapritinib is also 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 the EU, the UK and Switzerland 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. Currently, AYVAKIT is the only FDA-approved treatment for patients with D842V mutant PDGFRA-driven GIST. Through our collaboration with CStone, China's National Medicinal Products Administration 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 and approval in Hong Kong, both for adults with unresectable or metastatic GIST harboring PDGFRA D842V mutations. We also have distributor arrangements to commercialize AYVAKIT in global jurisdictions, including Israel and Canada, where approvals have been received. To date, AYVAKIT/AYVAKYT is approved and reimbursed for one or more indications in 15 countries, where we or our distribution partners are commercializing it. 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.

Avapritinib Clinical Data in SM

Registrational PIONEER Trial in Indolent SM

PIONEER is a randomized, double-blind, placebo-controlled, registration-enabling trial evaluating avapritinib in patients with indolent SM. The trial includes three parts: dose-finding Part 1, registration-enabling Part 2 and long-term treatment Part 3. All patients who completed Parts 1 or 2 had an opportunity to receive treatment with avapritinib in Part 3. Key trial endpoints include the change in patient-reported disease symptoms as measured by the Indolent SM Symptom Assessment Form Total Symptom Score, or ISM-SAF TSS, quantitative measures of mast cell burden and safety.

In June 2024, we presented data at EAACI and in February 2024, we presented data at American Academy of Allergy, Asthma, and Immunology (AAAAI) Annual Meeting. In February 2023 we presented fulsome results from PIONEER Part 2 at the AAAAI Annual Meeting and in August 2022 we presented top line data from PIONEER Part 2.

Data Presented at the European Academy of Allergy and Clinical Immunology (EAACI) Annual Meeting in June 2024

We presented long-term data from PIONEER, demonstrating that with a median follow-up of more than two years, AYVAKIT showed durable efficacy and a favorable safety profile in patients with indolent SM, and that safety data were consistent for the small number of patients who dose escalated to 50 mg once daily.

Data Presented at the AAAAI Annual Meeting in February 2024

We presented long-term data from PIONEER, demonstrating that AYVAKIT had a durable symptom impact and a well-tolerated safety profile, supporting long-term treatment and consistent with real-world experience observed in the commercial setting.

Data Presented at the AAAAI Annual Meeting in February 2023

In the randomized, double-blind, placebo-controlled part of the PIONEER trial, 141 patients received AYVAKIT 25 mg once daily plus best supportive care and 71 patients received placebo plus best supportive care (placebo) at 49 sites in 13 countries. The study included adults with an indolent SM diagnosis confirmed by central pathology review, and moderate-to-severe symptom burden despite an optimized regimen of best supportive care. All

patients were able to continue symptom-directed therapy throughout the trial and, following completion of the 24-week treatment period, had the option to receive AYVAKIT in an open-label extension study. Baseline patient demographics were balanced between treatment arms and reflected significant disease burden. Disease symptoms were assessed using the Indolent SM Symptom Assessment Form (ISM-SAF). Results were reported as of a data cutoff date of June 23, 2022.

Clinical Activity Data. Part 2 of the PIONEER study showed clinically meaningful and highly significant improvements across the primary and all key secondary endpoints, including patient-reported symptoms and objective measures of disease burden. For the avapritinib arm relative to the control arm, the trial achieved the primary endpoint with a highly significant difference in the mean change in TSS at 24 weeks ($p=0.003$). The avapritinib arm had a reduction of 15.6 points in mean TSS at 24 weeks, which continued to deepen to 20.2 points at 48 weeks in patients who rolled over to the Part 3 open-label extension study. At 24 weeks, the control arm had a reduction of 9.2 points in mean TSS. In addition, the trial met all key secondary endpoints, including significant improvements across measures of mast cell burden. More than half of AYVAKIT-treated patients had a greater than or equal to 50 percent reduction of serum tryptase, compared to no patients in the control arm (53.9% vs. 0%; $p<0.0001$).

Safety Data. Avapritinib had a favorable safety profile compared to the control arm. The rate of adverse events (AEs) was 90.8 percent in the avapritinib arm and 93.0 percent in the control arm. Serious AEs occurred in 5.0 percent of avapritinib-treated patients, compared to 11.3 percent of patients in the control arm. Discontinuations due to treatment-related AEs occurred in 0.7 percent of avapritinib-treated patients and 0 percent of patients in the placebo arm. The avapritinib arm had a lower rate of cognitive AEs than the control arm - 2.8% avapritinib vs. 4.2% control – and there were no intracranial bleeding events. Treatment-related AEs reported in at least three patients in either arm and at least 5 percent of avapritinib-treated patients included headache, nausea, peripheral edema and periorbital edema.

Elenestinib (BLU-263)

We are developing elenestinib 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 minimal penetration of the central nervous system 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. In December 2023, we presented HARBOR Part 1 trial data for elenestinib in indolent SM at the 65th American Society of Hematology (ASH) Annual Meeting and Exposition. We initiated the registration-enabling Phase 3 HARBOR trial of elenestinib in indolent SM in the fourth quarter of 2024.

Elenestinib Clinical Data in Indolent SM

Phase 2/3 HARBOR Trial in Indolent SM

HARBOR is a randomized, double-blind, placebo-controlled trial evaluating elenestinib in patients with indolent SM. The trial includes multiple parts including dose-finding Part 1, registration-enabling Part 2 and long-term treatment Part 3. All patients who complete Parts 1 or 2 will have an opportunity to receive treatment with elenestinib in Part 3. Key trial endpoints include the change in patient-reported disease symptoms as measured by the ISM-SAF TSS, quantitative measures of mast cell burden and safety.

Data Presented at the ASH Annual Meeting in December 2023

Part 1 of the HARBOR trial enrolled 29 patients who received elenestinib plus best available care, including 10 patients at 25 mg once daily, 10 patients at 50 mg once daily and nine patients at 100 mg once daily, and 10 patients who received placebo plus best available care. Baseline patient and disease characteristics were similar to those reported for the general ISM population. Results were reported as of a data cutoff date of October 17, 2022.

Clinical Activity Data. 12-week results from Part 1 of the HARBOR study showed elenestinib treatment led to rapid improvements in patient-reported symptoms, or TSS as measured by the ISM-SAF, as well as objective measures of mast cell burden. The elenestinib arms saw a mean percent reduction from baseline TSS of 28.5% at 25 mg, 31.8% at 50 mg, and 33.6% at 100 mg at 12 weeks, compared to a mean percent reduction from baseline TSS of 22.2% in the control arm. In addition, patients receiving elenestinib at doses of 25 mg, 50 mg, and 100 mg demonstrated dose-dependent mean percent reductions from baseline in serum tryptase levels, KIT D816V variant allele fraction (VAF), and bone marrow mast cells versus placebo.

Safety Data. Elenestinib safety results were consistent with its preclinical profile and a completed Phase 1 healthy volunteer trial. Elenestinib was generally well-tolerated at all dose levels with most AEs reported as Grade 1–2, and there were no discontinuations due to AEs. At the time of data cut-off, median treatment duration was 22 weeks and there were no grade 4 or 5 AEs, no treatment-related SAEs, no AEs that led to drug discontinuation, and all patients were still on treatment.

BLU-808

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 are developing 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. Wild-type KIT inhibition has an established proof-of-concept in chronic urticaria, and BLU-808 represents a small molecule approach with the opportunity to drive market expansion with an oral regimen. Beyond chronic urticaria, we plan to initiate proof of concept studies in other-related allergic-inflammatory indications, including but not limited to allergic rhinitis/allergic conjunctivitis, allergic asthma, and MCAS.

In February 2024, at the AAAAI Annual Meeting, we presented the preclinical attributes of BLU-808 that demonstrate its potency, selectivity, low potential for drug-drug interactions, and peripheral restriction. BLU-808 treatment led to dose-dependent inhibition and depletion of mast cells in multiple in vivo studies, and also improved lung function in an ovalbumin-induced asthma model. In June 2024, we submitted an Investigational New Drug (IND) application to FDA for BLU-808. We received FDA clearance to proceed with a Phase 1 study in healthy volunteers and initiated that study in the third quarter of 2024.

Data Presented at the J.P. Morgan Conference in January 2025

In January 2025, we presented results from the Phase 1 single-ascending dose (SAD; n=56) and multiple-ascending dose (MAD; n=31, 14-day dosing) trial of BLU-808, a highly potent and selective oral KIT inhibitor, in healthy volunteers at the J.P. Morgan Healthcare Conference.

Safety: BLU-808 was well-tolerated at all doses tested. All treatment-emergent adverse events (AEs) in the MAD cohorts 1-12 mg once daily (QD) in those who received BLU-808 were Grade 1. There were no serious AEs, no discontinuations or dose modifications due to AEs, and no clinically significant changes in laboratory measures.

Pharmacokinetics: BLU-808 showed a half-life of approximately 40 hours, enabling once-daily dosing, and consistent, dose-proportional increases in drug exposure. In the MAD cohorts, all BLU-808 doses led to sustained target coverage, with mean plasma concentrations exceeding predicted KIT IC_{50} levels at ≥1 mg QD and IC_{88} levels at ≥3 mg QD.

Pharmacodynamics: BLU-808 showed dose-dependent serum tryptase responses, reflecting evidence of mast cell target engagement across multiple dose levels. In the SAD cohorts, reductions in tryptase were observed after a single dose of BLU-808, exceeding 60 percent at 42 mg. In the MAD cohorts, rapid, robust and sustained reductions in tryptase were observed, with reductions exceeding 80 percent at 12mg and below the lower limit of quantification (LLOQ) at multiple dose levels.

Oncology/Hematology

Our oncology research program has delivered a number of innovative therapies and continues to be an active area of discovery. Based on early clinical success, we plan to further advance discovery research in oncology in 2025.

Cell Cycle Inhibition Programs

We are advancing multiple therapeutic candidates and research programs targeting the cell cycle as potential treatments for patients with hormone-receptor-positive/human epidermal growth receptor 2 negative (HR+/HER2-) breast cancer and other solid tumors. These include CDK2 and CDK4 targeted protein degraders, which have progressed rapidly in preclinical development toward potentially best-in-class development candidate profiles supporting our prioritization of these programs. We are completing the Phase 1 dose escalation study of our CDK2 inhibitor BLU-222 and are de-prioritizing any further investment in this program. We continue to engage strategic partners on potential opportunities to broadly advance our franchise of CDK programs.

Discovery Platform

We continue to drive organic growth with our innovative and highly productive research platform, which has nominated 17 development candidates to date. With drug design capabilities spanning small molecule inhibitors and targeted protein degraders, our approach begins by choosing the best modality for the targets we are pursuing and designing highly potent and selective therapeutic candidates. Within our focus areas of allergy/inflammation and oncology/hematology, we pursue targets where the biology is clear and there is opportunity to impact large patient populations. We consistently aim to achieve first- or best-in-class profiles with the potential to disrupt the current standard of care and dramatically improve patient outcomes. In addition, we prioritize opportunities where early data can de-risk future investment and we deeply integrate the insights and capabilities of our R&D and commercial functions to create significant and sustainable growth opportunities.

Collaborations, Licenses and Other Agreements Summary

Roche—Pralsetinib Collaboration. In July 2020, we entered into a collaboration agreement with Roche, which we refer to as the Roche pralsetinib collaboration, to develop and commercialize pralsetinib for the treatment of RET-altered cancers. Under the Roche pralsetinib collaboration, we and Genentech co-commercialized GAVRETO in the U.S., and Roche was granted exclusive commercialization rights for pralsetinib outside of the U.S., excluding Mainland China, Hong Kong, Macau and Taiwan (each a CStone region and, collectively, the CStone Territory). In February 2023, we received written notice from Roche of their election to terminate for convenience the Roche pralsetinib collaboration agreement. The termination became effective on February 22, 2024, at which time we entered into a transition agreement with Roche (the Roche transition agreement) and sold the U.S. rights to research, develop, manufacture and commercialize pralsetinib to Rigel Pharmaceuticals (Rigel). In January 2024, we decided to discontinue global development and marketing of GAVRETO in territories excluding the U.S. and CStone Territory, due to a lack of an alternate partner in these regions. We continue to work with Roche on the transition and wind-down activities contemplated in the Roche transition agreement. For additional information, see Note 11, *Collaborations, License and Other Agreements*, to our consolidated financial statements included in this Form 10-K.

CStone. In June 2018, we entered into a collaboration with CStone to develop and commercialize avapritinib, pralsetinib and fisogatinib, as well as any back-up and other forms thereof, 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, which we refer to as the Clementia license agreement. Pursuant to the Clementia license agreement, 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 has an ongoing Phase 2 clinical trial of BLU-782, now referred to as fidrisertib.

Zai Lab. In November 2021, we entered into a license and collaboration agreement with Zai Lab, which we refer to as the Zai Lab agreement, 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, which currently includes BLU-945 and BLU-525. In January 2024 at the J.P. Morgan Healthcare Conference, we announced that we are discontinuing further investment in early clinical-stage therapies for EGFR-mutant NSCLC globally; however, Zai Lab retains its rights to BLU-945 and BLU-525 under the Zai Lab agreement.

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 of Series A preferred stock pursuant to the anti-dilution provision in the IDRx Stock Purchase Agreement.

In January 2025, IDRx announced that they had entered into an agreement under which GSK plc will acquire IDRx for $1.0 billion upfront with an additional $150.0 million regulatory approval-based milestone payment. The transaction is expected to close in the first quarter 2025.

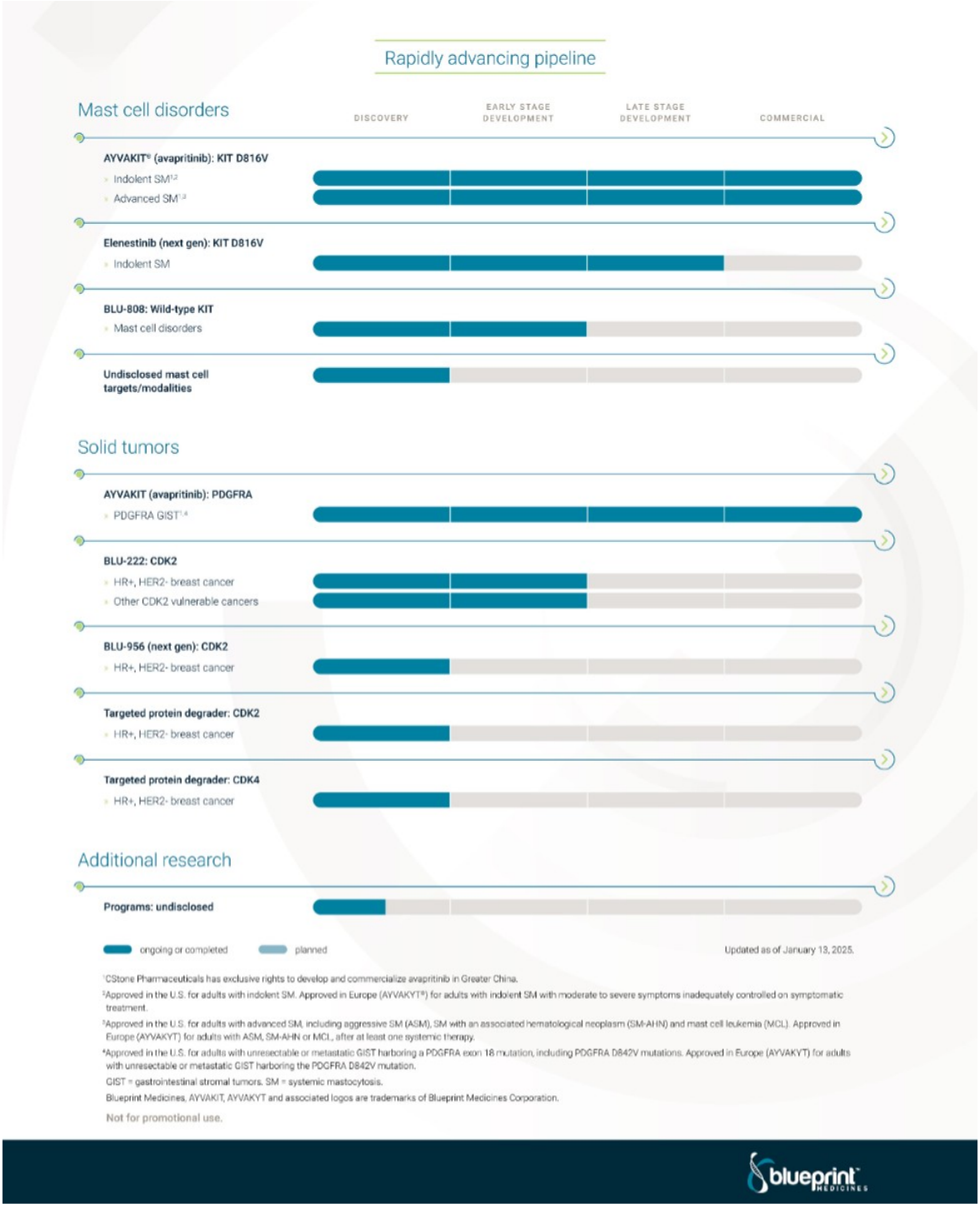
Financing Arrangements Summary

Royalty Purchase Agreement. In June 2022, we entered into a purchase and sale agreement with Royalty Pharma, which we refer to as the Royalty Purchase Agreement. Pursuant to the Royalty Purchase Agreement, we received an upfront cash payment of $175.0 million 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, we received written notice from Roche of their election to terminate for convenience the Roche pralsetinib collaboration agreement. The termination became effective in February 2024. In connection with and effective upon the termination of the Roche pralsetinib collaboration agreement, on February 22, 2024, we and Royalty Pharma agreed to terminate the Royalty Purchase Agreement, which we refer to as the Royalty Pharma Termination Agreement. Following the termination of the Royalty Purchase Agreement, we have no outstanding obligations under the Royalty Purchase Agreement, other than the remaining royalty payment obligation related to GAVRETO net sales as of the termination effective date, which has since been paid. As of December 31, 2024, we have no plans to enter into a new arrangement to commercialize GAVRETO outside of the U.S. and the CStone Territory.

Synthetic Royalty Facility. In June 2022, we entered into a purchase and sale agreement with Sixth Street Partners, which we refer to as the Future Revenue Purchase Agreement. 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 and (ii) if it is approved, aggregate worldwide annual net product sales of elenestinib, 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, which we refer to as the Financing Agreement. 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 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 and in May 2024, we received the second tranche in the amount of $150.0 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.

Our Pipeline



Our Strategy

As a global, fully-integrated biopharmaceutical company that invents life-changing medicines, we seek to alleviate human suffering by solving important medical problems in two core focus areas: allergy/inflammation and oncology/hematology. Our approach targets the root causes of disease, using deep scientific knowledge in our core focus areas and drug discovery expertise across multiple therapeutic modalities. Our goal is to pursue discovery, development, and commercialization of therapies that potently and selectively target known drivers of disease, with focused investment in therapeutic areas where we can leverage our core expertise and business infrastructure to bring scale to our science, to bring the benefit of Blueprint therapies to as many patients as possible. To achieve this goal, key elements of our strategy are as follows:

- Accelerate the adoption of our approved medicines, including AYVAKIT/AYVAKYT in the U.S. and Europe, continue to strengthen and expand our global commercial capabilities and prepare for future potential commercial launches of new investigational medicines.
- Deepen our strategic focus on mast cell diseases, including systemic mastocytosis, chronic urticaria, and other diseases implicated by KIT-mediated signaling, by continuing the development of elenestinib and BLU-808.
- Advance our innovative research programs, including our CDK2 and CDK4 targeted protein degraders, and our other preclinical programs, rapidly through development as we continue ongoing discussions for potential strategic partnership.
- Expand our focused, differentiated pipeline, with prioritization towards mast cell diseases within allergy/inflammation and solid tumors within oncology/hematology, and continued internal discovery research and innovation, inclusive of targeted protein degradation, as well as opportunities to acquire or in-license complementary technologies or therapies.
- Evaluate potential additional collaborations, partnerships and licenses that could maximize the value of our existing 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.
- Maintain a commitment to building a corporate culture centered by our focus on patient needs, science-driven approach to drug development, and organizational strength through the diversity of experience and perspective across our workforce.

Collaborations, Licenses and Other Agreements

Roche

Pralsetinib Collaboration. In July 2020, we entered into a collaboration agreement with Roche, which we refer to as the Roche pralsetinib collaboration, to develop and commercialize pralsetinib for the treatment of RET-altered cancers. Under the Roche pralsetinib collaboration, we and Genentech co-commercialized GAVRETO in the U.S., and Roche was granted exclusive commercialization rights for pralsetinib outside of the U.S., excluding Mainland China, Hong Kong, Macau and Taiwan (each a CStone region and, collectively, the CStone Territory). In February 2023, we received written notice from Roche of their election to terminate for convenience the Roche pralsetinib collaboration agreement. The termination became effective on February 22, 2024, at which time we entered into the Roche transition agreement and sold the U.S. rights to research, develop, manufacture and commercialize pralsetinib to Rigel pursuant to an Asset Purchase Agreement and certain supporting agreements, including a customary transition agreement (such agreements collectively referred to as the Rigel Agreement). In January 2024, we decided to discontinue global development and marketing of GAVRETO in territories excluding the U.S. and CStone Territory, due to a lack of an alternate partner in these regions. We continue to work with Roche on the transition and wind-down activities contemplated in the Roche transition agreement.

CStone

On June 1, 2018, we entered into a collaboration and license agreement, or the CStone agreement, with CStone pursuant to which we granted CStone exclusive rights to develop and commercialize avapritinib, pralsetinib and fisogatinib, as well as any back-up and other forms thereof, which we refer to collectively as the licensed products, in the CStone Territory, either as a monotherapy or as part of a combination therapy. We will retain exclusive rights to the licensed products outside the CStone Territory.

We received an upfront cash payment of $40.0 million, and through December 31, 2024, we have received $38.5 million in milestone payments under this collaboration. Subject to the terms of the CStone agreement, in addition to upfront and milestone payments received through December 31, 2024, we 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 will be obligated to pay us 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 is shared by us 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 region-by-region basis until the later of (i) 12 years after the first commercial sale of a licensed product in a region in the CStone Territory and (ii) the date of expiration of the last valid patent claim related to our 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 us, and CStone may terminate the CStone agreement with respect to a licensed product for convenience at any time by providing written notice to us following the occurrence of specified events. In addition, we may terminate the CStone agreement under specified circumstances if CStone or certain other parties challenges our 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 our uncured material breach, we will be obligated to pay CStone a low single digit percentage royalty on a licensed product-by-licensed product on annual net sales of such licensed product in the CStone Territory, subject to a cap and other specified exceptions.

Clementia

On October 15, 2019, we entered into a license agreement, or the Clementia agreement, with Clementia. Under the Clementia agreement, we granted an exclusive, worldwide, royalty-bearing license to Clementia to develop and commercialize BLU-782, an oral, highly selective investigational ALK2 inhibitor in clinical development for the treatment of FOP, as well as specified other compounds related to the BLU-782 program, which we refer to as the Clementia licensed products.

We received an upfront cash payment of $25.0 million in the fourth quarter of 2019, and through December 31, 2024, we have received $50.0 million in milestone payments under this license agreement. Subject to the terms of the Clementia agreement, in addition to the upfront and milestone payments received, we will be eligible to receive up to $460.0 million in development, regulatory and sales-based milestone payments for the Clementia licensed

products. In addition, Clementia is obligated to pay to us royalties on aggregate annual worldwide net sales of Clementia licensed products at tiered percentage rates ranging from the low- to mid-teens, subject to adjustment in specified circumstances under the Clementia agreement, and to purchase specified manufacturing inventory from our company.

Under the terms of the Clementia agreement, we were responsible for specified activities during a transition period, which has been completed, and Clementia is responsible for conducting all development and commercialization activities related to the Clementia licensed products, including the design, timing and conduct of any Phase 2 clinical trial evaluating BLU-782 for the treatment of FOP.

During the term of the agreement, we have agreed not to exploit any compound covered by the licensed patents for the treatment of FOP or multiple osteochondromas, or MO. In addition, with respect to any small molecule compound not covered by the licensed patents, we have agreed not to research, develop or manufacture any small molecule compound for the treatment of FOP or MO for a period of five years from the effective date of the Clementia agreement and not to commercialize any small molecule compound for the treatment of FOP or MO for a period of seven years from the effective date of the Clementia agreement.

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 us. 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, we are entitled to retain specified licenses to be able to continue to exploit the Clementia licensed products.

Zai Lab

On November 8, 2021, we entered into a license and collaboration agreement, or the Zai Lab agreement, with Zai Lab. Under the Zai Lab agreement, we granted an exclusive license for the development and commercialization of BLU-945 and BLU-525, including any back-up and other forms thereof, for the treatment of EGFR-driven NSCLC in Greater China, including Mainland China, Hong Kong, Macau and Taiwan, either as a monotherapy or as part of a combination therapy. We retain exclusive rights to the licensed products outside the Zai Lab territory.

We received an upfront cash payment of $25.0 million in the fourth quarter of 2021. Subject to the terms of the Zai Lab agreement, in addition to the upfront payment received, we will be eligible to receive up to $590.0 million in potential development, regulatory and sales-based milestone payments, and tiered royalties on a product-by-product basis ranging from the low-teens to mid-teens on annual net sales of the licensed products in Greater China, subject to adjustment in specified circumstances under the Zai Lab agreement.

Under the terms of the agreement, Zai Lab is responsible for all the development costs for the licensed products, which currently include BLU-945 and BLU-525, occurring in Greater China. In January 2024 at the J.P. Morgan Healthcare Conference, we announced that we will discontinue further investment in these early clinical-stage therapies for EGFR-mutant NSCLC globally (other than with respect to Greater China for BLU-525 and BLU-945, which remain licensed to Zai Lab for that territory) BLU-945 and BLU-525; however, Zai Lab retains its rights to BLU-945 and BLU-525 under the agreement.

IDRx

In August 2022, we entered into the IDRx License Agreement, pursuant to which we granted IDRx an exclusive, worldwide, royalty-bearing license to exploit our internally discovered KIT exon 13 inhibitor, IDRX-73. IDRx is a clinical-stage biopharmaceutical company and among IDRx's founders are Alexis Borisy, Nicholas Lydon, Ph.D. and George Demetri, M.D., each of whom were then-current members of our board of directors. Due to these relationships, the transaction was approved by only the non-interested members of the Company's board of directors.

In connection with the IDRx License Agreement, we also entered in the IDRx Stock Purchase Agreement, pursuant to which we received 4,509,105 shares of IDRx's Series A preferred stock and we have 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 of Series A preferred stock under the anti-dilution provision.

We are 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 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 us. We both can terminate the IDRx License Agreement for a material breach by the other party or for insolvency, and we 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 IDRx License Agreement in its entirety, all rights and obligations under the agreement will terminate and revert back to us, and we have 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.

In January 2025, IDRx announced that they had entered into an agreement under which GSK plc will acquire IDRx for $1.0 billion upfront with an additional $150.0 million regulatory approval-based milestone payment. The transaction is expected to close in the first quarter 2025.

Financing Arrangements

Royalty Purchase Agreement. In June 2022, we entered into a Royalty Purchase Agreement with Royalty Pharma. Pursuant to this Royalty Purchase Agreement, we received an upfront cash payment of $175.0 million. However, in February 2023, Roche provided written notice of their election to terminate the Roche pralsetinib collaboration agreement for convenience. In connection with and effective upon the termination of the Roche pralsetinib collaboration agreement, on February 22, 2024, we and Royalty Pharma agreed to terminate the Royalty Pharma Agreement pursuant to the Royalty Pharma Termination Agreement. Following the termination of the Royalty Purchase Agreement, we have no outstanding obligations under the Royalty Purchase Agreement, other than the remaining royalty payment obligation related to GAVRETO net sales as of the termination effective date, which has since been paid. As of December 31, 2024, we have no plans to enter into a new arrangement to commercialize GAVRETO outside of the U.S. and the CStone territory. The termination of the Roche pralsetinib collaboration agreement did not affect the upfront cash payment we received from Royalty Pharma.

Synthetic Royalty Facility. In June 2022, we entered a 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, the Financing Agreement, for up to $660.0 million with Sixth Street Partners. The Financing Agreement 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. The loans will mature on June 30, 2028 and bear interest at a variable rate equal to either the 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 and in May 2024, we received the second tranche in the amount of $150.0 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.

Intellectual Property

Our commercial success depends in part on our ability to obtain and maintain proprietary or intellectual property protection for our drugs and drug candidates, as well as our core technologies, including our novel target discovery engine, our proprietary compound library, targeted protein degrader platform and other know-how; to operate without infringing on the proprietary rights of others; and to prevent others from infringing our proprietary or intellectual property rights. Our policy is to seek to protect our proprietary and intellectual property position by, among other methods, filing U.S., international and foreign patent applications related to our proprietary compounds, technology, inventions and improvements that are important to the development and implementation of our business. We also rely on trade secrets, know-how and continuing technological innovation to develop and maintain our proprietary and intellectual property position.

We devote considerable effort and resources to protecting inventions, trade-secrets, and know-how related to our approved medicines AYVAKIT®/AYVAKYT® and our drug candidates in an effort to establish strong intellectual property positions regarding these new chemical entities and their uses and other technologies, including formulations, solid forms, manufacturing processes, and patient selection markers that may be useful with our drugs and drug candidates. We have patent rights that are the subject of U.S. and foreign patents and patent applications in the U.S. and a number of other jurisdictions, including Australia, Canada, certain Central and South American countries, certain Asian countries (including Greater China), the EU, certain Eurasian countries, certain Middle Eastern countries, New Zealand, and certain African countries. Our issued patents and patent applications of our most advanced programs pertain to our approved medicine AYVAKIT and clinical candidates.

We file trademarks to protect our products. Typically, we file trademark applications in the U.S., Europe, and elsewhere in the world as appropriate. In addition to multiple pending trademark applications in the U.S. and other major countries, we have registered trademarks, including but not limited to AYVAKIT in the U.S. and to AYVAKYT in the EU. In addition to patents and trademarks for our drug products, we seek to obtain all available regulatory exclusivities for our marketed products, including data and orphan exclusivities in the relevant jurisdictions.

The patent portfolios relating to our approved medicines and most advanced programs as of December 31, 2024 are summarized below.

Mast Cell Diseases - AYVAKIT/AYVAKYT (avapritinib), Elenestinib (BLU-263), and BLU-808

The patent portfolios relating to our approved medicines and most advanced programs as of December 31, 2024 are summarized below.

KIT D816V Mutant Program - AYVAKIT/AYVAKYT (avapritinib) and elenestinib

The patent portfolio for our mutant KIT programs contain patents and patent applications directed to compositions of matter for AYVAKIT/AYVAKYT, elenestinib, and other compound families, including solid forms and methods of use and manufacture. As of December 31, 2024, we own 16 U.S. patents, 4 European patents, validated in multiple states and 34 other foreign patents and multiple pending patent applications in the U.S., Europe and in various foreign jurisdictions. The patents that have issued or will issue covering AYVAKIT/AYVAKYT and elenestinib will have a statutory expiration date between 2034 and 2043. Patent term adjustments, patent term extensions, and supplementary protection certificates could result in later expiration dates.

In addition, in connection with our FDA approval on January 9, 2020, the FDA granted AYVAKIT new chemical entity, or NCE, exclusivity until January 9, 2025 and Orphan Drug Exclusivity, or ODE, until January 9, 2027. In connection with our FDA approval on June 16, 2021, the FDA granted AYVAKIT new clinical indication exclusivity for two indications until June 16, 2024 and ODE until June 16, 2028. In connection with our FDA approval on May 22, 2023, the FDA granted AYVAKIT new clinical indication exclusivity until May 22, 2026 and ODE until May 22, 2030.

In connection with notification of our EMA approval on September 25, 2020, the EMA granted AYVAKYT Orphan marketing exclusivity until September 25, 2030. Additionally, 1 year of market protection was granted after authorization of new therapeutic indication representing a significant clinical benefit in comparison with existing therapies until September 25, 2031. In connection with notification of our EMA approval on March 25, 2022, the EMA granted AYVAKYT Orphan marketing exclusivity until March 25, 2032. In connection with notification of our EMA approval on December 12, 2023, the EMA granted AYVAKYT Orphan marketing exclusivity December 12, 2033.

Wild-type KIT Program — BLU-808

The patent portfolio for our wild-type KIT program contains patents and patent applications directed to compositions of matter for BLU-808 and other compound families, as well as solid forms and methods of use and manufacture. As of December 31, 2024, we own 8 pending patent applications in the U.S., Argentina and Taiwan. The patents that will issue covering our wild-type KIT program will have a statutory expiration date between 2043 and 2045. Patent term adjustments, patent term extensions, and supplementary protection certificates could result in later expiration dates.

Cell Cycle Inhibition Program - CDK2 Inhibitors (BLU-222, BLU-956) and CDK Protein Degraders

The patent portfolio for our Cell Cycle Inhibition program contains patent applications directed to CDK2 inhibitors and CDK protein degraders, including compositions of matter for BLU-222, BLU-956 and other compound families, as well as solid forms and methods of use and manufacture. As of December 31, 2024, we own 2 issued U.S. patents, 1 issued foreign patent and 88 patent applications pending in the U.S., PCT and in various foreign jurisdictions. The patents that will issue covering our Cell Cycle Inhibition program will have a statutory expiration date between 2042 and 2045. Patent term adjustments, patent term extensions, and supplementary protection certificates could result in later expiration dates.

Other Considerations

The term of individual patents depends upon the legal term for patents in the countries in which they are obtained. In most countries, including the U.S., the patent term is 20 years from the earliest filing date of a non-provisional patent application. In the U.S., a patent's term may be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the USPTO in examining and granting a patent or may be shortened if a patent is terminally disclaimed over an earlier filed patent. The term of a patent that covers a drug or biological product may also be eligible for patent term extension when FDA approval is granted, provided statutory and regulatory requirements are met. See "— *Government Regulation — U.S. Patent Term Restoration and Marketing Exclusivity*" below for additional information on such exclusivity. In the future, if applicable and when our drug candidates receive approval by the FDA or foreign regulatory authorities, we expect to apply for patent term extensions on issued patents covering those drugs, depending upon the length of the clinical trials for each drug and other factors. There can be no assurance that any of our pending patent applications will issue or that we will benefit from any patent term extension or favorable adjustment to the term of any of our patents.

As with other biotechnology and pharmaceutical companies, our ability to maintain and solidify our proprietary and intellectual property position for our drug, drug candidates and technologies will depend on our success in obtaining effective patent claims and enforcing those claims if granted. However, our pending patent applications, and any patent applications that we may in the future file or license from third parties may not result in the issuance of patents. We also cannot predict the breadth of claims that may be allowed or enforced in our patents. Any issued patents that we may receive in the future may be challenged, invalidated or circumvented. For example, we cannot be certain of the priority of inventions covered by pending third-party patent applications. If third parties prepare and file patent applications in the U.S. that also claim technology or therapeutics to which we have rights, we may have to participate in interference proceedings in the U.S. Patent and Trademark Office (USPTO) to determine priority of invention, which could result in substantial costs to us, even if the eventual outcome is favorable to us, which is highly unpredictable. In addition, because of the extensive time required for clinical development and regulatory review of a drug or drug candidate we may develop, it is possible that, before any of our approved drugs or drug candidates can be commercialized, any related patent may expire or remain in force for only a short period following commercialization, thereby limiting protection such patent would afford the respective product and any competitive advantage such patent may provide.

In addition to patents, we rely upon unpatented trade secrets and know-how and continuing technological innovation to develop and maintain our competitive position. We seek to protect our proprietary information, in part, by executing confidentiality agreements with our collaborators, third-party service providers, and scientific advisors, and non-competition, non-solicitation, confidentiality, and invention assignment agreements with our employees. We have also executed agreements requiring assignment of inventions with selected scientific advisors, consultants, and collaborators. The confidentiality agreements we enter into are designed to protect our proprietary information and the agreements or clauses requiring assignment of inventions to us are designed to grant us ownership of drugs, drug candidates and technologies that are developed through our relationship with the respective counterparty. We cannot guarantee, however, that these agreements will afford us adequate protection of our intellectual property and proprietary information rights.

With respect to the building of our discovery platform, including our proprietary compound library and targeted protein degrader platform, we consider trade secrets and know-how to be our primary intellectual property. Trade secrets and know-how can be difficult to protect. In particular, we anticipate that with respect to our discovery platform, these trade secrets and know-how will over time be disseminated within the industry through independent development and public presentations describing the methodology.

Competition

The pharmaceutical and biotechnology industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary drugs. While we believe that our technology, development experience and scientific knowledge provide us with competitive advantages, we face potential competition from many different sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions and governmental agencies and public and private research institutions worldwide. Any drug or drug candidates that we successfully develop and commercialize will compete with existing drugs and new drugs that may become available in the future.

We compete in two core focus areas: allergy/inflammation and oncology/hematology, developing kinase inhibitors and targeted protein degraders. There are other companies working to develop therapies in these areas. These companies include divisions of large pharmaceutical companies and biotechnology companies of various sizes.

Many of the companies against which we are competing or against which we may compete in the future have significantly greater financial resources and expertise in research and development, manufacturing, 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 our drugs and our current or future drug candidates, if approved, are likely to be their efficacy, safety, convenience, price, the level of generic competition and the availability of reimbursement from government and other third party payors.

Our approved drugs and drug candidates, to the extent they receive marketing approval in the future for indications for which we are currently conducting or planning clinical trials, compete with or will compete with the drugs discussed below and will likely compete with other drugs that are currently in development.

SM

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 Alys Pharmaceuticals Inc., Cogent Biosciences, Inc. and Hoth Therapeutics, 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., Alys Pharmaceuticals Inc., Celldex Therapeutics, Inc., Cogent Biosciences, Inc., Hoth Therapeutics, Inc., Invea Therapeutics Inc., and Telios Pharma Inc.

GIST

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, Cogent Biosciences, Inc., Deciphera Pharmaceuticals, LLC, Exelixis, Inc., Ningbo Tai Kang Medical Technology Co. Ltd. and Xencor, Inc.

Chronic Urticaria, Asthma, Allergic Rhinitis, and Mast Cell Activation Syndrome

We are developing BLU-808 for chronic urticaria, asthma, allergic rhinitis, MCAS and other allergy/inflammation indications, which if approved, will face competition from omalizumab developed by Genentech and Novartis. In addition, BLU-808 may face competition from drug candidates in development, including those developed by Alivexis, Inc., Amgen Inc., AstraZeneca plc, Celldex Therapeutics, Inc., Eli Lilly, Enanta Pharmaceuticals, Inc, Escient Pharmaceuticals, Inc., Evommune, Inc, Hangshou Highlightll Pharma, Incyte Corp., Jasper Therapeutics, Inc., Leo Pharma A/S, LongBio Pharma, Novartis AG, Regeneron Pharmaceuticals, Inc., Sanofi S.A., Third Harmonic Bio, Inc,-Taiho Pharmaceutical Co., LTD, and United BioPharma.

Commercialization

We are a global, fully-integrated biopharmaceutical company that invents life-changing medicines. We seek to alleviate human suffering by solving important medical problems in two core focus areas: allergy/inflammation and oncology/hematology. Our approach targets the root causes of disease, using deep scientific knowledge in our core focus areas and drug discovery expertise across multiple therapeutic modalities. We have established our own commercial organization in the U.S. and Europe in connection with our commercial launch of AYVAKIT in the U.S. and AYVAKYT in Europe. We have also entered into collaborations with our partners, including CStone, for global commercialization activities for AYVAKIT/AYVAKYT. We are continuing to expand our commercialization capabilities and to build our distribution capabilities to accelerate global adoption of AYVAKIT and to prepare for additional planned commercial launches.

We may also evaluate opportunities to establish collaborations with pharmaceutical companies to leverage their capabilities to maximize the potential of our pipeline from time to time.

Manufacturing and Supply

We do not own or operate, and currently have no plans to establish, any manufacturing facilities. We currently rely, and expect to continue to rely, on third parties for the manufacture of our drug candidates for preclinical and clinical testing, as well as for commercial manufacture of any drug we may commercialize. To date, we have obtained materials for avapritinib, elenestinib and BLU-808 for our ongoing and planned clinical testing from third-party manufacturers. We obtain our supplies from these manufacturers on a purchase order basis and do not have a long-term supply arrangement in place other than for the commercial supply of AYVAKIT/AYVAKYT. Although we have negotiated manufacturing agreements with certain venders for the commercial supply of AYVAKIT/AYVAKYT, we may also obtain our supplies for these approved drugs from these manufacturers on a purchase order basis from time to time. We rely primarily on single-source third-party suppliers to manufacture and supply our drugs and may from time to time explore opportunities to identify and qualify additional manufacturers to provide the API, drug substance and drug products.

All of our approved drugs and drug candidates are compounds of low molecular weight, generally called small molecules. They can be manufactured in reliable and reproducible synthetic processes from readily available starting materials. The chemistry is amenable to scale-up and does not require unusual equipment in the manufacturing process. We expect to continue developing drug candidates that can be produced cost-effectively at contract manufacturing facilities.

Government Regulation

Government authorities in the U.S. at the federal, state and local level and in other countries extensively regulate, among other things, the research and clinical development, testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, post-approval monitoring and reporting, marketing, and export and import of drug products, such as those we are developing. Generally, before a new drug can be marketed, considerable data demonstrating its quality, safety and efficacy must be obtained, organized into a format specific to each regulatory authority, submitted for review and approved by the regulatory authority.

The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources. Failure to comply with the applicable regulatory requirements at any time during the product development process, approval process or after approval may subject an applicant to administrative or judicial sanctions. These sanctions could include, among other actions, the regulatory authority's refusal to approve pending applications, withdrawal of an approval, clinical holds, untitled or warning letters, voluntary product recalls or withdrawals from the market, product seizures, total or partial suspension of production or distribution, injunctions, debarment, fines, refusals of government contracts, restitution, disgorgement, or civil or criminal penalties. Any agency or judicial enforcement action could have a material adverse effect on us.

U.S. Drug Development

In the U.S., the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and its implementing regulations. Drugs are also subject to other federal, state and local statutes and regulations. Our drug candidates must be approved by the FDA through the NDA process before they may be legally marketed in the U.S. The process required by the FDA before a drug may be marketed in the U.S. generally involves the following:

- completion of extensive nonclinical tests, sometimes referred to as preclinical laboratory tests, animal studies and formulation studies performed in accordance with applicable regulations, including the FDA's good laboratory practice, or GLP, regulations;
- submission to the FDA of an IND, which must become effective before human clinical trials may begin and must be actively maintained, including by submitting 15- or 7-day safety reports and annual safety reports;
- performance of adequate and well-controlled human clinical trials in accordance with applicable IND and other clinical trial-related regulations, sometimes referred to as good clinical practices, or GCPs, to establish the safety and efficacy of the proposed drug for its proposed indication;
- submission to the FDA of an NDA for a new drug;
- a determination by the FDA within 60 days of its receipt of an NDA to file the NDA for review;
- review of the drug candidate by an FDA advisory committee, where appropriate or if applicable;
- payment of user fees for FDA review of the NDA (unless a fee waiver applies);
- satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities at which the API and finished drug product are produced to assess compliance with the FDA's current good manufacturing practice, or cGMP, requirements, where appropriate or if applicable;

- potential FDA audit of the preclinical study sites and/or clinical trial sites that generated the data in support of the NDA; and

- FDA review and approval of the NDA prior to any commercial marketing or sale of the drug in the U.S.

The data required to support an NDA is generated in two distinct development stages: preclinical and clinical. For new chemical entities, the preclinical development stage generally involves synthesizing the active component, developing the formulation and determining the manufacturing process, as well as carrying out non-human toxicology, pharmacology and drug metabolism studies in the laboratory as well as supporting starting dose determinations, which support subsequent clinical testing. The conduct of the preclinical tests must comply with federal regulations, including GLPs, where applicable. The sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and a proposed clinical protocol, to the FDA as part of the IND. An IND is a request for authorization from the FDA to administer an investigational drug product to humans. The central focus of an IND submission is on the preclinical data, general investigational plan and the protocol(s) for human trials. The IND becomes effective 30 days after receipt by the FDA, unless the FDA raises concerns or questions regarding the proposed clinical trials and places the IND on clinical hold within that 30-day time period. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns or questions before the clinical trial can begin. The FDA may also impose clinical holds on a drug candidate at any time before or during clinical trials due to safety concerns or non-compliance. Accordingly, we cannot be sure that submission of an IND will result in the FDA allowing clinical trials to begin, or that, once begun, issues will not arise that could cause the trial to be suspended or terminated.

The clinical stage of development involves the administration of the drug candidate to healthy volunteers and/or patients under the supervision of qualified investigators, generally physicians not employed by or under the trial sponsor's control, in accordance with GCPs, which include the requirement that all research subjects provide their informed consent for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria, and the parameters to be used to monitor subject safety and assess efficacy. Each protocol, and any subsequent amendments to the protocol, must be submitted to the FDA as part of the IND. Further, each clinical trial must be reviewed and approved by an independent institutional review board, or IRB, at or servicing each institution at which the clinical trial will be conducted. An IRB is charged with protecting the welfare and rights of trial participants and considers such items as whether the risks to individuals participating in the clinical trials are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the informed consent form that must be provided to each clinical trial subject or his or her legal representative and must monitor the clinical trial until completed. There are also requirements governing the reporting of ongoing clinical trials and completed clinical trial results to public registries. Failure to timely register a clinical trial or to submit study results to such public registries can give rise to civil monetary penalties and also prevent a non-compliant party from receiving future grant funds from the federal government.

Clinical trials are generally conducted in three sequential phases that may overlap or be combined, known as Phase 1, Phase 2 and Phase 3 clinical trials. Phase 1 clinical trials generally involve a small number of healthy volunteers and/or disease-affected patients who are treated with the drug candidate in escalating dose cohorts. The primary purpose of these clinical trials is to assess the pharmacokinetic, or PK, profile, pharmacologic action, side effect tolerability and safety of the drug and further support dose-finding and selection. Phase 1 clinical trials may also evaluate preliminary evidence of clinical activity. Phase 2 clinical trials typically involve studies in disease-affected patients to determine the dose required to produce the desired benefits. At the same time, safety and further PK and PD information is collected, as well as identification of possible AEs and safety risks and preliminary evaluation of efficacy. Phase 3 clinical trials generally involve large numbers of patients (from several hundred to several thousand subjects) at multiple sites, in multiple countries and are designed to provide the data necessary to demonstrate the efficacy of the drug for its intended use and patient population, its safety in use, and to establish the overall benefit/risk relationship of the drug and provide an adequate basis for physician and patient labeling. Phase 3 clinical trials may include comparisons with placebo and/or other comparator treatments. The duration of treatment is often extended to mimic the actual use of a drug during marketing. Generally, two adequate and well-controlled Phase 3 clinical trials are required by the FDA for approval of an NDA. However, in settings of rare diseases and genetically-driven cancers, regulatory flexibility is given on a case-by-case basis.

Post-approval trials, sometimes referred to as Phase 4 clinical trials, may be conducted after initial marketing approval. These trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication. In certain instances, FDA may mandate the performance of Phase 4 clinical trials as post-marketing commitments or requirements.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and written IND safety reports must be submitted to the FDA and the investigators for serious and unexpected adverse reactions, any finding from other clinical studies, tests in laboratory animals, or *in vitro* testing that suggests a significant risk for human subjects, or any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, if at all. The FDA or the clinical trial sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients. In addition, some clinical trials are overseen by an independent group of qualified experts organized by the clinical trial sponsor, known as a data safety monitoring board or committee. This group provides authorization for whether or not a trial may move forward at designated check points based on access to certain data from the trial. A sponsor may also suspend or terminate a clinical trial based on evolving business objectives and/or competitive climate. Concurrent with clinical trials, companies usually complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the drug as well as finalize a process for manufacturing the drug in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the drug candidate and, among other things, cGMPs impose extensive procedural, substantive and recordkeeping requirements to ensure and preserve the long-term stability and quality of the final drug product. In addition, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the drug candidate does not undergo unacceptable deterioration over its shelf life.

NDA and FDA Review Process

Following trial completion, trial data are analyzed to assess safety and efficacy. The results of preclinical studies and clinical trials are then submitted to the FDA as part of an NDA, along with proposed labeling for the drug and information about the manufacturing process and facilities that will be used to ensure drug quality, results of analytical testing conducted on the chemistry of the drug, and other relevant information. The NDA is a request for approval to market the drug and must contain adequate evidence of safety and efficacy, which is demonstrated by extensive preclinical and clinical testing. The application includes both negative or ambiguous results of preclinical studies and clinical trials as well as positive findings. Data may come from company-sponsored clinical trials intended to test the safety and efficacy of a use of a drug, or from a number of alternative sources, including studies initiated by investigators. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety and efficacy of the investigational drug product to the satisfaction of the FDA. FDA approval of an NDA must be obtained before a drug may be offered for sale in the U.S.

In addition, under the Pediatric Research Equity Act, or PREA, as amended, an NDA or supplement to an NDA must contain data to assess the safety and efficacy of the drug for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the drug is safe and effective. The FDA may grant deferrals for submission of pediatric data or full or partial waivers.

Under the Prescription Drug User Fee Act, or PDUFA, as amended, each NDA must be accompanied by a user fee, if applicable. The FDA adjusts the PDUFA user fees on an annual basis. According to the FDA's fiscal year 2025 fee schedule, effective October 1, 2024 through September 31, 2025, the user fee for an application requiring clinical data, such as an NDA, is $4,310,002. PDUFA also imposes an annual prescription drug product program fee for human drugs ($403,889 for the current fiscal year per approved product strength). Fee waivers or reductions are available in certain circumstances, including a waiver of the application fee for the first application filed by a small business. In addition, no user fees are assessed on NDAs for products designated as orphan drugs, unless the product also includes a non-orphan indication.

The FDA reviews all NDAs submitted before it accepts them for filing and may request additional information rather than accepting an NDA for filing. The FDA must make a decision on accepting an NDA for filing within 60 days of receipt. Once the submission is accepted for filing, the FDA begins an in-depth review of the NDA. Under the goals and policies agreed to by the FDA under PDUFA, for a new molecular entity the FDA has ten months from the filing date in which to complete its initial review of a standard NDA and respond to the applicant, and six months from the filing date for a priority NDA. The submission of a major amendment at any time during the review cycle may extend the PDUFA action date by up to three months. Only one extension can be given per review cycle. The FDA does not always meet its PDUFA goal dates for standard and priority NDAs, and the review process is often significantly extended by FDA requests for additional information or clarification.

After the NDA submission is accepted for filing, the FDA reviews the NDA to determine, among other things, whether the proposed drug is safe and effective for its intended use and patient population, and whether the drug is being manufactured in accordance with cGMP to assure and preserve the drug's identity, strength, quality and purity. The FDA may refer applications for novel drugs or drug candidates that present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians, patient advocates, and other experts, for review, evaluation and a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions. The FDA will likely re-analyze the clinical trial data, which could result in extensive discussions between the FDA and us during the review process.

Before approving an NDA, the FDA may conduct a pre-approval inspection of the manufacturing facilities for the new drug to determine whether they comply with cGMPs. The FDA will not approve the drug unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the drug within required specifications. In addition, before approving an NDA, the FDA may also audit data from clinical trials by inspecting the sponsor or clinical trial sites to ensure compliance with GCP requirements. After the FDA evaluates the application, manufacturing process and manufacturing facilities where the drug product and/or its API will be produced, it may issue an approval letter or a Complete Response Letter or defer action on an application where required inspections cannot be conducted. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. A Complete Response Letter indicates that the review cycle of the application is complete, and the application is not ready for approval. A Complete Response Letter usually describes all of the specific deficiencies in the NDA identified by the FDA. The Complete Response Letter may require additional clinical data and/or an additional pivotal clinical trial(s), and/or other significant, expensive and time-consuming requirements related to clinical trials, preclinical studies or manufacturing. If a Complete Response Letter is issued, the applicant may either resubmit the NDA, addressing all of the deficiencies identified in the letter, withdraw the application or request a hearing. Even if such data and information is submitted, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval.

There is no assurance that the FDA will ultimately approve a drug product for marketing in the U.S. and we may encounter significant difficulties or costs during the review process. If a drug receives marketing approval, the approval may be significantly limited to specific diseases and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the drug. Further, the FDA may require that certain contraindications, warnings or precautions be included in the drug labeling or may condition the approval of the NDA on other changes to the proposed labeling, development of adequate controls and specifications, or a commitment to conduct post-market testing or clinical trials and surveillance to monitor the effects of approved drugs. For example, the FDA may require Phase 4 testing which involves clinical trials designed to further assess a drug's safety and effectiveness and may require testing and surveillance programs to monitor the safety of approved drugs that have been commercialized. The FDA may also place other conditions on approvals including the requirement for a Risk Evaluation and Mitigation Strategy, or REMS to assure the safe use of the drug. If the FDA concludes a REMS is needed, the sponsor of the NDA must submit a proposed REMS. The FDA will not approve the NDA without an approved REMS, if required. A REMS could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. Any of these limitations on approval or marketing could restrict the commercial promotion, distribution, prescription or dispensing of drugs. Drug approvals may be withdrawn for non-compliance with regulatory requirements or if problems occur following initial marketing.

Special FDA Expedited Review and Approval Programs

The FDA has various programs, including fast track designation, accelerated approval, priority review and breakthrough therapy designation, that are intended to expedite or simplify the process for the development and FDA review of drugs that are intended for the treatment of serious or life-threatening diseases or conditions and demonstrate the potential to address unmet medical needs. The purpose of these programs is to provide important new drugs to patients earlier than under standard FDA review procedures. To be eligible for fast track designation, the FDA must determine, based on the request of a sponsor, that a drug is intended to treat a serious or life-threatening disease or condition and based on preclinical or preliminary clinical data demonstrates the potential to address an unmet medical need. The FDA will determine that a product will fill an unmet medical need if it will provide a therapy where none exists or provide a therapy that may be potentially superior to existing therapy based on efficacy or safety factors.

The FDA may give a priority review designation to drugs that offer major advances in treatment or provide a treatment where no adequate therapy exists. A priority review means that the goal for the FDA to review an application is six months, rather than the standard review of ten months under current PDUFA guidelines. These six- and ten-month review periods are measured from the "filing" date rather than the receipt date for NDAs for new molecular entities, which typically adds approximately two months to the timeline for review and decision from the date of submission. Products that are eligible for fast track designation are also likely to be considered appropriate to receive a priority review.

In addition, drugs studied for their safety and effectiveness in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit over existing treatments may receive accelerated approval and may be approved on the basis of adequate and well-controlled clinical trials establishing that the drug has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity or prevalence of the condition and the availability or lack of alternative treatments. As a condition of approval, the FDA may require a sponsor of a drug receiving accelerated approval to perform post-marketing studies to verify and describe the predicted effect on irreversible morbidity or mortality or other clinical endpoint and under the Food and Drug Omnibus Reform Act of 2022 (FDORA), the FDA is now permitted to require, as appropriate, that such trials be underway and fully enrolled prior to approval or within a specific time period after the date of approval for a product granted accelerated approval. Under FDORA, the FDA has increased authority for expedited procedures to withdraw approval of a drug or indication approved under accelerated approval if, for example, the confirmatory trial fails to verify the predicted clinical benefit of the product, the post-marketing studies are not conducted with due diligence or the company disseminates false or misleading promotional materials with respect to the product. In addition, the FDA generally requires, unless otherwise informed by the agency, pre-approval of promotional materials, which could adversely impact the timing of the commercial launch of the product.

Moreover, a sponsor can request designation of a drug candidate as a "breakthrough therapy." A breakthrough therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. Drugs designated as breakthrough therapies are also eligible for accelerated approval and priority review. The FDA must take certain actions, such as holding timely meetings and providing advice, intended to expedite the development and review of an application for approval of a breakthrough therapy.

Clinical Trial Diversity Plans

Diversity Action Plans must specify the sponsor's rationale and goals for clinical study enrollment (separated by the age group, ethnicity, sex and race of clinically relevant study populations) and describe how the sponsor intends to meet those goals. The guidance also urges sponsors and investigators to consider the many dimensions of clinical trial diversity, even those that extend beyond age, ethnicity, sex, and race to enroll populations that represent the patients who will be treated is the product is approved. The requirement for sponsors to submit Diversity Action Plans comes from new provisions of the FDORA. This guidance applies to Phase 3 clinical studies or, as appropriate, other pivotal clinical studies of a drug or biological product, as well as for certain clinical studies of devices, including those intended to serve as the primary basis for the FDA's evaluation of the safety and effectiveness and benefit-risk determination of the device. The requirement to submit a Diversity Action Plan applies to clinical studies for which enrollment begins 180 days after publication of the final guidance. The Trump administration's plans regarding the finalization of this guidance remain unknown at this time.

Pediatric Trials

A sponsor who is planning to submit a marketing application for a drug that includes a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration must submit an initial Pediatric Study Plan, or PSP, within sixty days of an end of Phase 2 meeting or as may be agreed between the sponsor and FDA. The initial PSP must include an outline of the pediatric study or studies that the sponsor plans to conduct, including study objectives and design, age groups, relevant endpoints and statistical approach, or a justification for not including such detailed information, and any request for a deferral of pediatric assessments or a full or partial waiver of the requirement to provide data from pediatric studies along with supporting information. FDA and the sponsor must reach agreement on the PSP. A sponsor can submit amendments to an agreed upon initial PSP at any time if changes to the pediatric plan need to be considered based on data collected from preclinical studies, early phase clinical trials, and/or other clinical development programs.

Post-Marketing Requirements

Following approval of a new drug, a pharmaceutical company and the approved drug are subject to continuing regulation by the FDA, including, among other things, monitoring and recordkeeping activities, reporting to the applicable regulatory authorities of adverse experiences with the drug, providing the regulatory authorities with updated safety and efficacy information, drug sampling and distribution requirements, and complying with promotion and advertising requirements, which include, among others, standards for direct to consumer advertising, restrictions on promoting drugs for uses or in patient populations that are not described in the drug's approved labeling, which is known as "off-label use", and requirements for promotional activities involving the internet. Although physicians may prescribe legally available drugs for off-label uses, manufacturers may not market or promote such off-label uses. Prescription drug promotional materials must be submitted to the FDA in conjunction with their first use. There are also limitations on industry sponsored scientific and educational activities. Modifications or enhancements to the drug or its labeling or changes of the site of manufacture are often subject to the approval of the FDA and other regulators, which may or may not be received or may result in a lengthy review process. Any distribution of prescription drugs and pharmaceutical samples must comply with the U.S. Prescription Drug Marketing Act, or the PDMA, a part of the FDCA.

In the U.S., once a drug is approved, its manufacture is subject to comprehensive and continuing regulation by the FDA. The FDA regulations require that drugs be manufactured in specific approved facilities and in accordance with cGMP. We rely, and expect to continue to rely, on third parties for the production of clinical and commercial quantities of our drugs in accordance with cGMP regulations. cGMP regulations require among other things, quality control and quality assurance as well as the corresponding maintenance of records and documentation and the obligation to investigate and correct any deviations from cGMP. Drug manufacturers and other entities involved in the manufacture and distribution of approved drugs, and those supplying products, ingredients, and components of them, are required to register their establishments with the FDA and certain state agencies and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP and other laws. Additionally, manufacturers and other parties involved in the drug supply chain for prescription drug products must also comply with product tracking and tracing requirements and notify the FDA of counterfeit, diverted, stolen and intentionally adulterated products or products that are otherwise unfit for distribution in the United States. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP

compliance. These regulations also impose certain organizational, procedural and documentation requirements with respect to manufacturing and quality assurance activities. NDA holders using contract manufacturers, laboratories or packagers are responsible for the selection and monitoring of qualified firms, and, in certain circumstances, qualified suppliers to these firms. These firms and, where applicable, their suppliers are subject to inspections by the FDA at any time, and the discovery of violative conditions, including failure to conform to cGMP, could result in enforcement actions that interrupt the operation of any such facilities or the ability to distribute drugs manufactured, processed or tested by them. Discovery of problems with a drug after approval may result in restrictions on a drug, manufacturer, or holder of an approved NDA, including, among other things, recall or withdrawal of the drug from the market, and may require substantial resources to correct.

The FDA also may require post-approval commitments, which may include testing that are sometimes referred to as post-marketing studies or clinical studies, risk minimization action plans and post-marketing surveillance to monitor the effects of an approved drug or place conditions on an approval that could restrict the distribution or use of the drug. Discovery of previously unknown problems with a drug or the failure to comply with applicable FDA requirements can have negative consequences, including adverse publicity, judicial or administrative enforcement, untitled or warning letters from the FDA, mandated corrective advertising or communications with doctors, and civil or criminal penalties, among others. Newly discovered or developed safety or effectiveness data may require changes to a drug's approved labeling, including the addition of new warnings and contraindications, require new post-marketing studies, and also may require the implementation of other risk management measures. The distribution of pharmaceutical drugs is subject to additional requirements and regulations, including extensive record-keeping, licensing, storage and security requirements intended to prevent the unauthorized sale of pharmaceutical drugs. In addition, under FDORA, sponsors of approved drugs must notify the FDA of any changes in marketing status, such as withdrawal of a drug, within 180 days. If the sponsor fails to meet this marketing status reporting requirement, the FDA could add the applicable products to a list of discontinued products, which would revoke the product's ability to be marketed.

Also, new government requirements, including those resulting from new legislation, may be established, or the FDA's policies may change, which could delay or prevent regulatory approval of our drugs under development.

Other Regulatory Matters

Manufacturing, sales, promotion and other activities following drug approval are also subject to regulation by numerous regulatory authorities in addition to the FDA, including, in the U.S., the Centers for Medicare & Medicaid Services, other divisions of the Department of Health and Human Services, the Drug Enforcement Administration for controlled substances, the Consumer Product Safety Commission, the Federal Trade Commission, the Occupational Safety & Health Administration, the Environmental Protection Agency and state and local governments. In the U.S., sales, marketing and scientific/educational programs must also comply with state and federal fraud and abuse laws. Pricing and rebate programs must comply with the Medicaid rebate requirements of the U.S. Omnibus Budget Reconciliation Act of 1990 and more recent requirements in the Patient Protection and Affordable Care Act, as well as the 340B drug pricing program administered by the Health Resources Services Administration within the U.S. Department of Health and Human Services as amended by the Health Care and Education Reconciliation Act of 2010, or collectively, the Affordable Care Act, as well as the 340B drug pricing program administered by the Health Resources Services Administration within the U.S. Department of Health and Human Services. If drugs are made available to authorized users of the Federal Supply Schedule of the General Services Administration, additional laws and requirements apply. The handling of any controlled substances must comply with the U.S. Controlled Substances Act and Controlled Substances Import and Export Act. Drugs must meet applicable child-resistant packaging requirements under the U.S. Poison Prevention Packaging Act. Manufacturing, sales, promotion and other activities are also potentially subject to federal and state consumer protection and unfair competition laws.

The failure to comply with regulatory requirements and changes to regulatory requirements subjects firms to possible legal or regulatory action. In addition, even if a firm complies with FDA and other requirements, new information regarding the safety or efficacy of a product could lead the FDA to modify or withdraw product approval.

U.S. Patent Term Restoration and Marketing Exclusivity

Depending upon the timing, duration and specifics of the FDA approval of our drug candidates, some of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term

Restoration Act of 1984, commonly referred to as the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date. The patent term restoration period is generally one-half the time between the effective date of an IND and the submission date of an NDA plus the time between the submission date of an NDA and the approval of that application. Only one patent applicable to an approved drug is eligible for the extension and the application for the extension must be submitted prior to the expiration of the patent. The USPTO, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. In the future, we intend to apply for restoration of patent term for one of our currently owned or licensed patents to add patent life beyond its current expiration date, depending on the expected length of the clinical trials and other factors involved in the filing of the relevant NDA.

Marketing exclusivity provisions under the FDCA can also delay the submission or the approval of certain marketing applications. The FDCA provides a five-year period of non-patent marketing exclusivity within the U.S. to the first applicant to obtain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not accept for review an abbreviated new drug application, or ANDA, or a 505(b)(2) NDA submitted by another company for another drug based on the same active moiety, regardless of whether the drug is intended for the same indication as the original innovator drug or for another indication, where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement to one of the patents listed with the FDA by the innovator NDA holder. The FDCA also provides three years of marketing exclusivity for an NDA, or supplement to an existing NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example new indications, dosages or strengths of an existing drug. This three-year exclusivity covers only the modification for which the drug received approval on the basis of the new clinical investigations and does not prohibit the FDA from approving ANDAs for drugs containing the active agent for the original indication or condition of use. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness. Orphan drug exclusivity, as described below, may offer a seven-year period of marketing exclusivity, except in certain circumstances. Pediatric exclusivity is another type of regulatory market exclusivity in the U.S. Pediatric exclusivity, if granted, adds six months to existing exclusivity periods for all formulations, dosage forms, and indications of the active moiety and patent terms. This six month exclusivity, which runs from the end of other exclusivity protection or patent term, may be granted based on the voluntary completion of a pediatric trial in accordance with an FDA issued "Written Request" for such a trial, provided that at the time pediatric exclusivity is granted there is not less than nine months of term remaining.

Orphan Drug Designation

The FDA may grant orphan drug designation to drugs intended to treat a rare disease or condition that affects fewer than 200,000 individuals in the U.S., or if it affects more than 200,000 individuals in the U.S., there is no reasonable expectation that the cost of developing and marketing the drug for this type of disease or condition will be recovered from sales in the 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. In addition, if a product receives the first FDA approval for the indication for which it has orphan designation, the product is entitled to orphan drug exclusivity, which means the FDA may not approve any other application to market the same drug for the same indication for a period of seven years, except in limited circumstances, such as a showing of clinical superiority over the product with orphan exclusivity. Orphan drug designation must be requested before submitting an application for marketing approval. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

Rare Pediatric Disease Designation and Priority Review Vouchers

Under the FDCA, the FDA incentivizes the development of drugs products that meet the definition of a "rare pediatric disease," defined to mean a serious or life-threatening disease in which the serious of life-threatening manifestations primarily affect individuals aged from birth to 18 years and the disease affects fewer than 200,000 individuals in the United States or affects more than 200,000 in the United States and for which there is no reasonable expectation that the cost of developing and making in the United States a drug product for such disease or condition will be received from sales in the United States of such drug product. The sponsor of a product candidate for a rare pediatric disease may be eligible for a voucher that can be used to obtain a priority review for a subsequent human drug product application after the date of approval of the rare pediatric disease drug product, referred to as a priority review voucher, or PRV. A sponsor may request rare pediatric disease designation from the FDA prior to the submission of its NDA. A rare pediatric disease designation does not guarantee that a sponsor will receive a PRV upon approval of its NDA. Moreover, a sponsor who chooses not to submit a rare pediatric disease designation request may nonetheless receive a PRV upon approval of their marketing application if they request such a voucher in their original marketing application and meet all of the eligibility criteria. If a PRV is received, it may be sold or transferred an unlimited number of times. The FDA's rare pediatric disease priority voucher program began to sunset on December 20, 2024, on failure of Congress to pass a continuing resolution package that included its reauthorization. Under the amended statutory sunset provisions, after December 20, 2024, the FDA may award a priority review voucher for an approved rare pediatric disease product application only if the sponsor has rare pediatric disease designation for the drug and if that designation was granted by December 20, 2024. After September 30, 2026, the FDA may not award any rare pediatric disease priority review vouchers. Congress may vote to reauthorize this program, but its future remains unknown at this time.

European Union Drug Development

In the EU, our existing and future drugs will also be subject to extensive regulatory requirements. As in the U.S., medicinal products can only be marketed if a marketing authorization from the competent regulatory agencies has been obtained.

Clinical Trial Approval

In April 2014, the EU adopted a new Clinical Trials Regulation (EU) No 536/2014, or the Clinical Trials Regulation, which replaced the previous Clinical Trials Directive 2001/20/EC on January 31, 2022. The Clinical Trials Regulation is directly applicable in all EU Member States meaning no national implementing legislation in each EU Member State is required. The legislation aims at simplifying and streamlining the approval of clinical trials in the EU. For instance, the new Clinical Trials Regulation provides for a streamlined application procedure via a single entry point, rules on the protection of subjects and informed consent, and transparency requirements, and strictly defined deadlines for the assessment of clinical trial applications.

Drug Review and Approval

In the EU, medicinal products can only be commercialized after obtaining a marketing authorization, or MA. There are two types of MA:

The centralized MA, which is issued by the European Commission through the centralized procedure, based on the opinion of the CHMP of the EMA and which is valid throughout the entire territory of the EU, and in the additional Member States of the EEA. The centralized procedure is mandatory for certain types of products, including medicines produced by certain biotechnological processes, advanced therapy medicinal products (gene-therapy, somatic cell-therapy or tissue-engineered medicines), products designated as orphan medicinal products, and products containing a new active substance indicated for the treatment of HIV, AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune and other immune dysfunctions and viral diseases. The centralized procedure is optional for products containing a new active substance not yet authorized in the EU, or for products that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the EU.

National MAs, which are issued by the competent authorities of the Member States of the EU and only cover their respective territory, are available for products not falling within the mandatory scope of the centralized procedure.

Where a product has already been authorized for marketing in a Member State of the EU, this national MA can be recognized in another Member State through the mutual recognition procedure. If the product has not received a national MA in any Member State at the time of application, it can be approved simultaneously in various Member States through the decentralized procedure. Under the decentralized procedure an identical dossier is submitted to the competent authorities of each of the Member States in which the MA is sought, one of which is selected by the applicant as the reference member state.

Under the above described procedures, before granting the MA, the EMA or the competent authorities of the Member States of the EU make an assessment of the risk-benefit balance of the product on the basis of scientific criteria concerning its quality, safety and efficacy.

Orphan Drug Designation

In the EU, the European Commission, after receiving the opinion of the EMA's Committee for Orphan Medicinal Products, or COMP, grants orphan medicinal product designation in respect of products that are intended for the diagnosis, prevention or treatment of a life threatening or chronically debilitating condition affecting not more than five in 10,000 persons in the EU. In addition, designation may be granted 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 drug in the EU would be sufficient to justify the necessary investment in developing the drug or biological product. In each case, there must be no satisfactory method of diagnosis, prevention or treatment of the applicable condition authorized for marketing in the EU, or, if such a method exists, the sponsor must establish that its product would be of significant benefit to those affected by the condition. In the EU, orphan medicinal product designation also entitles a party to financial incentives such as reduction of fees or fee waivers and ten years of market exclusivity is granted following the grant of an MA. This period may be reduced to six years if, at the end of the fifth year, it is established that the orphan designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity

Pediatric Investigation Plan

In the EU, marketing authorization applications for new medicinal products have to include the results of studies conducted in the pediatric population, in compliance with a pediatric investigation plan, or PIP, agreed with the EMA's Pediatric Committee, or PDCO, unless the EMA has granted a product-specific waiver, a class waiver, or a deferral for one or more of the measures included in the PIP. This requirement also applies when a company wants to add a new indication, pharmaceutical form or route of administration for a medicine that is already authorized. The PIP sets out the timing and measures proposed to generate data to support a pediatric indication of the product for which marketing authorization is being sought. The PDCO can grant a deferral of the obligation to implement some or all of the measures of the PIP until there are sufficient data to demonstrate the efficacy and safety of the product in adults. Further, the obligation to provide pediatric clinical trial data can be waived by the PDCO when this data is not needed or appropriate because the product is likely to be ineffective or unsafe in children, the disease or condition for which the product is intended occurs only in adult populations, or when the product does not represent a significant therapeutic benefit over existing treatments for pediatric patients. If an MA is obtained and trial results are included in the product information, even when negative, the product is eligible for six-months' supplementary protection certificate extension. In the case of orphan medicinal products, a two-year extension of the orphan market exclusivity may be available. This pediatric reward is subject to specific conditions and is not automatically available when data in compliance with the PIP are developed and submitted.

Data and Market Exclusivity

In the EU, innovative medicinal products approved on the basis of a complete and independent data package qualify for eight years of data exclusivity upon marketing authorization and an additional two years of market exclusivity. The data exclusivity, if granted, prevents generic or biosimilar applicants from referencing the innovator's preclinical and clinical trial data contained in the dossier of the reference product, when applying for a generic or biosimilar (abbreviated) marketing authorization for eight years from the date on which the reference product was first authorized in the EU. During an additional two-year period of market exclusivity, a generic or biosimilar marketing authorization application can be submitted, and the innovator's data may be referenced, but no generic or biosimilar medicinal product can be placed on the EU market until the expiration of the market exclusivity. The overall ten-year

period may be extended to a maximum of 11 years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are determined to bring a significant clinical benefit in comparison with existing therapies. There is no guarantee that a product will be considered by the EMA to be an innovative medicinal product, and products may not qualify for data exclusivity. Even if a product is considered to be an innovative medicinal product so that the innovator gains the prescribed period of data exclusivity, another company could nevertheless also market another version of the product if such company obtained an MA based on an application with a complete and independent data package of pharmaceutical tests, preclinical tests and clinical trials.

Orphan Drug Designation and Exclusivity

Regulation (EC) No. 141/2000, as implemented by Regulation (EC) No. 847/2000 provides that a product can be designated as an orphan medicinal product by the European Commission if its sponsor can establish: that (1) the product is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition; (2) either (a) such condition affects no more than five (5) in ten thousand (10,000) persons in the EU when the application is made, or (b) it is unlikely that the product, without the benefits derived from orphan status, would generate sufficient return in the EU to justify the necessary investment in its development; and (3) there exists no satisfactory method of diagnosis, prevention or treatment of such condition authorized for marketing in the EU or, if such method exists, the product will be of significant benefit to those affected by that condition. Orphan medicinal products are eligible for financial incentives such as reduction of fees or fee waivers. The application for orphan designation must be submitted before the application for marketing authorization. The applicant will receive a fee reduction for the marketing authorization application if the orphan designation has been granted, but not if the designation is still pending at the time the marketing authorization is submitted. Orphan designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

Products receiving orphan designation in the EU can receive ten years of market exclusivity, during which time no "similar medicinal product" may be placed on the market in the EU. A "similar medicinal product" is defined as a medicinal product containing a similar active substance or substances as contained in an authorized orphan medicinal product, and which is intended for the same therapeutic indication.

However, a marketing authorization may be granted to a similar medicinal product with the same indication an authorized orphan product during the ten-year period with the consent of the marketing authorization holder for the original orphan medicinal product or if the manufacturer of the original orphan medicinal product is unable to supply sufficient quantities. Marketing authorization may also be granted to a similar medicinal product with the same indication if the applicant can establish that its similar product is safer, more effective or otherwise clinically superior to the original orphan medicinal product. The period of market exclusivity may, in addition, be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for orphan designation, for example, if the product is sufficiently profitable not to justify maintenance of market exclusivity.

Regulatory Requirements After a Marketing Authorization has been Obtained

If an authorization for a medicinal product in the EU is obtained, the holder of the marketing authorization is required to comply with a range of requirements applicable to the manufacturing, marketing, promotion and sale of medicinal products. These include:

- Compliance with the EU's stringent pharmacovigilance or safety reporting rules must be ensured. These rules can impose post-authorization studies and additional monitoring obligations.
- The manufacturing of authorized medicinal products, for which a separate manufacturer's license is mandatory, must also be conducted in strict compliance with the applicable EU laws, regulations and guidance, including Directive 2001/83/EC, Directive 2017/1572, Regulation (EC) No 726/2004 and the European Commission Guidelines for Good Manufacturing Practice. These requirements include compliance with EU cGMP standards when manufacturing medicinal products and active pharmaceutical ingredients, including the manufacture of active pharmaceutical ingredients outside of the EU with the intention to import the active pharmaceutical ingredients into the EU.
- The marketing and promotion of authorized medicinal products, including industry-sponsored continuing medical education and advertising directed toward the prescribers of medicinal products and/or the general public, are strictly regulated in the EU. Direct-to-consumer advertising of prescription medicines is prohibited across the EU.

The aforementioned EU rules are generally applicable in the EEA, which consists of the EU Member States, plus Iceland, Liechtenstein and Norway.

Reform of the Regulatory Framework in the European Union

The European Commission introduced legislative proposals in April 2023 that, if implemented, will replace the current regulatory framework in the EU for all medicines (including those for rare diseases and for children). The European Commission has provided the legislative proposals to the European Parliament and the European Council for their review and approval and, in April 2024, the European Parliament proposed amendments to the legislative proposals. Once the European Commission's legislative proposals are approved (with or without amendment), they will be adopted into EU law.

Brexit and the Regulatory Framework in the United Kingdom

The UK formally left the EU on January 31, 2020. As a result of the Northern Ireland Protocol, following Brexit, the EMA remained responsible for approving novel medicines for supply in Northern Ireland under the EU centralized procedure, and a separate authorization was required to supply the same medicine in Great Britain (England, Wales and Scotland). A new framework named the Windsor Framework was approved by the EU-UK Joint Committee on March 24, 2023, and the medicines aspects of the Windsor Framework have applied since January 1, 2025. This new framework fundamentally changes the previous system under the Northern Ireland Protocol, including with respect to the regulation of medicinal products in the UK. In particular, the MHRA is now responsible for approving all medicinal products destined for the UK market (i.e., Great Britain and Northern Ireland), and the EMA no longer has any role in approving medicinal products destined for Northern Ireland under the EU centralized procedure. A single UK-wide MA will be granted by the MHRA for all novel medicinal products to be sold in the UK, enabling products to be sold in a single pack and under a single authorization throughout the UK. However, although a separate authorization is now required to market medicinal products in the UK, under an international recognition procedure which was put in place by the MHRA on January 1, 2024, the MHRA may take into account decisions on the approval of an MA from the EMA (and certain other regulators) when considering an application for a UK MA.

Rest of the World Regulation

For other countries outside of the EU and the U.S., such as countries in Eastern Europe, Latin America or Asia, the requirements governing the conduct of preclinical trials, clinical trials, manufacturing, drug licensing, pricing and reimbursement vary from country to country. In all cases the clinical trials must be conducted in accordance with GCP requirements and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

If we fail to comply with applicable foreign regulatory requirements, we may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

Data Privacy and Security Laws

Pharmaceutical companies may be subject to U.S. federal and state health information privacy, security and data breach notification laws, which may govern the collection, use, disclosure and protection of health-related and other personal information. State laws may be more stringent, broader in scope or offer greater individual rights with respect to protected health information, or PHI, than the federal Health Insurance Portability and Accountability Act of 1996, as amended, and its implanting regulations, which are collectively referred to as HIPAA, and state laws may differ from each other, which may complicate compliance efforts. Entities that are found to be in violation of HIPAA as the result of a breach of unsecured PHI, a complaint about privacy practices or an audit by the Department of Health and Human Services, or HHS, may be subject to significant civil, criminal and administrative fines and penalties and/or additional reporting and oversight obligations if required to enter into a resolution agreement and corrective action plan with HHS to settle allegations of HIPAA non-compliance.

In addition to federal regulation, many states have begun to focus on efforts to regulate privacy and data security. For example, in California the California Consumer Protection Act, or CCPA, which went into effect on January 1, 2020 and was expanded by the California Consumer Privacy Rights Act, or CPRA, which went into effect on January 1, 2023, collectively establishes a privacy framework for covered businesses by creating an expanded definition

of personal information, establishing new data privacy rights for consumers in the State of California, imposing special rules on the collection of consumer data from minors, and creating a new and potentially severe statutory damages framework for violations and for businesses that fail to implement reasonable security procedures and practices to prevent data breaches. Numerous other states have enacted or proposed comprehensive privacy laws that are similar to the CCPA. The California Confidentiality of Medical Information Act also applies to pharmaceutical companies, including requirements for written authorization to use and disclose medical information and restrictions on the circumstances under which medical information can be used for marketing purposes. Furthermore, all fifty states, the District of Columbia, Puerto Rico, and U.S. territories have enacted data breach notification laws. These various state laws differ from one another and impose significant compliance efforts.

EEA Member States, the UK, Switzerland and other jurisdictions have also adopted data protection laws and regulations, which impose significant compliance obligations. In the EEA and the UK, the collection and use of personal data, including clinical trial data, is governed by the provisions of the General Data Protection Regulation, or GDPR. The GDPR, together with national legislation, regulations and guidelines of the EEA Member States, the UK and Switzerland governing the processing of personal data, impose strict obligations and restrictions on the ability to collect, analyze and transfer personal data, including health data from clinical trials and adverse event reporting. In particular, these obligations and restrictions concern the consent of the individuals to whom the personal data relates, the information provided to the individuals, the transfer of personal data out of the EEA, the UK or Switzerland, data breach notifications, security and confidentiality, responding and handling data subject rights, ensuring appropriate assessments are carried out on processing operations and documented. Under these laws data protection authorities can impose substantial potential fines for breaches of the data protection obligations. European data protection authorities may interpret the GDPR and national laws differently and impose additional requirements, which add to the complexity of processing personal data in or from the EEA, UK or Switzerland. Guidance on implementation and compliance practices are often updated or otherwise revised. Additionally, multiple jurisdictions outside the EEA, UK, and Switzerland have adopted data protection regulations with similar requirements for companies.

Coverage and Reimbursement

Sales of our drugs will depend, in part, on the extent to which our drugs will be covered by third-party payors, such as government health programs, commercial insurance and managed healthcare organizations. In the U.S. and markets in other countries, patients and health care providers generally rely on third-party payors to reimburse all or part of prescription medications and associated healthcare costs. Thus, even if a drug has marketing approval in a country, sales of the drug will depend, in part, on the extent to which third-party payors, including government health programs, including Medicare and Medicaid in the U.S., commercial health insurers and managed care organizations, provide coverage for the cost of the patient's use of the drug, and establish adequate reimbursement levels for the product. In the U.S., no uniform policy of coverage and reimbursement for drug products exists among third-party payors. Therefore, coverage and reimbursement for drug products can differ significantly from payor to payor. The process for determining whether a third-party payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the approved products for a particular indication. The insurance coverage and reimbursement status of newly-approved products is uncertain. Failure to obtain or maintain adequate coverage and reimbursement for any of our drug and drug candidates, if approved, could limit our ability to market those products and decrease our ability to generate revenue. Factors payors, including government health programs globally, consider in determining reimbursement are based on whether the product is:

- a covered benefit under its health plan;
- safe, effective and medically necessary;
- appropriate for the specific patient;

- cost-effective; and
- neither experimental nor investigational.

These third-party payors are increasingly reducing or restricting reimbursements for medical drugs and services. In addition, the containment of healthcare costs has become a priority of federal and state governments, and the prices of drugs have been a focus in this effort. The U.S. government, state legislatures and foreign governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic drugs. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit our net revenue and results. Decreases in third-party reimbursement for our drug candidates, if approved, or a decision by a third-party payor to not cover our drug candidates could reduce usage of such drugs and have a material adverse effect on our sales, results of operations and financial condition.

The Medicaid Drug Rebate Program requires pharmaceutical manufacturers to enter into and have in effect a national rebate agreement with the Secretary of the Department of Health and Human Services as a condition for states to receive federal matching funds for the manufacturer's outpatient drugs furnished to Medicaid patients. The ACA made several changes to the Medicaid Drug Rebate Program, including increasing pharmaceutical manufacturers' rebate liability by raising the minimum basic Medicaid rebate on most branded prescription drugs from 15.1% of average manufacturer price (AMP), to 23.1% of AMP and adding a new rebate calculation for "line extensions" (i.e., new formulations, such as extended release formulations) of solid oral dosage forms of branded products, as well as potentially impacting their rebate liability by modifying the statutory definition of AMP. The ACA also expanded the universe of Medicaid utilization subject to drug rebates by requiring pharmaceutical manufacturers to pay rebates on Medicaid managed care utilization and by enlarging the population potentially eligible for Medicaid drug benefits.

The Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or the MMA, established the Medicare Part D program to provide a voluntary prescription drug benefit to Medicare beneficiaries. Under Part D, Medicare beneficiaries may enroll in prescription drug plans offered by private entities that provide coverage of outpatient prescription drugs. Unlike Medicare Part A and B, Part D coverage is not standardized. Part D prescription drug plan sponsors are not required to pay for all covered Part D drugs, and each drug plan can develop its own drug formulary that identifies which drugs it will cover and at what tier or level. However, Part D prescription drug formularies must include drugs within each therapeutic category and class of covered Part D drugs, though not necessarily all the drugs in each category or class. Any formulary used by a Part D prescription drug plan must be developed and reviewed by a pharmacy and therapeutic committee. Government payment for some of the costs of prescription drugs may increase demand for drugs for which we receive marketing approval. Any negotiated prices for our drugs covered by a Part D prescription drug plan may be lower than the prices we might otherwise obtain. Moreover, while the MMA applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own payment rates. Any reduction in payment that results from the MMA may result in a similar reduction in payments from non-governmental payors. If third-party payors do not consider our drugs to be cost-effective compared to other available therapies, they may not cover our drugs after approval as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow us to sell our drugs on a profitable basis.

For a drug product to receive federal reimbursement under the Medicaid or Medicare Part B programs or to be sold directly to U.S. government agencies, the manufacturer must extend discounts to entities eligible to participate in the 340B drug pricing program. The required 340B discount on a given product is calculated based on the AMP and Medicaid rebate amounts reported by the manufacturer. As of 2010, the ACA expanded the types of entities eligible to receive discounted 340B pricing, although, under the current state of the law, with the exception of children's hospitals, these newly eligible entities will not be eligible to receive discounted 340B pricing on orphan drugs. In addition, as 340B drug pricing is determined based on AMP and Medicaid rebate data, the revisions to the Medicaid rebate formula and AMP definition described above could cause the required 340B discount to increase.

As noted above, the marketability of any products for which we receive regulatory approval for commercial sale may suffer if the government and third-party payors fail to provide coverage and reimbursement. Obtaining coverage and reimbursement for newly approved drugs and biologics is a time-consuming and costly process, and

coverage may be more limited than the purposes for which a drug is approved by the FDA or comparable foreign regulatory authorities. Assuming coverage is obtained for a given product by a third-party payor, the resulting reimbursement payment rates may not be adequate or may require co-payments that patients find unacceptably high. Additionally, coverage policies and third-party reimbursement rates may change at any time. Patients who are prescribed medications for the treatment of their conditions, and their prescribing physicians, generally rely on third-party payors to reimburse all or part of the costs associated with their prescription drugs. Patients are unlikely to use products unless coverage is provided and reimbursement is adequate to cover all or a significant portion of the cost of prescribed products.

In addition, in some foreign countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. For example, the EU provides options for its member states to restrict the range of medicinal drugs for which their national health insurance systems provide reimbursement and to control the prices of medicinal drugs for human use. A member state may approve a specific price for the medicinal drug or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal drug on the market. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical drugs will allow favorable reimbursement and pricing arrangements for any of our drugs. Historically, drugs launched in the EU do not follow price structures of the U.S. and generally tend to be significantly lower.

Healthcare Reform

In the United States, there have been and continue to be a number of legislative initiatives to contain healthcare costs. The Affordable Care Act, for example, enacted in 2010, has had a significant impact on the health care industry. The Affordable Care Act expanded coverage for the uninsured while at the same time containing overall healthcare costs. With regard to pharmaceutical products, the Affordable Care Act, among other things, increased the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extended the rebate program to individuals enrolled in Medicaid managed care organizations, and established annual fees and taxes on manufacturers of certain branded prescription drugs.

In August 2022, the Inflation Reduction Act of 2022, or the IRA, was signed into law. The IRA includes several provisions that may impact our business, depending on how various aspects of the IRA are implemented. Provisions that may impact our business include a $2,000 out-of-pocket cap for Medicare Part D beneficiaries, the imposition of new manufacturer financial liability on most drugs in Medicare Part D, permitting 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, requiring companies to pay rebates to Medicare for drug prices that increase faster than inflation, and delay until January 1, 2032 the implementation of the HHS rebate rule that would have limited the fees that pharmacy benefit managers can charge. 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 orphan 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 effects of the IRA on our business and the healthcare industry in general is not yet known.

In addition, other legislative and regulatory changes have been proposed and adopted in the United States since the ACA was enacted:

- On August 2, 2011, the Budget Control Act of 2011, and subsequent legislation, among other things, included aggregate reductions of Medicare payments to providers of 2% per fiscal year. These reductions went into effect on April 1, 2013 and, due to subsequent legislative amendments to the statute, will remain in effect through 2031.

- On May 23, 2019, CMS published a final rule to allow Medicare Advantage Plans the option of using step therapy for Part B drugs beginning January 1, 2020.

- The Creating and Restoring Equal Access to Equivalent Samples Act, or 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.

In addition, there have been several changes to the 340B drug pricing program, which imposes ceilings on prices that drug manufacturers can charge for medications sold to certain health care facilities. On November 3, 2023, the U.S. District Court of South Carolina issued an opinion in Genesis Healthcare Inc. v. Becerra et al. that may lead to an expansion of the scope of patients eligible to access prescriptions at 340B pricing. The outcome of this judicial proceeding is uncertain. We continue to review developments impacting the 340B program.

There has also been increasing legislative and enforcement interest in the United States with respect to drug pricing practices. Specifically, there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several U.S. Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, and review the relationship between pricing and manufacturer patient programs. At a federal level, President Trump reversed some of President Biden's executive orders including rescinding Executive Order 14087 entitled "Lowering Prescription Drug Costs for Americans." President Trump may issue new executive orders designed to impact drug pricing. A number of these and other proposed measures may require authorization through additional legislation to become effective. Congress and the Trump administration have indicated that they will continue to seek new legislative measures to control drug costs.

We expect that additional U.S. federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that the U.S. Federal Government will pay for healthcare drugs and services, which could result in reduced demand for our drug candidates or additional pricing pressures.

Individual states in the U.S. have also become increasingly active in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or reimbursement constraints, discounts, restrictions on certain drug access, marketing cost disclosure, comprehensive price transparency disclosure requirements, and designed to encourage importation from other countries and bulk purchasing. Legally mandated price controls on payment amounts by third-party payors or other restrictions could harm our business, financial condition, results of operations and prospects. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. This could reduce the ultimate demand for our drugs or put pressure on our drug pricing, which could negatively affect our business, financial condition, results of operations and prospects.

In addition, in some foreign countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. Many foreign countries' health authorities are authorized to restrict the range of medicinal drugs for which their national health insurance systems provide reimbursement to control the prices of medicinal drugs for human use. In addition, countries may approve a specific price for the medicinal drug or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the drug on the market. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical drugs will allow favorable reimbursement and pricing arrangements for any of our drugs. Historically, drugs launched in Europe and elsewhere globally do not follow price structures of the U.S. and generally tend to be significantly lower. More recently, developments in Europe include reforms to national reimbursement and pricing in Germany, France, Italy and the UK, that are expected to increase pressure on prices. For example, the German Federal Ministry of Health announced the SHI Financial Stabilisation Act which includes an extension of price moratorium for another 4 years, increases manufacturer mandatory discounts, and other measures intended to generate savings. Additionally, there is increased interest in cross-border collaboration on technology assessments, data/knowledge sharing, and group price negotiations as a means of controlling costs, such as the Beneluxa Initiative which includes Belgium, Luxembourg, the Netherlands, Austria and Ireland, and also the Nordic Pharmaceutical Forum.

Other Healthcare Laws

We may also be subject to healthcare regulation and enforcement by the federal government and the states and foreign governments where we may market our drug candidates, if approved. These laws include, without limitation, fraud and abuse, false claims, privacy and data security, and sunshine laws and regulations. Many of which differ from each other in significant ways, thus complicating compliance efforts.

For example, in the United States, the federal Anti-Kickback Statute prohibits, among other things, any person from knowingly and willfully offering, soliciting, receiving or paying remuneration, directly or indirectly, to induce either the referral of an individual, for an item or service or the purchasing or ordering of a good or service, for which payment may be made under federal healthcare programs such as the Medicare and Medicaid programs. The government has enforced the Anti-Kickback Statute to reach large settlements with healthcare companies based on sham consulting and other financial arrangements with physicians. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal False Claims Act or civil monetary penalties. The majority of states also have anti-kickback laws, which establish similar prohibitions and, in some cases, may apply to items or services reimbursed by any third-party payor, including commercial insurers.

In addition, the federal civil and criminal False Claims Act prohibits, among other things, knowingly presenting or causing the presentation of a false, fictitious or fraudulent claim for payment to the U.S. government. Actions under the False Claims Act may be brought by the Attorney General or as a qui tam action by a private individual in the name of the government. Violations of the False Claims Act can result in very significant monetary penalties and treble damages. The federal government is using the False Claims Act, and the accompanying threat of significant liability, in its investigation and prosecution of pharmaceutical and biotechnology companies throughout the U.S., for example, in connection with the promotion of drug for unapproved uses and other sales and marketing practices. Manufacturers can be held liable under the federal False Claims Act even when they do not submit claims directly to government payors if they are deemed to "cause" the submission of false or fraudulent claims. The federal False Claims Act also permits a private individual acting as a "whistleblower" to bring an action on behalf of the federal government alleging violations of the federal False Claims Act and to share in any monetary recovery. In September 2024, a federal district court in Florida ruled that the qui tam provision of the False Claims Act is unconstitutional, for violating the Constitution's Appointments Clause. The U.S. government has appealed that decision. But if the decision is upheld and/or other federal courts adopt its reasoning, those decisions could reduce the number of False Claims Act investigations and lawsuits. The government has obtained multi-million and multi-billion dollar settlements under the False Claims Act in addition to individual criminal convictions under applicable criminal statutes. Given the significant size of actual and potential settlements, it is expected that the government will continue to devote substantial resources to investigating healthcare providers' and manufacturers' compliance with applicable fraud and abuse laws.

HIPAA also created new federal criminal statutes that prohibit among other actions, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private third-party payors, knowingly and willfully embezzling or stealing from a healthcare benefit program, willfully obstructing a criminal investigation of a healthcare offense, and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.

HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH and their respective implementing regulations, including the Final Omnibus Rule published in January 2013, which impose requirements on certain covered healthcare providers, health plans, and healthcare clearinghouses as well as their respective business associates, independent contractors or agents of covered entities, that perform services for them that involve the creation, maintenance, receipt, use, or disclosure of, individually identifiable health information relating to the privacy, security and transmission of individually identifiable health information. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys' fees and costs associated with pursuing federal civil actions. In addition, numerous states have enacted comprehensive data privacy laws that impact our business in

different and inconsistent ways, and there may be additional federal, state and non-U.S. laws which govern the privacy and security of health and other personal information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

We may be subject to consumer protection and unfair competition laws enacted at the country and state level, which broadly regulate marketplace activities and activities that potentially harm consumers.

There has also been a recent global trend of increased regulation of payments made to physicians and other healthcare providers. For example, in the United States, the Affordable Care Act, among other things, imposes reporting requirements on drug manufacturers for payments made by them to physicians, certain other licensed healthcare practitioners and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Failure to submit required information may result in civil monetary penalties for all payments, transfers of value or ownership or investment interests that are not timely, accurately and completely reported in an annual submission. Drug manufacturers are required to submit annual reports to the CMS, which publicly posts the data on its website. Certain countries as well as U.S. states also mandate implementation of compliance programs, impose restrictions on drug manufacturer marketing practices and/or require the tracking and reporting of gifts, compensation and other remuneration to physicians.

We are also subject to federal price reporting laws, which require manufacturers to calculate and report complex pricing metrics to government programs, where such reported prices may be used in the calculation of reimbursement and/or discounts on approved products. Likewise, we must comply with federal consumer protection and unfair competition laws. These laws broadly regulate marketplace activities and activities that potentially harm consumers.

Additionally, we may be subject to analogous state and foreign laws and regulations, such as fraud and abuse, anti-kickback, false claims laws, consumer protection, and unfair competition laws, which may apply to pharmaceutical business practices, including but not limited to, research, distribution, sales, and marketing arrangements as well as submitting claims involving healthcare items or services reimbursed by any third-party payor, including commercial insurers. Such laws are enforced by various governmental agencies and through private actions. Some laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant country-level government compliance guidance that otherwise restricts payments that may be made to healthcare providers and other potential referral sources, require drug manufacturers to report information related to pricing and marketing information, such as the tracking and reporting of gifts, compensations, and other remuneration and items of value provided to physicians and other healthcare providers and entities, require the registration of pharmaceutical sales representatives, and restrict marketing practices or require disclosure of marketing expenditures.

Human Capital Resources

We provide an inclusive, collaborative and safe work environment for our employees, who enjoy innovative work and development opportunities. As of January 31, 2025, we had 649 full- and part-time employees globally, approximately 569 of whom are employed in the U.S. and approximately 80 are employed in foreign countries. Of those employees, 350 are engaged in research and development activities and 212 hold Doctorate or Master's degrees. To allow us flexibility in meeting varying workflow demands, we also engage consultants and temporary workers when needed.

We believe our employees are among the most important assets to our company and are key to achieving our goals and expectations. Accordingly, we focus significant attention on attracting and retaining talented individuals. Our management teams and function leaders regularly review employee engagement and satisfaction surveys and monitor employee turnover rates. To recruit and retain our employees, we offer robust compensation packages, including competitive base pay, incentive compensation and equity programs, and provide a broad range of benefits, including 401(k) plan (pension outside the U.S.), healthcare and insurance benefits, paid time off, paid family and medical leave, flexible work schedules, and various innovative health and wellness programs. In addition, we are committed to the professional development of our employees, who can take advantage of various learning opportunities, such as our mentorship, lunch & learn and skill builder accelerator programs, as well as various training programs.

None of our U.S. employees are represented by a labor union or covered by a collective bargaining agreement. Outside the U.S., our employees in France, Germany and Italy, respectively, are covered by a collective bargaining agreement applicable to our industry as required by applicable local law. We consider our relationship with our employees to be good.

Corporate Information

We were incorporated in the State of Delaware in October 2008 under the name ImmunoCo, Inc. In May 2010, we changed our name to Hoyle Pharmaceuticals, Inc., and in June 2011, we changed our name again to Blueprint Medicines Corporation. Our principal executive offices are located at 45 Sidney Street, Cambridge, Massachusetts 02139, and our telephone number is (617) 374-7580.

Information Available on the Internet

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

Investors and others should note that we announce material information to our investors using one or more of the following: SEC filings, press releases, public conference calls and webcasts and our corporate website (https://www.blueprintmedicines.com/), including without limitation the "Investors & Media" and "Presentations & Publications" sections of our website. We use these channels, as well as social media channels such as "X" (formerly Twitter @BlueprintMeds) and LinkedIn, to communicate with the public about our company, our business, our approved drugs and drug candidates and other matters. It is possible that the information we post on our corporate website or other social media could be deemed to be material information. Therefore, we encourage investors, the media, and others interested in our company to review the information we post on the "Investors & Media" and "Presentations & Publications" sections of our corporate website and on the social media channels listed on the "Investors & Media" section of our corporate website. The contents of our corporate website and social media channels are not, however, a part of this Annual Report on Form 10-K.

Item 1A. Risk Factors

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

Risks Related to Commercialization

We continue to grow as a commercial company and the marketing and sale of AYVAKIT/AYVAKYT or any future approved drugs may be unsuccessful or less successful than anticipated.

We have had two approved precision therapies, AYVAKIT/AYVAKYT and GAVRETO. While we have been commercializing AYVAKIT in the U.S. and AYVAKYT in Europe and prior to the sale of the related assets to Rigel

pursuant to the Rigel Agreement, co-commercializing GAVRETO with Roche in the U.S., we only became a commercial company in 2020, and our track record of demonstrating our ability to successfully overcome the many risks and uncertainties encountered by companies commercializing drugs in the biopharmaceutical industry is somewhat limited. 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 key collaborations;
- 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, 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, 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, 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, GIST, chronic urticaria, asthma, allergic rhinitis, mast cell activation syndrome (MCAS), and other allergy/inflammation indications 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, healthcare claims data, 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 diseases and the number of patients may turn out to be lower than expected. For example, new claims data and epidemiology data suggest that SM prevalence is greater than previously thought; however, other future studies could contradict such findings. 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 our areas of focus, including allergy/inflammation and hematology/oncology. 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, which could be more successful than ours. 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 Alys Pharmaceuticals Inc., Cogent Biosciences, Inc. and Hoth Therapeutics, Inc. Avapritinib and elenestinib may face non-advanced SM competition from drug candidates in development, including those being developed by AB Science S.A., Alys Pharmaceuticals Inc., Celldex Therapeutics, Inc., Cogent Biosciences, Inc., Hoth Therapeutics, Inc., Invea Therapeutics Inc., and Telios Pharma 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, Cogent Biosciences, Inc., Deciphera Pharmaceuticals, LLC, Exelixis, Inc., Ningbo Tai Kang Medical Technology Co. Ltd. and Xencor, Inc.

We are developing BLU-808 for chronic urticaria, asthma, allergic rhinitis/conjunctivitis, MCAS, and other allergy/inflammation indications, which if approved, will face competition from omalizumab developed by Genentech and Novartis. In addition, BLU-808 may face competition from drug candidates in development, including those developed by Alivexis, Inc., Allakos Inc., Amgen Inc., AstraZeneca plc, Celldex Therapeutics, Inc., Eli Lilly, Enanta Pharmaceuticals, Inc, Escient Pharmaceuticals, Inc., Evommune, Inc, Hangshou Highlightll Pharma, Incyte Corp., Jasper Therapeutics, Inc., Leo Pharma A/S, LongBio Pharma, Novartis AG, Regeneron Pharmaceuticals, Inc., Sanofi S.A., Third Harmonic Bio, Inc, Taiho Pharmaceutical Co., LTD, and United BioPharma.

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 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.

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 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, 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. 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;
- 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. 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.

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. 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, 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 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 expect to rely on third-party contract research organizations, or 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 the 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, the FDA has stated that it generally intends to issue a complete response letter. Further, if there is inadequate information to make a determination on the acceptability of a facility, the FDA may defer action on the application until an inspection can be completed. 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, interpretations or agency discretion during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted new drug application, or NDA, for a drug candidate, may cause delays in the approval or rejection of an application. Moreover, the U.S. Supreme Court's July 2024 decision to overturn prior established case law giving deference to regulatory agencies' interpretations of ambiguous statutory language has introduced uncertainty regarding the extent to which the FDA's regulations, policies, and decisions may become subject to increasing legal challenges, delays, and/or changes. Additionally, 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;
- 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, 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, 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.

Currently, federal agencies in the U.S. are operating under a continuing resolution that is set to expire on March 14, 2025. Without appropriation of additional funding to federal agencies, our business operations related to our product development activities for the U.S. market could be impacted. 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 investigational and approved 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, such as off-target toxicity, 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 have later been found to cause side effects that prevented further development of the compound.

Further, clinical trials by their nature utilize a sample of the potential patient population. With a limited number of patients and limited duration of exposure, rare and severe side effects of our drugs or drug candidates may only be uncovered with a significantly larger number of patients exposed to the drugs or drug candidate. If we or others identify undesirable side effects caused by any of our approved drugs or drug candidates (or any other similar drugs) after marketing approval, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw or limit their approval of such drug;
- regulatory authorities may require the addition of labeling statements, such as a "boxed" warning or a contraindication;
- we may be required to create a medication guide outlining the risks of such side effects for distribution to patients;
- we may be required to change the way such drug is distributed or administered, conduct additional clinical trials or change the labeling of such drug;
- regulatory authorities may require a Risk Evaluation and Mitigation Strategy, or REMS, plan to mitigate risks, which could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools;
- we may be subject to regulatory investigations and government enforcement actions;
- we may decide to remove such drug from the marketplace;
- we could be sued and held liable for injury caused to individuals exposed to or taking our drugs and drug candidates; and
- our reputation may suffer.

We believe that any of these events could prevent us from achieving or maintaining market acceptance of the affected drugs or drug candidates and could substantially increase the costs of commercializing our approved drugs and drug candidates, if approved, and significantly impact our ability to successfully commercialize our approved drugs and drug candidates and generate revenues.

A 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 granted breakthrough therapy designation to AYVAKIT for the treatment of certain patients with GIST, advanced SM, and moderate to severe indolent SM and RET-altered cancers. The FDA also granted fast track designation to BLU-782 for the treatment of FOP, which we have out licensed to Clementia.

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, or 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 the Food and Drug Omnibus Reform Act of 2022 (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.

We may be unsuccessful in obtaining or may be unable to maintain the benefits associated with orphan drug designation, including the potential for market exclusivity.

The FDA has granted orphan drug designation to avapritinib for the treatment of GIST and the treatment of mastocytosis, to pralsetinib for the treatment of RET-rearranged NSCLC, JAK1/2-positive NSCLC or TRKC-positive NSCLC and to fisogatinib for the treatment of HCC. In addition, the European Commission, or EC, has granted orphan medicinal product designation to avapritinib for the treatment of GIST and the treatment of mastocytosis. Both the FDA and EC have granted orphan drug designation to elenestinib for 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 EC 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, in order to obtain orphan designation, there must be no satisfactory method of diagnosis, prevention, or treatment authorized for marketing in the EU for the applicable orphan

condition (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, at the end of the fifth year, the 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 small molecule inhibitors and targeted protein degraders, and design highly potent and selective therapeutic candidates where there is an opportunity to impact large patient populations. 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. However, we may not be able to identify any drug candidates for our pipeline through such transactions.

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-808, elenestinib, 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 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, or 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. 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.

The Drug Supply Chain Security Act, or DSCSA, was enacted in 2013 with the aim of building an electronic system to identify and trace certain prescription drugs and biologics distributed in the United States. The DSCSA mandates phased-in and resource-intensive obligations for pharmaceutical manufacturers, wholesale distributors, and dispensers over a 10-year period that culminated in November 2023. The FDA established a one-year stabilization period until November 2024 for trading partners to continue to build and validate interoperable systems and processes to meet certain requirements of the DSCSA. In late 2024, the FDA announced it is allowing a further exemption period for eligible trading partners who have successfully completed or made documented efforts to complete data connections with their immediate trading partners, but still face challenges exchanging data. The exemption period for eligible manufacturers and repackagers now extends until May 27, 2025. The DSCSA requirements include the quarantine and prompt investigation of a suspect product, to determine if it is illegitimate, notifying trading partners and the FDA of any illegitimate product, and compliance with product tracking and tracing requirements. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP requirements and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance.

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*".

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 U.S., 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 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 U.S. 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 addition, both Congress and

the Trump administration have indicated that they will continue to seek new legislative measures to control drug costs. See section entitled *"Business – Healthcare Reform."*

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. For example, by Executive Order, FDA works with states and Indian Tribes that propose to develop Section 804 Importation Programs in accordance with the Medicare Prescription Drug, Improvement, and Modernization Act of 2003. The FDA released implementing regulations on September 24, 2020, which went into effect on November 30, 2020, providing guidance for states to build and submit importation plans for drugs from Canada. On January 5, 2024, the FDA issued to Florida the first approval for a state importation plan. Several states now have pending applications with the FDA, including Colorado, Maine, New Hampshire and New Mexico. If successfully implemented, importation of drugs from Canada may materially and adversely affect the price we receive for any of our product candidates. In addition, a handful of states have passed legislation to establish state drug importation programs. Legislation or regulations allowing the reimportation of drugs, if enacted and successfully implemented, could decrease the price we receive for any products that we may develop and adversely affect our future revenues and prospects for profitability.

The Creating and Restoring Equal Access to Equivalent Samples Act, or 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.

We cannot predict the initiatives that may be adopted in the future. The continuing efforts of the government, insurance companies, managed care organizations and other payors of healthcare services to contain or reduce costs of healthcare and/or impose price controls may adversely affect:

- the demand for AYVAKIT/AVAKYT and any current and future drug candidates, for which we receive marketing approval;
- our ability to set a price that we believe is fair for our approved products;
- our ability to generate revenue and achieve or maintain profitability;
- the level of taxes that we are required to pay; and
- the availability of capital.

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), as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 (HITECH), the Physician Payment Sunshine Act, 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*".

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. In addition, we have a co-pay support program for commercially insured patients. Government enforcement agencies have shown increased interest in pharmaceutical companies' product and patient assistance programs, including reimbursement support services, and a number of investigations into these programs have resulted in significant civil and criminal settlements. In addition, at least one insurer has directed its network pharmacies to no longer accept co-pay coupons for certain specialty drugs the insurer identified. Our co-pay coupon programs could become the target of similar insurer actions. In addition, in November 2013, the CMS issued guidance to the issuers of qualified health plans sold through the ACA's marketplaces encouraging such plans to reject patient cost-sharing support from third parties and indicating that the CMS intends to monitor the provision of such support and may take regulatory action to limit it in the future. The CMS subsequently issued a rule requiring individual market qualified health plans to accept third-party premium and cost-sharing payments from certain government-related entities. In September 2014, the Office of the Inspector General, or OIG, of the HHS issued a Special Advisory Bulletin warning manufacturers that they may be subject to sanctions under the federal anti-kickback statute and/or civil monetary penalty laws if they do not take appropriate steps to exclude Part D beneficiaries from using co-pay coupons. Accordingly, companies exclude these Part D beneficiaries from using co-pay coupons. It is possible that changes in insurer policies regarding co-pay coupons and/or the introduction and enactment of new legislation or regulatory action could restrict or otherwise negatively affect these patient support programs, which could result in fewer patients using affected products, and therefore could have a material adverse effect on our sales, business, and financial condition.

Third party patient assistance programs that receive financial support from companies have become the subject of enhanced government and regulatory scrutiny. The OIG has established guidelines that suggest that it is lawful for pharmaceutical manufacturers to make donations to charitable organizations who provide co-pay assistance to Medicare patients, provided that such organizations, among other things, are bona fide charities, are entirely independent of and not controlled by the manufacturer, provide aid to applicants on a first-come basis according to consistent financial criteria and do not link aid to use of a donor's product. However, donations to patient assistance programs have received some negative publicity and have been the subject of multiple government enforcement actions, related to allegations regarding their use to promote branded pharmaceutical products over other less costly alternatives. Specifically, in recent years, there have been multiple settlements resulting out of government claims challenging the legality of their patient assistance programs under a variety of federal and state laws. It is possible that we may make grants to independent charitable foundations that help financially needy patients with their premium, co-pay, and co-insurance obligations.

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 are found not to be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government-funded healthcare programs.

If we fail to comply with our reporting and payment obligations under the Medicaid Drug Rebate Program or other governmental pricing programs, we could be subject to additional reimbursement requirements, penalties, sanctions and fines, which could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

We participate in the Medicaid Drug Rebate program, the 340B drug pricing program, and the Department of Veterans Affairs (VA)'s Federal Supply Schedule (FSS) pricing program. Under the Medicaid Drug Rebate program, we are required to pay a rebate to each state Medicaid program for our covered outpatient drugs that are dispensed to Medicaid beneficiaries and paid for by a state Medicaid program as a condition of having federal funds being made available to the states for our drugs under Medicaid and Medicare Part B. Those rebates are based on pricing data reported by us on a monthly and quarterly basis to CMS, the federal agency that administers the Medicaid Drug Rebate program. These data include the average manufacturer price and, in the case of innovator products, the best price for each drug which, in general, represents the lowest price available from the manufacturer to any entity in the U.S. in any pricing structure, calculated to include all sales and associated rebates, discounts and other price concessions. Our failure to comply with these price reporting and rebate payment obligations could negatively impact our financial results.

The ACA made significant changes to the Medicaid Drug Rebate program. CMS issued a final regulation, which became effective on April 1, 2016, to implement the changes to the Medicaid Drug Rebate program under the ACA. The issuance of the final regulation has increased and will continue to increase our costs and the complexity of compliance, has been and will continue to be time-consuming to implement, and could have a material adverse effect on our results of operations, particularly if CMS challenges the approach we take in our implementation of the final regulation.

Federal law requires that any company that participates in the Medicaid Drug Rebate program also participate in the Public Health Service's 340B drug pricing program in order for federal funds to be available for the manufacturer's drugs under Medicaid and Medicare Part B. The 340B program requires participating manufacturers to agree to charge statutorily defined covered entities no more than the 340B "ceiling price" for the manufacturer's covered outpatient drugs. These 340B covered entities include a variety of community health clinics and other entities that receive health services grants from the Public Health Service, as well as hospitals that serve a disproportionate share of low-income patients. The 340B ceiling price is calculated using a statutory formula based on the average manufacturer price and Medicaid rebate amount for the covered outpatient drug as calculated under the Medicaid Drug Rebate program, and in general, products subject to Medicaid price reporting and rebate liability are also subject to the 340B ceiling price calculation and discount requirement. Any additional future changes to the definition of average manufacturer price and the Medicaid rebate amount under the ACA, other legislation, or in regulation could affect our 340B ceiling price calculations and negatively impact our results of operations.

The Health Resources and Services Administration, or HRSA, which administers the 340B program, issued a final regulation regarding the calculation of the 340B ceiling price and the imposition of civil monetary penalties on manufacturers that knowingly and intentionally overcharge covered entities, which became effective on January 1, 2019. We also are required to report our 340B ceiling prices to HRSA on a quarterly basis. Implementation of the civil monetary penalties regulation and the issuance of any other final regulations and guidance could affect our obligations under the 340B program in ways we cannot anticipate. In addition, legislation may be introduced that, if passed, would further expand the 340B program to additional covered entities or would require participating manufacturers to agree to provide 340B discounted pricing on drugs used in the inpatient setting.

Pricing and rebate calculations vary across products and programs, are complex, and are often subject to interpretation by us, governmental or regulatory agencies and the courts. In the case of our Medicaid pricing data, if we become aware that our reporting for a prior quarter was incorrect, or has changed as a result of recalculation of the

pricing data, we are obligated to resubmit the corrected data for up to three years after those data originally were due. Such restatements and recalculations increase our costs for complying with the laws and regulations governing the Medicaid Drug Rebate program and could result in an overage or underage in our rebate liability for past quarters. Price recalculations also may affect the ceiling price at which we are required to offer our products under the 340B program or could require us to issue refunds to 340B covered entities.

Significant civil monetary penalties can be applied if we are found to have knowingly submitted any false pricing information to CMS, or if we fail to submit the required price data on a timely basis. Such conduct also could be grounds for CMS to terminate our Medicaid drug rebate agreement, in which case federal payments may not be available under Medicaid or Medicare Part B for our covered outpatient drugs. Significant civil monetary penalties also can be applied if we are found to have knowingly and intentionally charged 340B covered entities more than the statutorily mandated ceiling price. We cannot assure you that our submissions will not be found by CMS or HRSA to be incomplete or incorrect.

In order to be eligible to have our products paid for with federal funds under the Medicaid and Medicare Part B programs and purchased by certain federal agencies and grantees, as noted above, we participate in the VA's FSS pricing program. As part of this program, we are obligated to make our products available for procurement on an FSS contract under which we must comply with standard government terms and conditions and charge a price that is no higher than the statutory Federal Ceiling Price, or FCP, to four federal agencies (the VA, U.S. Department of Defense, or DOD, Public Health Service, and the U.S. Coast Guard). The FCP is based on the Non-Federal Average Manufacturer Price, or Non-FAMP, which we calculate and report to the VA on a quarterly and annual basis. Pursuant to applicable law, knowing provision of false information in connection with a Non-FAMP filing can subject a manufacturer to significant penalties for each item of false information. These obligations also contain extensive disclosure and certification requirements.

We also participate in the Tricare Retail Pharmacy program, under which we pay quarterly rebates on utilization of innovator products that are dispensed through the Tricare Retail Pharmacy network to Tricare beneficiaries. The rebates are calculated as the difference between the annual Non-FAMP and FCP. We are required to list our covered products on a Tricare Agreement in order for these products to be eligible for DOD formulary inclusion. If we overcharge the government in connection with our FSS contract or Tricare Agreement, whether due to a misstated FCP or otherwise, we are required to refund the difference to the government. Failure to make necessary disclosures and/or to identify contract overcharges can result in allegations against us under the FCA and other laws and regulations. Unexpected refunds to the government, and responding to a government investigation or enforcement action, would be expensive and time-consuming, and could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

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, for example, 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 may never become and remain profitable.

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 December 31, 2024, we have received an aggregate of $3.9 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, $1.1 billion in upfront payments and milestone payments under our collaborations with CStone and Zai Lab, our now terminated collaborations with Roche, our license agreement with Clementia, our agreement with Rigel, and our former collaboration with Alexion Pharma Holding, or Alexion and $400.0 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 $67.1 million for the year ended December 31, 2024. Our net losses were $507.0 million and $557.5 million for the years ended December 31, 2023 and 2022, respectively. As of December 31, 2024, we had an accumulated deficit of $2,407.0 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;
- 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 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 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. 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;
- the success of our collaborations with CStone, and our license agreements with Clementia, IDRx (which has recently entered into an agreement to be acquired by GSK plc) and our agreement with Rigel, 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 if needed 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 collaboration with CStone and the license agreements with Clementia and IDRx (which recently entered into an agreement to be acquired by GSK plc), the Financing Agreement with Sixth Street Partners, and the Rigel Agreement, which are limited in scope and duration and subject to the achievement of milestones or royalties on sales of licensed products, if any. In addition, we may sell additional shares of our common stock pursuant to our at-the-market (ATM) Facility with Cowen. 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 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.

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. In August 2023, we received tranche A of the senior secured delayed draw term loan facility in the amount of $100.0 million in gross proceeds. In May 2024, we received tranche B of the senior secured delayed draw term loan facility in the amount of $150.0 million in gross proceeds. 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. As borrowings under the facility bear interest at a variable rate, we are exposed to market risk for changes in interest rates.

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, licenses and other agreements with third parties for the development and commercialization of several of our drugs and drug candidates. If such collaborations or arrangements 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, licenses and other agreements with CStone, VantAI, Clementia, and Rigel for the development and commercialization of several of our drugs and drug candidates, and may enter into additional collaborations, licenses and other arrangements with other third parties in the future. The success of these arrangements will depend heavily on the efforts and activities of our collaborators, licensing partners and other contracting parties. Collaborators and other contracting parties generally have significant discretion in determining the efforts and resources that they will apply to these arrangements. 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 or other arrangement regarding clinical development and commercialization matters can lead to delays in the development process or commercializing the applicable drug or drug candidate and, in some cases, termination of the collaboration or other 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, VantAI, Clementia or IDRx (which has recently entered into an agreement to be acquired by GSK plc), 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. The termination became effective on February 22, 2024.

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, or 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 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. 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. As a result, 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 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. Therefore, 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.

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 a marketing authorization application 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 2025.

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 or future legislative proposals in the U.S., such as the previously considered BIOSECURE bill, that, if enacted, could significantly impact our ability to work with 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 discovery platform technology or obtain and maintain patent protection for our technology, drugs and drug candidates or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize technology, drugs and drug candidates similar or identical to ours, and our ability to successfully commercialize our technology, drugs and drug candidates 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 uses 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, processes, 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. 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, drug or drug candidates 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, drugs or drug candidates 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. 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 abbreviated new drug application, or 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 U.S. 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 U.S. 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 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 biotechnology and pharmaceutical companies, our success is heavily dependent on the intellectual property we maintain, particularly patents. Obtaining and enforcing patents in the biotechnology and pharmaceutical 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, or D&O insurance. We may not be able to maintain D&O insurance at a reasonable cost or in an amount adequate to satisfy any liability that may arise. An inability to secure and maintain D&O insurance may make it difficult for us to retain and attract talented and skilled directors and officers to serve our company, which could adversely affect our business. We do not maintain "key person" insurance for any of our executives or other employees.

In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. If we are unable to continue to attract and retain high quality personnel, our ability to pursue our growth strategy will be limited.

We expect to continue hiring qualified development personnel. Recruiting and retaining qualified scientific, clinical, regulatory, manufacturing and sales and marketing personnel is critical to our success. The loss of the services of our executive officers or other key employees could impede the achievement of our research, development and commercialization objectives and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing key employees and executive officers may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval of and commercialize drugs. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. Failure to succeed in clinical trials may make it more challenging to recruit and retain qualified scientific personnel.

We will need to develop and expand our company, and we may encounter difficulties in managing this development and expansion, which could disrupt our operations.

As of January 31, 2025, we had 649 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 increased inflation, increased U.S. trade tariffs and trade disputes with other countries, 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. Additionally, the impacts of the change in the U.S. presidential administration also remains unknown.

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 U.S. 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 cybersecurity incidents or data 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 (including phishing attacks) and other means to affect service reliability and threaten the confidentiality, integrity and availability of information. Cyber-attacks also could include wrongful conduct by employees or vendors, 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 (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. Although our business strategy, results of operations, and financial condition have not, to date, been materially affected by risks from cybersecurity threats, we and third parties upon whom we rely, like other companies in our industry, have, experienced threats and security incidents, including phishing attacks. Such events could 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 cybersecurity incident or data 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 cybersecurity incidents, data breaches, cyberattacks and other related security events.

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 cybersecurity incidents that result in the unauthorized access, release or transfer of sensitive information, including physician data, patient data, or any personally identifiable information, may require that we notify affected stakeholders and 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. Further, our contracts may not contain limitations of liability, and even where they do, there can be no assurance that limitations of liability in our contracts are sufficient to protect us from liabilities, damages, or claims related to our privacy and data security obligations. Although we maintain cyber liability insurance, this insurance may not provide adequate coverage against potential liabilities related to any experienced cybersecurity incident or breach.

Cybersecurity incidents 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.

The use of new and evolving technologies, such as artificial intelligence, in our business may result in spending material resources and presents risks and uncertainties that can impact our business including by posing security and other risks to our confidential and/or proprietary information, including personal information, and as a result we may be exposed to reputational harm and liability.

The increasing use of AI, and machine learning technology in the biopharmaceutical industry presents new risks and challenges. If we enable or offer solutions that draw controversy due to perceived or actual negative societal impact, we may experience brand or reputational harm, competitive harm or legal liability. The use of AI based software may lead to intellectual property risks, including intellectual property infringement and 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. We expect to see increasing government and supranational regulation related to artificial intelligence use and ethics, which may also significantly increase the burden

and cost of research, development and compliance in this area. For example, in Europe, the EU's Artificial Intelligence Act ("AI Act") — which entered into force on August 1, 2024 and, with some exceptions, will begin to apply as of August 2, 2026 — imposes significant obligations on providers and deployers of high-risk artificial intelligence systems, and encourages providers and deployers of artificial intelligence systems to account for EU ethical principles in their development and use of these systems. Furthermore, in the U.S., a number of states have proposed and passed laws regulating various uses of AI, and federal regulators have issued guidance affecting the use of AI in regulated sectors. If we develop or use AI systems that are governed by these AI laws, it may necessitate ensuring higher standards of data quality, transparency, and human oversight, as well as adhering to specific and potentially burdensome and costly ethical, accountability, and administrative requirements.

The rapid evolution of artificial intelligence will require the application of significant resources to design, develop, test and maintain our products and services to help ensure that artificial intelligence is implemented in accordance with applicable law and regulation and in a socially responsible manner and to minimize any real or perceived unintended harmful impacts. Our vendors may in turn incorporate artificial intelligence tools into their offerings, and the providers of these artificial intelligence tools may not meet existing or rapidly evolving regulatory or industry standards, including with respect to privacy and data security. Further, bad actors around the world use increasingly sophisticated methods, including the use of artificial intelligence, to engage in illegal activities involving the theft and misuse of personal information, confidential information and intellectual property. Any of these effects could damage our reputation, result in the loss of valuable property and information, cause us to breach applicable laws and regulations, and adversely impact our business.

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 victims of cyber-security incident or 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 remain 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. Additional regulations and guidance requiring data localization and restrictions on data transfer increase complexity for global corporations. 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, in Europe, the European General Data Protection Regulation 2016/679, which is commonly referred to as 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 imposes data protection obligations on processors and controllers of personal data, including, for example, disclosures about how personal information is to be used, stricter requirements for processing special category data (such as health data), having a valid legal basis or condition to process personal data, maintaining records

of our processing activities and documenting 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 are put in place to safeguard personal data and onerous obligations on services providers. Penalties under the GDPR include fines of up to €20 million or 4% of total worldwide annual turnover, whichever is higher. 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.

Further to the UK's exit from the European Union on January 31, 2020, the UK 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 currently still 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. Although the UK is regarded as a third country under the EU's GDPR, the European Commission 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. Likewise The UK government has confirmed that personal data transfers from the UK to the EEA remain free flowing. The UK Government has introduced a Data Protection and Digital Information Bill which failed in the UK legislative process. A new Data (Use and Access) Bill (UK Bill) has been introduced into parliament. If passed, the final version of the UK Bill may have the effect of further altering the similarities between the UK and EEA data protection regime and threaten the UK Adequacy Decision from the European Commission. This may lead to additional compliance costs and could increase our overall risk. The respective provisions and enforcement of the EU GDPR and UK GDPR may further diverge in the future and create additional regulatory challenges and uncertainties.

Given the breadth and depth of changes in data protection obligations, 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 UK or EEA.

Further, European data protection laws also regulates the transfer of personal data from the EEA, the UK and Switzerland to third countries that are not considered to provide adequate protections to personal data. On June 4, 2021, the European Commission, or the EC, issued Standard Contractual Clauses, or the SCCs, for data transfers from controllers or processors in the EEA (or otherwise subject to the EU GDPR) to controllers or processors established outside the EEA (and not subject to the EU GDPR). The UK is not subject to the EC's SCCs but has published its own standard clauses, the International Data Transfer Agreement, which enables transfers from the UK. We will be required to implement these new safeguards when conducting restricted data transfers under the EU GDPR and UK GDPR and doing so will require significant effort and cost. Where relying on the SCCs or UK IDTA for data transfers, we may also be required to carry out transfer impact assessments to assess whether the recipient is subject to local laws which allow public authority access to personal data.

On July 10, 2023, the EU adopted an adequacy decision for a new "Data Privacy Framework," which replaces the Privacy Shield, which the European Court of Justice invalidated in 2020 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 have registered and have active membership under the Framework, allowing for transfer of HR and non-HR data from Switzerland, UK and EEA member states. We will be required to maintain 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.

While we have taken steps to mitigate the impact on us with respect to transfers of data, such as registering with the U.S. governing bodies managing the Data Privacy Framework, and implementing the SCCs where necessary in new contracts with our service providers, customers, subsidiaries, the validity of these transfer mechanisms remains uncertain. The previous data transfer mechanisms providing adequacy to enable cross-border transfers between the US and the EEA have been invalidated, and the Data Privacy Framework has already been challenged in several

jurisdictions. 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 Europe 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, the Swiss federal Parliament enacted a revised version of the FADP which came into effect in September 2023. The new version of the FADP aligns Swiss data protection law with the GDPR. We have updated our agreements to reflect the new requirements per the FADP, but further modifications or changes may require revisiting these agreements.

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. It is unclear whether and/or when the Draft Regulation will enter into force.

Further, the EU Artificial Intelligence Act or AI Act came into force on August 1, 2024 with provisions effective between 2025 and 2026. The AI Act prescribes requirements on companies that publish, deploy or use AI systems to perform assessments and to ensure governance of process to ensure the transparency, fairness and accuracy of AI systems.

Preparing for and complying with the evolving application of the GDPR, national laws in Switzerland and the UK, ePrivacy Regulation (if and when it becomes effective) and the EU AI Act 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 US federal and state laws relating to privacy and data security. At the federal level, failing to take appropriate steps to keep consumers' personal information secure may constitute unfair acts or practices in or affecting commerce in violation of Section 5(a) of the Federal Trade Commission Act (the FTCA), 15 U.S.C § 45(a). The FTC expects a company's data security measures to be reasonable and appropriate in light of the sensitivity and volume of consumer information it holds, the size and complexity of its business and the cost of available tools to improve security and reduce vulnerabilities. Through executive and legislative action, the federal government has also taken steps to restrict data transactions involving certain sensitive data categories – including health data, genetic data, and biospecimens – with persons affiliated with China, Russia, and other countries of concern.

In addition, certain state laws govern the privacy and security of personal information. For example, the California Consumer Privacy Act (CCPA), which took effect on January 1, 2020 and imposed sweeping privacy and security obligations on many companies doing business in California that meet one of three thresholds 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 was amended by the California Privacy Rights Act (CPRA) which became effective on January 1, 2023. The CPRA imposed additional obligations on companies covered by the legislation and significantly modified the CCPA, including by expanding consumers' rights with respect to certain sensitive personal information. The CPRA also created a new state agency that is vested with authority to implement and enforce the CCPA. The effects of the CCPA are significant and requires us to incur substantial costs and expenses in an effort to comply and increase our potential exposure to regulatory enforcement and/or litigation.

In addition to the CCPA, similar laws have been passed in numerous other states, reflecting a trend toward more stringent privacy legislation in the U.S., which may accelerate. Further, other states have proposed new privacy laws which, 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 would 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.

Furthermore, a smaller number of states have passed or are considering laws that are specifically focused upon health privacy, such as Washington's My Health My Data Act which took effect on March 31, 2024 and regulates the collection and sharing of health information. This law also has a private right of action, which further increases the relevant compliance risk. Connecticut and Nevada have also passed similar laws regulating consumer health data. In addition, other states have proposed and/or passed legislation that regulates the privacy and/or security of certain specific types of information. For example, a small number of states have passed laws that regulate biometric data specifically.

These various privacy and security laws may impact our business activities, including our identification of research subjects, relationships with business partners and ultimately the marketing and distribution of our products. The effects of the CCPA and other state and federal privacy laws are significant and may require us to modify our data processing practices and policies and to incur substantial costs and potential liability in an effort to comply with such legislation. State laws are changing rapidly and there is discussion in the U.S. Congress of a new comprehensive federal data privacy law to which we may become subject, if enacted.

The widespread use of generative AI and natural language processing tools have significant risk when used in the healthcare space. We are exposed to risks associated with employees utilizing generative AI in methods and ways that are contrary to the framework laid out by the Executive Order or the subsequent complementary laws. We will need to invest resources to ensure appropriate development and use of any generative AI, or like-technology, and to develop internal compliance policies and procedures addressing this use.

The Department of Justice, or DOJ, issued the final rule carrying out Executive Order 14117, Preventing Access to Americans' Bulk Sensitive Personal Data and United States Government-Related Data by Countries of Concern. This rule imposes restrictions on data considered sensitive to certain countries. As a result, we are exposed to risks associated with required data sharing between ourselves and a vendor in a country of concern, and we will need to invest resources to ensure appropriate safeguards are in place prior to any sharing of sensitive data.

Cybersecurity presents an ongoing risk vector for our company. A cybersecurity incident or data breach impacting our internal systems or network could compromise sensitive information of patients and employees, requiring additional resources to enable us to ensure remediation and proper notification. Additionally, we rely on vendors to provide many services where they collect, use or process sensitive data on our behalf or jointly. An incident compromising the databases of our internal network or our vendor's information may materially impact our ability to continue development of our products or have appropriate data to complete FDA submissions. If data related to drug development is compromised, the integrity of that data might be impacted in such a way to render it unusable or potentially modified to a degree it will not be reliable. This type of attack may have material financial impacts resulting from a cybersecurity incident or data breach disclosing or making unavailable IP related to our drug development through a ransomware attack or similar method. The continued development and management of our Information Security function may require additional investment of resources to mature our ability to prevent and respond to cybersecurity incidents or data breaches.

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. The inability to deduct research and development expenditures in their entirety will continue to 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.

Additionally, the Organization for Economic Co-operation and Development, or the OECD, the EC, and individual taxing jurisdictions where we and our affiliates do business have recently focused on issues related to the taxation of multinational corporations. In December 2021, the OECD released its comprehensive plan to create an agreed set of international rules for fighting base erosion and profit shifting, including the implementation of minimum taxes. As a result, tax laws in the U.S. and other countries in which we operate could change and any such changes could materially affect our business, prospects, operating results and financial condition. As of December 31, 2024, the Company does not meet the revenue threshold requirements set forth by the OECD and as such has not included any tax impact.

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 February 11, 2025. 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;
- the announcement of, or developments in, any litigation matters; 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 the Sales Agreement with Cowen through which we may, from time to time, issue and sell shares of our common stock having an aggregate offering price of up to $300.0 million, subject to the terms and conditions of the Sales Agreement. Through December 31, 2024, we sold 544,719 shares of common stock pursuant to the Sales Agreement, at an average price of $91.88 per share, with aggregate net

proceeds of $48.9 million. If we sell additional shares of common stock under the 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. In addition, we are, and may from time-to-time become, involved in lawsuits and other disputes that could have a material impact on us. See the section titled "*Legal Proceedings*" in Note 19, *Commitments and Contingencies* to our consolidated financial statements included in this Annual Report on Form 10-K for information regarding currently pending litigation. It is possible that we may not prevail in any such lawsuits and disputes even after expending significant amounts of money and company resources in defending our positions in such lawsuits and disputes. The outcome of such lawsuits and disputes is inherently uncertain and may have a negative impact on our business, financial condition and results of operations.

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 program with Cowen. 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 ATM program, the ATM Facility with Cowen to raise additional capital. Under our ATM Facility, we entered into the Sales Agreement, pursuant to which we can sell common shares, up to a maximum aggregate market value of $300.0 million, through one or more at-the-market offerings. Through December 31, 2024, we sold 544,719 shares of common stock pursuant to the Sales Agreement, at an average price of $91.88 per share, with aggregate net proceeds of $48.9 million. 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, if we need additional capital.

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 any 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 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 Exchange Act or the Securities Act of 1933, as amended (Securities Act). Our bylaws further provide that, unless we consent in writing to an alternative forum, the federal district courts of the U.S. 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 U.S. 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 U.S. 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, or SEC, and Nasdaq have imposed various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel will need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will increase our legal and financial compliance costs and make some activities more time-consuming and costlier.

Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002 (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 the Financing Agreement preclude us, and the terms of any future debt agreements may preclude us from paying cash 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.

As part of the Inflation Reduction Act of 2022, for tax years beginning on or after December 31, 2022, U.S. Congress enacted a 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 percentage point 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, 2024, we had federal net operating loss carryforwards of approximately $859.2 million, and our ability to utilize those net operating loss carryforwards could be limited by an "ownership change" as described above, which could result in increased tax liability to us. In addition, pursuant to the TCJA, 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.

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 percentage point 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 greater than 50 percentage point ownership change. The Company has not performed an analysis through December 31, 2024 at this time.

Item 1B. Unresolved Staff Comments.

Not applicable.

Item 1C. Cybersecurity

Governance Related to Cybersecurity Risks

Our management, with involvement and input from our audit committee, performs an annual enterprise-wide risk management (ERM) assessment to identify and manage key existing and emerging risks for our company. Our ERM process seeks to identify both the potential impacts to our company of a particular risk and the likelihood and proximity of any such risk. Our management team is responsible for implementing and overseeing our ERM process. Cybersecurity is among the risks identified for board of directors' level risk oversight as a result of our most recent ERM assessment, with our audit committee of the board of directors having been delegated responsibility for overseeing our policies, practices and assessments with respect to cybersecurity and other information technology risks.

Our information security team is led by the SVP of IS, who reports to our chief financial officer. Our SVP of IS has over 25 years of experience managing and securing technology infrastructure. The information security team has responsibility for the planning and execution of our processes to manage cybersecurity and other information technology risks. The information security team also institutes and maintains controls for our systems, applications, and databases.

The audit committee receives periodic updates on our cybersecurity risks from our information security team, which include biannual presentations on the status of our cybersecurity risk management program by the SVP IS. These reports include updates on our performance preparing for, preventing, detecting, responding to and recovering from cyber incidents, if any. In addition, as needed, management updates the audit committee regarding any notable cybersecurity incidents. We have also implemented an annual process for employees to complete security awareness training.

Cyber Risk Management and Strategy

Our processes to identify, assess, and manage risks presented by cybersecurity threats are informed by the National Institute of Standards and Technology Cybersecurity Framework. Our SVP of IS, with support from the information security team, is informed about and monitors the prevention, detection, mitigation, and remediation of cybersecurity risks and incidents through various means, which include leveraging external third parties for security testing.

The information security team monitors security alerts from information security research sources and peer networking, and we have implemented processes and technologies for monitoring our networks for exfiltration of sensitive company information. Before contracting with third parties or purchasing third party technology or other solutions that involve exposure to sensitive company information the team assesses vendor risk, including by requesting SOC2 reports and/or security documentation from a vendor, where appropriate, and we receive and review security updates and alerts from these third parties. Penetration testing is performed periodically across our network boundaries to identify issues for remediation. Additionally, we maintain off-site back-ups and disaster recovery plans to restore our information and systems in the event of a disruptive event.

The information security team also has processes in place to inform and update management and, as needed, the audit committee about cybersecurity incidents that may pose significant risk to the company. Although risks from cybersecurity threats have to date not materially affected us, our business strategy, results of operations or financial condition, we have, from time to time, experienced threats and security incidents relating to our and our third-party vendors' data and systems. For more information, please see "*Item 1A, Risk Factors.*"

Item 2. Properties.

Our headquarters are located at 45 Sidney Street in Cambridge, Massachusetts where we occupy approximately 139,216 rentable square feet of office and laboratory space under a lease that will expire on November 30, 2029, unless terminated sooner.

We also lease approximately 39,000 rentable square feet at our former corporate headquarters at 38 Sidney Street in Cambridge, Massachusetts under a lease that was extended in December 2021, and will now expire on November 30, 2029.

We believe that our existing office and laboratory space is sufficient to meet our needs for the foreseeable future and that suitable additional space will be available as and when needed.

Item 3. Legal Proceedings.

For a description of our material legal proceedings, please see the section titled "*Legal Proceedings*" in Note 19, *Commitments and Contingencies* to our consolidated financial statements included in this Annual Report on Form 10-K.

Item 4. Mine Safety Disclosures.

Not applicable.

PART II

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

Certain Information Regarding the Trading of Our Common Stock

Our common stock trades under the symbol "BPMC" on the Nasdaq Global Select Market and has been publicly traded since April 30, 2015.

Holders

As of January 31, 2025, there were 7 holders of record of our common stock. This number does not include beneficial owners whose shares are held by nominees in street name.

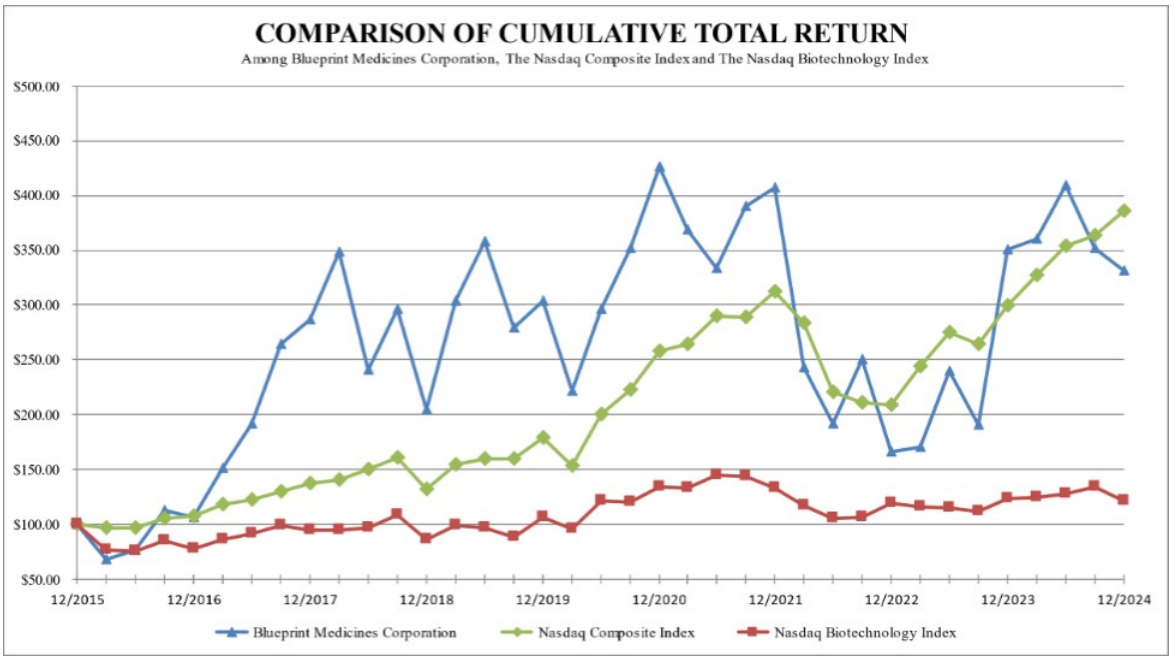
Dividends

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all available funds and any future earnings, if any, to fund the development and expansion of our business, and we do not anticipate paying any cash dividends in the foreseeable future. Any future determination to pay dividends will be made at the discretion of our board of directors and will depend on various factors, including applicable laws, our results of operations, financial condition, future prospects and any other factors deemed relevant by our board of directors. Investors should not purchase our common stock with the expectation of receiving cash dividend.

Stock Performance Graph

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

The following performance graph compares the performance of our common stock to the Nasdaq Composite Index and to the Nasdaq Biotechnology Index from December 31, 2015 through December 31, 2024. The comparison assumes $100 was invested in our common stock and in each of the foregoing indices after the market closed on December 31, 2015, and it assumes reinvestment of dividends, if any. The stock price performance included in this graph is not necessarily indicative of, nor is it intended to forecast, future stock price performance.



Securities Authorized for Issuance under Equity Compensation Plans

Information about our equity compensation plans will be included in our definitive proxy statement to be filed with the SEC with respect to our 2025 Annual Meeting of Stockholders and is incorporated herein by reference.

Unregistered Sales of Equity Securities and Use of Proceeds

None.

Recent Sales of Unregistered Equity Securities

None.

Purchases of Equity Securities by the Issuer and Affiliated Purchasers

We did not purchase any of our registered equity securities during the period covered by this Annual Report on Form 10-K.

Item 6. [Reserved]

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

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

Information pertaining to fiscal year 2022 was included in the Company's Annual Report on Form 10-K for the year ended December 31, 2023 on pages 105 through 113 under Part II, Item 7, "Management's Discussion and Analysis of Financial Position and Results of Operations," which was filed with the Securities and Exchange Commission (the "SEC") on February 15, 2024.

Overview

We are a global, fully-integrated biopharmaceutical company that invents life-changing medicines. We seek to alleviate human suffering by solving important medical problems in two core focus areas: allergy/inflammation and oncology/hematology. Our approach targets the root causes of disease, using deep scientific knowledge in our core focus areas and drug discovery expertise across multiple therapeutic modalities. We have a track record of success with two approved medicines, including AYVAKIT®/AYVAKYT® (avapritinib), which we are bringing to patients with systemic mastocytosis (SM) and PDGFRA Exon 18 mutant GIST in the U.S. and Europe. Leveraging our established research, development, and commercial capability and infrastructure, we now aim to significantly scale our impact by advancing a broad pipeline of programs ranging from early science to advanced clinical trials in mast cell diseases including SM and chronic urticaria, breast cancer and other solid tumors.

Since 2011, we have advanced a drug discovery approach that combines evolving biological insights with our proprietary research platform and drug design capabilities, which currently includes kinase inhibition and targeted protein degradation. We aim to rapidly and reproducibly translate science into durable clinical benefit for broad populations of patients with significant medical needs, including patients with mast cell diseases, breast cancer and other solid tumors. Our focused business model integrates our research engine with robust clinical development and commercial capabilities in allergy/inflammation and solid tumors to create a sustainable cycle of innovation**.**

As described in Part I, Item 1. "*Business*," of this Annual Report on Form 10-K, we currently have two products that have received marketing approval, including one partnered product, and multiple investigational programs of various stages advancing towards potential commercialization. In Part I, Item 1. "*Business*," you can also find a summary of key events from 2023 and 2024 to-date related to our marketed products and our clinical development programs.

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 December 31, 2024, we have received an aggregate of $3.9 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, $1.1 billion in upfront and milestone payments under our collaborations with CStone and Zai Lab, our now terminated collaborations with Roche, our license agreement with Clementia, our agreement with Rigel and our former collaboration with Alexion Pharma Holding (Alexion) and $400.0 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 $67.1 million for the year ended December 31, 2024. Our net losses were $507.0 million and $557.5 million for the years ended December 31, 2023 and 2022, respectively. As of December 31, 2024, we had an accumulated deficit of $2,407.0 million. We expect to continue to incur significant expenses over the next few years, with anticipated variability in these expenses due to our ongoing activities, particularly as we:

- maintain and expand our sales, marketing and distribution infrastructure to continue to commercialize avapritinib and any current or future drug candidates for which we may obtain marketing approval;
- seek marketing approval for avapritinib in additional geographies;
- 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) 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 trials as we develop our drugs and drug candidates either as potential combination therapies or for use as comparator agents;
- conduct research and development activities under current or future collaborations;
- 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 for avapritinib under the brand name 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. 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 and in December 2023, the European Commission approved AYVAKYT for the treatment of adult patients with indolent SM with moderate to severe symptoms inadequately controlled on symptomatic treatment.

For the year ended December 31, 2024, our revenue primarily consisted of product sales of AYVAKIT/AYVAKYT as well as some collaboration, license and other revenue. Our collaboration, license and other revenue primarily included revenue related to the Rigel Agreement.

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, license and other 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, license or other agreements, if any.

In 2025, we anticipate a robust increase in net product revenues compared to 2024, as we continue to add new patients onto AYVAKIT/AYVAKYT, including those with indolent SM and advanced SM.

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, distribution, freight, and indirect overhead costs as well as amounts written down as a result of excess, obsolescence, unmarketability or other reasons. 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 years ended December 31, 2023 and 2022. This pre-launch inventory was fully sold through during 2023 and as a result, it did not have an impact on the cost of goods sold during the year ended December 31, 2024. We estimate our costs of goods sold related to product sales to be within the low to the mid-single digit percentage range. Cost of goods sold related to sales of drug products to our collaboration partners are at lower margins.

Expenses

Collaboration Loss Sharing

Roche was the principal for recording GAVRETO product sales to customers in the U.S. under our Roche pralsetinib collaboration, and we recognized a portion of the profit as revenue and losses as collaboration loss sharing in our consolidated statements of operations and comprehensive loss. The Roche pralsetinib collaboration agreement was terminated in February 2024. We continued to share any profit or loss from GAVRETO sales in the U.S. until February 22, 2024. For additional information, see Note 11, *Collaboration, License and Other Agreements*, to our consolidated financial statements included in this Form 10-K.

Research and Development Expenses

Research and development expenses consist primarily of costs incurred for our research and development activities, including our drug discovery efforts, and the development of our drug candidates, which include:

- employee-related expenses including salaries, benefits, and stock-based compensation expense;
- expenses incurred under agreements with third parties that conduct research and development, preclinical activities, clinical activities and manufacturing on our behalf;
- expenses incurred in connection with development activities under our now terminated collaboration for pralsetinib with Roche and research and development activities under our collaboration with VantAI;
- 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 pre-validated commercial supply materials; and
- facilities, depreciation, and other expenses, which include direct and allocated lease, information technology and maintenance of facilities expenses, 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 our drug candidates;
- commercializing our drug candidates, if and when approved, whether alone or in collaboration with others;
- market acceptance of AYVAKIT/AYVAKYT 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 allocate our internal research and development expenses to specific drug candidate programs as they are deployed across multiple projects under development.

The following table summarizes our research and development expenses by principal program for the years ended December 31, 2024 and 2023 (in thousands). Other development and pre-development candidate expenses, unallocated expenses and internal research and development expenses have been classified separately.

	Year Ended December 31,			
	2024	2023	Dollar Change	% Change
Avapritinib external expenses	$ 16,240	$ 32,383	$ (16,143)	(50)%
Pralsetinib external expenses*	1,260	20,512	(19,252)	(94)
Elenestinib external expenses	15,571	24,431	(8,860)	(36)
EGFR franchise (BLU-451/525/701/945) external expenses	6,276	57,177	(50,901)	(89)
BLU-222 external expenses	18,015	42,945	(24,930)	(58)
BLU-808 external expenses	23,777	12,094	11,683	97
Other development and pre-development candidate expenses and unallocated expenses	101,780	89,845	11,935	13
Internal research and development expenses	158,514	148,333	10,181	7
Total research and development expenses	$ 341,433	$ 427,720	$ (86,287)	(20)%

* Pralsetinib external expenses include expenses reimbursable to Roche under our now terminated collaboration for pralsetinib with Roche.

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 (API), drug product and drug substance for current and future clinical trials will vary depending on clinical data results and our resource 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.

In 2025, we anticipate a modest increase in our research and development expenses compared to 2024. This is due to increased investment in our priority programs to advance the associated clinical trials, in contrast to our focused approach towards optimizing operational efficiency across our portfolio in 2024.

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.

In 2025, we anticipate a modest increase in selling, general, and administrative expenses compared to 2024. This increase is driven by our enhanced efforts to expand our global commercial and compliance infrastructure to support the commercialization of AYVAKIT/AYVAKYT.

Interest Expense, net

Interest expense, net, consists primarily of interest expense related to our financing arrangements with Sixth Street Partners. Interest expense on liabilities related to the sale of future revenues consists of the periodic interest calculated using the effective interest rate method over the future estimated royalty payments due to Sixth Street Partners over the life of the Future Revenue Purchase Agreement. 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 consolidated financial statements included in this Form 10-K.

Interest 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 gains on our equity investment and the impacts of foreign currency exchange differences.

In 2025, we anticipate an increase in other income, net, compared to 2024. This increase is driven by a gain on our equity investment in IDRx we expect to recognize upon closing of the acquisition of IDRx by GSK plc. For additional information, see Note 20, *Subsequent Events*, to our consolidated financial statements included in this Form 10-K.

Debt Extinguishment Gain

Debt extinguishment gain consists of the gain recognized as a result of the Royalty Pharma Termination Agreement entered into on February 22, 2024. For additional information, see Note 3, *Financing Arrangements*, to our consolidated financial statements included in this Form 10-K.

Income Tax Expense

Income tax expense consists of U.S. state and foreign income taxes incurred.

Critical Accounting Policies and Estimates

Our management's discussion and analysis of our financial condition and results of operations are based on our consolidated financial statements, which have been prepared in accordance with U.S. generally accepted accounting principles. The preparation of these consolidated financial statements requires us to make judgments and estimates that affect the reported amounts of assets, liabilities, revenues, and expenses and the disclosure of contingent assets and liabilities in our consolidated financial statements. We base our estimates on historical experience, known trends and events, and various other factors that are believed to be reasonable under the circumstances. Some of those judgments can be subjective and complex, and consequently actual results could differ from those estimates. For any given individual estimate or assumption we make, it is possible that other people applying reasonable judgment to the same facts and circumstances could develop different estimates. We believe that, given current facts and circumstances, it is unlikely that applying any such other reasonable judgment would cause a material adverse effect on our consolidated results of operations, financial position, or liquidity for the periods presented in this report. We evaluate our judgments and estimates in light of changes in circumstances, facts and experience on an ongoing basis.

Critical accounting estimates are those estimates that, in accordance with generally accepted accounting principles, involve a significant level of estimation uncertainty and have had or are reasonably likely to have a material impact on our consolidated financial statements. Management has determined that our most critical accounting estimates are those relating to revenue recognition, accrued research and development expenses, equity investments, liabilities related to the sale of future royalties and revenues, and modification of debt. We have reviewed our critical accounting estimates with our audit committee. For further discussion about our general accounting policies, see Note 2 *Summary of Significant Accounting Policies and Recent Accounting Pronouncements,* to our consolidated financial statements included in this Form 10-K.

Revenue Recognition

We recognize revenue when we transfer control of goods or services to our customers. Revenue is measured as the amount of consideration we expect to receive in exchange for goods and services. We generate revenue from product sales and revenue transactions under our collaboration, license and other agreements.

Product Revenue

For product sales to customers, provisions for returns, rebates and discounts are established in the same period the related product sales are recognized. To determine the appropriate transaction price for our product sales at the time we recognize a sale to a direct customer, we estimate any rebates, chargebacks or discounts that ultimately will be due to

the direct customer and other customers in the distribution chain under the terms of our contracts. Significant judgments are required in making these estimates. The largest of our sales rebate and discount amounts are rebates associated with sales covered by Medicaid and chargeback contracts in the U.S. We utilize the expected value method to determine the appropriate amount for estimates of variable consideration based on factors such as historical rebate payments for these programs, the current contractual and statutory requirements, specific known market events and sales trends, industry data and forecasted customer buying and payment patterns, the percentage of our products that are sold via these programs, and our product pricing. Actual amounts of consideration ultimately received may differ from our estimates. If actual results vary from our estimates, we adjust these estimates, which would affect net product revenue and earnings in the period such variances become known.

Collaboration, License and Other Revenue

Revenue recognized from collaboration, license and other agreements includes estimated royalties on drug sales, upfront, milestone, profit sharing and other payments, if any, under any current or future collaboration, license and other agreements, including revenues related to the supply of our drug candidates or approved drugs to our various collaboration partners under these types of contracts.

Accrued Research and Development Expenses

As part of the process of preparing our consolidated financial statements, we are required to estimate our accrued expenses as of each balance sheet date. This process involves reviewing open contracts and purchase orders, communicating with our personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of the actual cost. The majority of our service providers invoice us monthly in arrears for services performed or when contractual milestones are met. We make estimates of our accrued expenses as of each balance sheet date based on facts and circumstances known to us at that time. We periodically confirm the accuracy of our estimates with the service providers and make adjustments if necessary. The significant estimates in our accrued research and development expenses include the costs incurred for services performed by our vendors in connection with research and development activities for which we have not yet been invoiced.

We base our expenses related to research and development activities on our estimates of the services received and efforts expended pursuant to quotes and contracts with vendors that conduct research and development on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the research and development expense. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrual or prepaid accordingly. Non-refundable advance payments for goods and services that will be used in future research and development activities are expensed when the activity has been performed or when the goods have been received rather than when the payment is made.

Although we do not expect our estimates to be materially different from amounts actually incurred, if our estimates of the status and timing of services performed differ from the actual status and timing of services performed, it could result in us reporting amounts that are too high or too low in any particular period. To date, there have been no material differences between our estimates of such expenses and the amounts actually incurred.

Equity Investment

Investments in non-marketable equity securities of privately-held companies that do not have readily determinable fair values and where we have no significant influence are measured at cost, less any impairments, plus or minus changes resulting from observable price changes in orderly transactions for the identical or a similar investment of the same issuer. Each period we assess relevant transactions to identify observable price changes, and regularly monitor these investments to evaluate whether there is an indication of impairment. Judgement is required in identifying the existence of impairment indicators. If indicators of impairment exist, we evaluate whether an investment’s fair value is less than its carrying value using an estimate of fair value.

Liabilities related to the sale of future royalties and revenues

We account for net proceeds from sales of our rights to receive future royalty payments and from sales of future revenues as liabilities related to the sale of future royalties and revenues as we have significant continuing involvement in the generation of the related future cash flows. Interest on the liabilities related to the sale of future royalties and revenues is recognized using the effective interest rate method over the life of the related royalty or revenue stream. The liabilities related to the sale of future royalties and revenues and the related interest expenses are based on our current estimates of future royalties and revenues as well as commercial milestones expected to be achieved and received over the life of the arrangement, which we determine by using forecasts of the underlying drug products of the underlying regions. We periodically assess the expected payments and to the extent the amount or timing of the future estimated payments is materially different than previous estimates, we account for any such change by adjusting carrying value of the liabilities related to the sale of future royalties and revenues, and prospectively recognizing the related interest expenses. An increase or decrease of 5% to the interest rate would result in an increase or decrease to our liability related to the sale of future royalties of approximately $0.3 million.

Modification of Debt Instruments

When a debt instrument in which we are the debtor is modified or exchanged, we analyze whether the modification should be accounted for as a modification or an extinguishment. Modified terms are considered substantially different if, after an exchange or modification of debt instruments with the same creditor, the present value of cash flows under the terms of the new debt instrument differs by at least 10% from the present value of the remaining cash flows under the terms of the original debt instrument. If the modified instrument is considered substantially different from the original debt instrument, the modification or exchange is accounted for as an extinguishment. The new instrument is recorded at its fair value and that fair value is used to determine the extinguishment gain or loss.

Results of Operations

Comparison of Years Ended December 31, 2024 and 2023

The following table summarizes our results of operations for the years ended December 31, 2024 and 2023, together with the changes in those items in dollars and as a percentage (in thousands):

	Year ended December 31,			
	2024	2023	Dollar Change	% Change
Total revenues	$ 508,824	$ 249,380	$ 259,444	104 %
Total cost and operating expenses	720,868	735,657	(14,789)	(2)
Total other income (expense), net	146,181	(19,739)	165,920	841
Loss before income taxes	(65,863)	(506,016)	440,153	87
Income tax expense	1,226	968	258	27
Net loss	$ (67,089)	$ (506,984)	$ 439,895	87 %

Total Revenues

Total revenues consist of the following (in thousands):

	Year ended December 31,			
	2024	2023	Dollar Change	% Change
Product revenue, net	$ 478,950	$ 204,207	$ 274,743	135 %
Collaboration, license and other revenue	29,874	45,173	(15,299)	(34)
Total revenues	$ 508,824	$ 249,380	$ 259,444	104 %

Product Revenue, Net

The following table summarizes revenue recognized from sales of AYVAKIT/AYVAKYT during the years ended December 31, 2024, and 2023 (in thousands):

	Year ended December 31,			
	2024	2023	Dollar change	% Change
United States	$ 421,837	$ 181,971	$ 239,866	132 %
Rest of World	57,113	22,236	34,877	157
Total product revenue, net	$ 478,950	$ 204,207	$ 274,743	135 %

Product revenue, net increased during the year ended December 31, 2024 as compared to the year ended December 31, 2023 primarily driven by growth in the number of indolent SM and advanced SM patients on therapy.

Collaboration, License and Other Revenue

The following table summarizes the revenue recognized from our collaboration, license and other agreements during the years ended December 31, 2024 and 2023 (in thousands):

	Year Ended December 31,			
	2024	2023	Dollar change	% Change
Rigel agreement	$ 24,273	$ —	24,273	100 %
CStone collaboration	3,304	17,312	(14,008)	(81)
Roche pralsetinib collaboration	1,920	2,143	(223)	(10)
Roche immunotherapy collaboration	—	25,706	(25,706)	(100)
Other	377	12	365	3,042
Total collaboration, license and other revenue	$ 29,874	$ 45,173	$ (15,299)	(34)%

Revenue recognized from our collaboration, license and other agreements decreased during the year ended December 31, 2024 as compared to the year ended December 31, 2023 primarily due to:

- The termination of the Roche immunotherapy collaboration effective in April 2023. As a result of the termination, the percentage of completion to fulfill the performance obligations under the Roche immunotherapy collaboration was increased, and therefore, the remaining transaction price associated with the agreement was recognized as collaboration, license and other revenue during the year ended December 31, 2023; and

- Decreased revenue under our CStone collaboration primarily due to a regulatory milestone of $9.0 million achieved during the year ended December 31, 2023 and a reduction in revenue recorded as a result of consideration payable to CStone in connection with commercial supply of pralsetinib for the CStone Territory.

The decrease in collaboration, license and other revenue was partially offset by the revenue recorded under the Rigel Agreement upon completion of the transition during the year ended December 31, 2024.

Cost of Sales

The following table summarizes the cost of sales during the years ended December 31, 2024 and 2023 (in thousands):

	Year Ended December 31,			
	2024	2023	Dollar change	% Change
Cost of product sales	$ 8,041	$ 6,465	$ 1,576	24 %
Cost of collaboration and other sales	12,122	2,075	10,047	484
Total cost of sales	$ 20,163	$ 8,540	$ 11,623	136 %

Cost of sales increased during the year ended December 31, 2024 as compared to the year ended December 31, 2023 primarily due to an increase in the cost of collaboration and other agreement related sales which was driven by GAVRETO product sales to Rigel and collaboration sales to CStone. The increase in cost of product sales was primarily due to an increase in product sales volume.

Collaboration Loss Sharing

During the year ended December 31, 2024, no collaboration loss sharing was recognized for the sales of GAVRETO to the customers in the U.S. because the commercialization activities of GAVRETO were profitable in the U.S. through its termination date of February 22, 2024 and generated profit sharing revenue of $1.4 million which was recorded as Roche pralsetinib collaboration revenue. During the year ended December 31, 2023, we recorded collaboration loss sharing of $4.3 million.

Research and Development Expense

The following table summarizes the research and development expenses during the years ended December 31, 2024 and 2023 (in thousands):

	Year Ended December 31,			
	2024	2023	Dollar change	% Change
Compensation and related expenses	$ 114,861	$ 110,740	$ 4,121	4 %
Early drug discovery and platform	76,970	70,383	6,587	9
Stock-based compensation	47,455	41,534	5,921	14
Clinical and manufacturing related activities	38,889	138,801	(99,912)	(72)
Facilities and IT	35,589	33,783	1,806	5
Consulting and professional services	24,182	29,189	(5,007)	(17)
Other	3,487	3,290	197	6
Total research and development expenses	$ 341,433	$ 427,720	$ (86,287)	(20)%

Research and development expense decreased during the year ended December 31, 2024 as compared to the year ended December 31, 2023, primarily due to a decrease in clinical and manufacturing related activities. This decrease is attributed to our focused approach towards optimizing operational efficiency across our portfolio while prioritizing our top programs, the timing of manufacturing clinical trial materials, and the termination of the Roche pralsetinib collaboration.

Selling, General and Administrative Expense

The following table summarizes the sales, general and administrative expenses during the years ended December 31, 2024 and 2023 (in thousands):

	Year Ended December 31,			
	2024	2023	Dollar change	% Change
Compensation and related expenses	$ 127,286	$ 120,756	$ 6,530	5 %
Commercial and related expenses	96,604	53,579	43,025	80
Stock-based compensation	61,456	51,138	10,318	20
Consulting and professional services	49,575	41,876	7,699	18
Facilities and IT	12,214	13,126	(912)	(7)
Other	12,137	14,666	(2,529)	(17)
Total sales, general and administrative expenses	$ 359,272	$ 295,141	$ 64,131	22 %

Selling, general and administrative expense increased during the year ended December 31, 2024 as compared to the year ended December 31, 2023 primarily due to:

- an increase in commercial and related activities primarily driven by efforts to support the commercialization of AYVAKIT/AYVAKYT; and
- an increase in stock-based compensation expense primarily driven by the higher valuation of newly granted equity awards as a result of the Company's rising stock price, and an increase in equity awards granted to support headcount growth within our commercial operations.

Interest Expense, Net

The following table summarizes the interest expense, net, during the years ended December 31, 2024 and 2023 (in thousands):

	Year ended December 31,			
	2024	2023	Dollar Change	% Change
Interest income	$ 40,655	$ 32,812	$ 7,843	24 %
Interest expense	(68,806)	(51,605)	(17,201)	(33)
Interest expense, net	$ (28,151)	$ (18,793)	$ (9,358)	(50)%

Interest expense, net, increased during the year ended December 31, 2024 as compared to the year ended December 31, 2023 primarily due to higher interest charges on the term loan with Sixth Street Partners driven by the additional delayed draw term loan facilities, partially offset by higher interest income earned on our available-for-sale investments during the year ended December 31, 2024 as compared to the year ended December 31, 2023.

Other Income (Expense), Net

The following table summarizes the other income (expense), net, during the years ended December 31, 2024 and 2023 (in thousands):

	Year ended December 31,			
	2024	2023	Dollar Change	% Change
Other income (expense), net	$ 656	$ (946)	$ 1,602	169 %

Other income, net, increased during the year ended December 31, 2024 as compared to the year ended December 31, 2023 primarily due to the gain recorded associated with our equity investment in IDRx in connection with the Series B preferred stock financing completed by IDRx during the year ended December 31, 2024.

Debt extinguishment gain

During the year ended December 31, 2024, a debt extinguishment gain of $173.7 million was recognized as a result of the Royalty Pharma Termination Agreement entered into on February 22, 2024. For additional information, see Note 3, *Financing Arrangements*, to our consolidated financial statements included in this Form 10-K.

Income Tax Expense

The following table summarizes the income tax expense during the years ended December 31, 2024 and 2023 (in thousands):

	Year ended December 31,			
	2024	2023	Dollar Change	% Change
Income tax expense	$ 1,226	$ 968	$ 258	27 %

Income tax expense increased during the year ended December 31, 2024 as compared to the year ended December 31, 2023 primarily due to state income tax and taxable income from jurisdictions in which the Company is subject to tax. For additional information, see Note 15, *Income Taxes*, to our consolidated financial statements included in this Form 10-K.

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 December 31, 2024, we have received an aggregate of $3.9 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, $1.1 billion in upfront payments and milestone payments under our collaborations with CStone and Zai Lab, our now terminated collaborations with Roche, our license agreement with Clementia, our agreement with Rigel and our former collaboration with Alexion, and $400.0 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 December 31, 2024, we had cash, cash equivalents and marketable securities of $863.9 million.

Cash Flows

The following table provides information regarding our cash flows for the years ended December 31, 2024 and 2023:

	Year Ended December 31,	
(in thousands)	**2024**	**2023**
Net cash used in operating activities	$ (192,586)	$ (436,847)
Net cash provided by (used in) investing activities	(47,501)	274,040
Net cash provided by financing activities	273,111	119,225
Net increase (decrease) in cash, cash equivalents, and restricted cash	$ 33,024	$ (43,582)

Net Cash Used in Operating Activities. For the year ended December 31, 2024, compared to the same period in 2023, the $244.3 million decrease in net cash used in operating activities was primarily due to the decrease in net loss of $439.9 million. The decrease was partially offset by the non-cash adjustment for the debt extinguishment gain of $173.7 million and changes in our operating assets and liabilities of $23.6 million.

Net Cash Provided by (Used in) Investing Activities. For the year ended December 31, 2024, compared to the same period in 2023, the $321.5 million decrease in net cash provided by investing activities was primarily due to a $333.0 million increase in net purchases of investments classified as available for sale.

Net Cash Provided by Financing Activities. For the year ended December 31, 2024, compared to the same period in 2023, the $153.9 million increase in net cash provided by financing activities was primarily due to the increase of $48.9 million in proceeds from the ATM Facility (as defined below), the $56.4 million increase in net proceeds received from stock option exercises and employee stock purchase plan and the $49.0 million increase in net proceeds from 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. In connection with and effective upon the termination of the Roche pralsetinib collaboration agreement, on February 22, 2024, we and Royalty Pharma agreed to terminate the Royalty Purchase Agreement. As of December 31, 2024, the net carrying value of liability related to this arrangement was $0.7 million, which we subsequently paid in February 2025.

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 December 31, 2024, the net carrying value of the liability related to this arrangement was $254.4 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 May 2024, we received the second tranche in the amount of $150.0 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 December 31, 2024, the net carrying value of the term loan was $387.0 million.

Our obligations under the Financing Agreement are secured, subject to certain exceptions, by security interests in substantially all of our assets and certain of our subsidiaries' assets. The Financing Agreement contains customary 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 $80.0 million.

For additional information, see Note 3, *Financing Arrangements*, to our consolidated financial statements included in this Form 10-K.

Sales Agreement with Cowen

In February 2022, we entered into an at-the-market (ATM) Facility with Cowen and Company, LLC (Cowen), pursuant to which we may offer and sell, from time to time at our sole discretion, shares of our common stock having an aggregate offering price of up to $300.0 million through Cowen as sales agent. During the year ended December 31, 2024, we issued and sold 544,719 shares of our common stock under the ATM Facility, at an average price of $91.88 per share, and received net proceeds of $48.9 million. As of December 31, 2024, we had $250.0 million of remaining capacity available under the ATM Facility.

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 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 December 31, 2024, we had cash, cash equivalents and marketable securities of $863.9 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 collaboration with CStone, our license agreements with Clementia and IDRx, our agreement with Rigel, 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, license or other 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 collaboration with CStone, the license agreements with Clementia and IDRx, the agreement with Rigel 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. In addition, we may sell additional shares of our common stock pursuant to our ATM Facility with Cowen, as further discussed above. 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

We have entered into arrangements that contractually obligate us to make payments that will affect our liquidity and cash flows in future periods. Our contractual obligations primarily consist of our obligations under unconditional purchase obligations related to certain commercial manufacturing agreements, research service commitments, non-cancellable operating leases, term loan and defined benefit obligation.

Supply agreements

The aggregate amount of future minimum purchase obligations under the manufacturing agreements over the period of next five years was approximately $2.0 million as of December 31, 2024, of which $1.0 million are expected to be paid within one year.

Lease commitments

The aggregate amount of future operating lease obligations over the term of our leases was $97.8 million as of December 31, 2024, of which $18.8 million are expected to be paid within one year. For additional information on our leases and timing of future payments, see Note 16, *Leases*, to our consolidated financial statements included in this Form 10-K.

Long-term debt obligations

The long-term debt obligation related to our term loan over the period of next five years was $553.6 million as of December 31, 2024, of which $43.9 million are expected to be paid within one year. For additional information on the term loan, see Note 3, *Financing Arrangements*, to our consolidated financial statements included in this Form 10-K.

Defined benefit obligation

The future benefits expected to be paid under our pension plan covering employees of our Swiss subsidiary, Blueprint Medicines (Switzerland) GmbH was $6.8 million as of December 31, 2024, of which $0.5 million is expected to become payable from the plan within one year. For additional information on the defined benefit plan, see Note 17, *Employee Benefit Plans*, to our consolidated financial statements included in this Form 10-K.

Research service commitments

We also have obligations to make future payments to third parties that become due and payable on the achievement of certain development and sales milestones, including future payments to third parties with whom we have entered into agreements to develop and commercialize certain of our research and development programs. As of December 31, 2024, we have an obligation to pay $5.0 million under one of such commitments within one year. We have not included these other such commitments on our balance sheet or in the contractual obligations above because the achievement and timing of these milestones is not fixed and determinable.

Other obligations

In the normal course of business, we enter into agreements with contract research organizations for clinical trials and vendors for clinical supply manufacturing, preclinical research studies, synthetic chemistry and other services and products for operating purposes. We have not included all of these payments in the contractual obligations above since majority of the contracts are generally cancelable at any time by us upon less than 180 days' prior written notice. Certain of these agreements require us to pay milestones to such third parties upon achievement of certain development, regulatory or commercial milestones. Amounts related to contingent milestone payments are not considered contractual obligations as they are contingent on the successful achievement of certain development, regulatory approval and commercial milestones, which may not be achieved.

Recently Issued and Adopted Accounting Pronouncements

A description of recently issued accounting pronouncements that may potentially impact our financial position and results of operations is disclosed in Note 2, *Summary of Significant Accounting Policies and Recent Accounting Pronouncements*, to our consolidated financial statements included in this Form 10-K.

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

As of December 31, 2024 and 2023, we had cash, cash equivalents and marketable securities of $863.9 million and $767.2 million, respectively, consisting primarily of money market funds and investments in U.S. government agency securities and treasury obligations.

Our primary exposure to market risk is interest rate sensitivity in our fixed income portfolio, which is affected primarily by changes in the general level of U.S. interest rates resulting from the Federal Reserve's raising or lowering 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 materially affected to any significant degree by the effect of a change in market interest rates on our investment portfolio.

We are also exposed to interest rate risk in connection with our borrowings under our senior secured term loan with Sixth Street Partners. As of December 31, 2024, we had $387.0 million of outstanding borrowings under the senior secured term loan. Pursuant to the Financing Agreement, outstanding indebtedness under the term loan bears interest at a 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 effective annual interest was 12.0% as of December 31, 2024. We currently do not engage in any interest rate hedging activity, and we have no intention to do so in the foreseeable future. Based on the current interest rate of the term loan and the scheduled payments thereunder, we do not believe a 1.0% increase in interest rates would have a material impact on our financial condition or results of

operations. For more information regarding the Financing Agreement and the term loan with Sixth Street Partners, see Note 3, *Financing Arrangements*, to our consolidated financial statements included in this Form 10-K.

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 December 31, 2024 and 2023, we held considerable funds and 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. We have not seen a significant impact from inflation on our business, financial condition or results of operations during the years ended December 31, 2024 and 2023. However, a significant or prolonged period of high inflation could adversely impact our results if costs were to increase at a rate higher than the increase in the revenues we generate.

Item 8. Financial Statements and Supplementary Data.

The financial statements and the report of our independent registered public accounting firm (PCAOB ID:42) required to be filed pursuant to this Item 8 are appended to this Annual Report on Form 10-K. An index of those financial statements is found in Item 15 of this Annual Report on Form 10-K.

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

None.

Item 9A. Controls and Procedures

Management's Evaluation of our Disclosure Controls and Procedures

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

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer (our principal executive officer and principal financial officer, respectively), evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2024. Based upon such evaluation, our Chief Executive Officer and Chief Financial Officer have concluded that, as of December 31, 2024, our disclosure controls and procedures were effective at the reasonable assurance level.

Management's Annual Report on Internal Control Over Financial Reporting

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

statements for external purposes in accordance with generally accepted accounting principles and includes those policies and procedures that:

- pertain to the maintenance of records that in reasonable detail accurately and fairly reflect the transactions and dispositions of a company's assets;
- provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that a company's receipts and expenditures are being made only in accordance with authorizations of the company's management and directors; and
- provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of our assets that could have a material effect on the financial statements.

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

Under the supervision of and with the participation of our principal executive officer and principal financial officer, our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2024 based on the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission in Internal Control—Integrated Framework (2013 framework). Based on this assessment, management concluded that our internal control over financial reporting was effective as of December 31, 2024.

Our independent registered public accounting firm has issued an attestation report of our internal control over financial reporting. This report appears below.

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Blueprint Medicines Corporation

Opinion on Internal Control Over Financial Reporting

We have audited Blueprint Medicines Corporation's internal control over financial reporting as of December 31, 2024, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) (the COSO criteria). In our opinion, Blueprint Medicines Corporation (the Company) maintained, in all material respects, effective internal control over financial reporting as of December 31, 2024, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the consolidated balance sheets of the Company as of December 31, 2024 and 2023, the related consolidated statements of operations and comprehensive loss, stockholders' equity and cash flows for each of the three years in the period ended December 31, 2024, and the related notes and our report dated February 13, 2025 expressed an unqualified opinion thereon.

Basis for Opinion

The Company's management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting included in the accompanying Management's Annual Report on Internal Control Over Financial Reporting. Our responsibility is to express an opinion on the Company's internal control over financial reporting based on our audit. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audit in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was

maintained in all material respects.

Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, testing and evaluating the design and operating effectiveness of internal control based on the assessed risk, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

Definition and Limitations of Internal Control Over Financial Reporting

A company's internal control over financial reporting is a process designed 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. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

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

/s/ Ernst & Young LLP
Boston, Massachusetts
February 13, 2025

Changes in Internal Control over Financial Reporting

No change in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) occurred during the year ended December 31, 2024 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information

(b) Rule 10b5-1 Trading Arrangements

During the three months ended December 31, 2024, none of our officers or directors adopted a "Rule 10b5-1 trading arrangement," as the term is defined in Item 408(a) of Regulation S-K.

During the three months ended September 30, 2024, 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 which was not previously disclosed due to an administrative error. We describe the material terms of the 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
Christina Rossi *(Officer)*	Adoption August 27, 2024	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	August 27, 2024 – November 28, 2025	27,291

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections

Not applicable.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

The information required by this Item 10 will be included in our definitive proxy statement to be filed with the SEC with respect to our 2025 Annual Meeting of Stockholders and is incorporated herein by reference.

Item 11. Executive Compensation.

The information required by this Item 11 will be included in our definitive proxy statement to be filed with the SEC with respect to our 2025 Annual Meeting of Stockholders and is incorporated herein by reference.

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

The information required by this Item 12 will be included in our definitive proxy statement to be filed with the SEC with respect to our 2025 Annual Meeting of Stockholders and is incorporated herein by reference.

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

The information required by this Item 13 will be included in our definitive proxy statement to be filed with the SEC with respect to our 2025 Annual Meeting of Stockholders and is incorporated herein by reference.

Item 14. Principal Accounting Fees and Services.

The information required by this Item 14 will be included in our definitive proxy statement to be filed with the SEC with respect to our 2025 Annual Meeting of Stockholders and is incorporated herein by reference.

PART IV

Item 15. Exhibits and Financial Statement Schedules.

(1) Financial Statements

The following documents are included on pages F-1 through F-46 attached hereto and are filed as part of this Annual Report on Form 10-K.

(2) Financial Statement Schedules

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

(3) Exhibits

Exhibit Number	Description of Exhibit	Incorporated by Reference			
		Form	File No.	Exhibit Number	Filing Date
1.1	Sales Agreement, dated as of February 17, 2022, by and between Blueprint Medicines Corporation and Cowen and Company, LLC	10-K	001-37359	1.1	February 17, 2022
3.1	Fifth Amended and Restated Certificate of Incorporation of the Registrant	10-Q	001-37359	3.1	November 9, 2015
3.2	Amended and Restated Bylaws, as amended on November 30, 2022, of the Registrant	8-K	001-37359	3.1	December 6, 2022
4.1	Specimen Common Stock Certificate	S-1/A	333-202938	4.1	April 20, 2015
4.2	Description of the Registrant's securities registered pursuant to Section 12 of the Securities and Exchange Act of 1934, as amended	10-K	001-37359	4.3	February 13, 2020
10.1#	2011 Stock Option and Grant Plan, as amended, and forms of award agreements thereunder	S-1	333-202938	10.1	March 23, 2015
10.2#	2015 Stock Option and Incentive Plan and forms of award agreements thereunder	10-K	001-37359	10.2	February 13, 2020

10.3#	2015 Employee Stock Purchase Plan	10-K	001-37359	10.3	February 13, 2020
10.4#	2020 Inducement Plan and form of award agreements thereunder	S-8	333-238039	99.1	May 6, 2020
10.5	Lease Agreement, dated February 11, 2015, by and between the Registrant and 38 Sidney Street Limited Partnership	S-1	333-202938	10.4	March 23, 2015
10.6	First Amendment to Lease Agreement, dated January 26, 2018, by and between the Registrant and 38 Sidney Street Limited Partnership	10-K	001-37359	10.5	February 26, 2019
10.7	Second Amendment to Lease Agreement, dated April 6, 2021, by and between Blueprint Medicines Corporation and BRE-BMR 38 SIDNEY LLC	10-Q	001-37359	10.1	April 29,2021
10.8	Third Amendment to Lease Agreement, dated December 15, 2021, by and between Blueprint Medicines Corporation and BRE-BMR 38 SIDNEY LLC	10-K	001-37359	10.8	February 17, 2021
10.9	Lease Agreement, dated April 28, 2017, by and between the Registrant and UP 45/75 Sidney Street, LLC	10-Q	001-37359	10.1	May 3, 2017
10.10	First Amendment of Lease, dated September 19, 2018, between Blueprint Medicines Corporation and UP 45/75 Sidney Street, LLC	8-K	001-37359	10.1	September 25, 2018
10.11#	Amendment Agreement dated as of December 23, 2022 by and between the Registrant and Jeffrey W. Albers	8-K	001-37359	10.2	December 27, 2022
10.12#	Employment Agreement, dated March 10, 2016, by and between the Registrant and Kathryn Haviland	10-K	001-37359	10.9	March 11, 2016

10.13#	First Amendment to Employment Agreement, dated January 30, 2019, by and between the Registrant and Kathryn Haviland	8-K	001-37359	10.2	February 5, 2019
10.14#	Second Amendment to Employment Agreement, dated December 22, 2021, by and between the Registrant and Kathryn Haviland	8-K	001-37359	10.4	December 23, 2021
10.15#	First Amendment to Amended and Restated Employment Agreement, dated September 23, 2022, by and between the Registrant and Kathryn Haviland	8-K	001-37359	10.1	September 23, 2022
10.16#	Amended and Restated Employment Agreement, dated January 4, 2022 and effective as of April 4, 2022, by and between the Registrant and Kathryn Haviland	8-K	001-37359	10.2	January 5, 2022
10.17#	Employment Agreement, dated September 6, 2016, by and between the Registrant and Tracey L. McCain	10-Q	001-37359	10.3	November 10, 2016
10.18#	First Amendment to Employment Agreement, dated December 22, 2021, by and between the Registrant and Tracey L. McCain	8-K	001-37359	10.5	December 23, 2021
10.19#	Second Amendment to Employment Agreement, dated September 23, 2022, by and between the Registrant and Tracey L. McCain	8-K	001-37359	10.5	September 23, 2022
10.20#	Employment Agreement, dated November 22, 2017, by and between the Registrant and Michael Landsittel	8-K	001-37359	10.1	November 22, 2017
10.21#	First Amendment to Employment Agreement, dated January 30, 2019, by and between the Registrant and Michael Landsittel	8-K	001-37359	10.1	February 5, 2019

10.22#	Second Amendment to Employment Agreement, dated December 22, 2021, by and between the Registrant and Michael Landsittel	8-K	001-37359	10.2	December 23, 2021
10.23#	Third Amendment to Employment Agreement, dated September 23, 2022, by and between the Registrant and Michael Landsittel	8-K	001-37359	10.2	September 23, 2022
10.24#	Employment Agreement, dated October 29, 2018, by and between the Registrant and Christina Rossi	8-K	001-37359	10.1	October 29, 2018
10.25#	First Amendment to Employment Agreement, dated December 22, 2021, by and between the Registrant and Christina Rossi	8-K	001-37359	10.6	December 23, 2021
10.26#	Amended and Restated Employment Agreement, dated January 4, 2022 and effective as of April 4, 2022, by and between the Registrant and Christina Rossi	8-K	001-37359	10.3	January 5, 2022
10.27#	First Amendment to Amended and Restated Employment Agreement, dated September 23, 2022, by and between the Registrant and Christina Rossi	8-K	001-37359	10.3	September 23, 2022
10.28#	Employment Agreement, dated March 6, 2019, by and between the Registrant and Ariel Hurley	8-K	001-37359	10.1	March 8, 2019
10.29#	First Amendment to Employment Agreement, dated December 22, 2021, by and between the Registrant and Ariel Hurley	8-K	001-37359	10.11	December 23, 2021
10.30#	Second Amendment to Employment Agreement, dated September 23, 2022, by and between the Registrant and Ariel Hurley	8-K	001-37359	10.10	September 23, 2022

10.31#	Third Amendment to Employment Agreement, dated February 15, 2023, effective as of January 1, 2023, by and between the Registrant and Ariel Hurley	10-K	001-37359	10.39	February 16, 2023
10.32#	Employment Agreement, dated November 22, 2017, by and between the Registrant and Debra Durso-Bumpus, as amended by the First Amendment to Employment Agreement, dated February 10, 2020, by and between the Registrant and Debra Durso-Bumpus	10-K	001-37359	10.19	February 13, 2020
10.33#	Second Amendment to Employment Agreement, dated December 22, 2021, by and between the Registrant and Debra Durso-Bumpus	8-K	001-37359	10.10	December 23, 2021
10.34#	Third Amendment to Employment Agreement, dated September 23, 2022, by and between the Registrant and Debra Durso-Bumpus	8-K	001-37359	10.9	September 23, 2022
10.35#	Employment Agreement, effective September 1, 2020, by and between the Registrant and Fouad Namouni, M.D.	8-K	001-37359	10.1	September 1, 2020
10.36#	First Amendment to Employment Agreement, dated December 22, 2021, by and between the Registrant and Fouad Namouni, M.D.	8-K	001-37359	10.3	December 23, 2021
10.37#	Second Amendment to Employment Agreement, dated September 23, 2022, by and between the Registrant and Fouad Namouni, M.D.	8-K	001-37359	10.4	September 23, 2022
10.38#	Amended and Restated Employment Agreement, dated January 11, 2021, by and between the Registrant and Becker Hewes, M.D.	8-K	001-37359	10.2	January 11, 2021

10.39#	First Amendment to Amended and Restated Employment Agreement, dated December 22, 2021, by and between the Registrant and Lemuel Becker Hewes, M.D.	8K	001-37359	10.7	December 23, 2021
10.40#	Second Amendment to Employment Agreement, dated September 23, 2022, by and between the Registrant and Lemuel Becker Hewes, M.D.	8-K	001-37359	10.6	September 23, 2022
10.41#††	Employment Agreement, effective as of May 19, 2021, by and between the Registrant and Percy H. Carter, M.D., Ph.D.	10-Q	001-37359	10.1	July 29, 2021
10.42#	First Amendment to Employment Agreement, dated December 22, 2021, by and between the Registrant and Percy H. Carter, M.D., Ph.D.	8-K	001-37359	10.9	December 23, 2021
10.43#	Second Amendment to Employment Agreement, dated September 23, 2022, by and between the Registrant and Percy H. Carter, M.D., Ph.D.	8-K	001-37359	10.8	September 23, 2022
10.44#	Amended and Restated Employment Agreement, dated January 19, 2022 and effective as of April 4, 2022, by and between the Registrant and Philina Lee	8-K	001-37359	10.1	January 20, 2022
10.45#	First Amendment to Amended and Restated Employment Agreement, dated September 23, 2022, by and between the Registrant and Philina Lee	8-K	001-37359	10.11	September 23, 2022
10.46†	License and Collaboration Agreement, dated June 1, 2018, between the Registrant and CStone Pharmaceuticals	10-Q	001-37359	10.1	August 1, 2018
10.47††	License Agreement, effective October 15, 2019, by and between the Registrant and Clementia Pharmaceuticals, Inc.	10-Q	001-37359	10.1	November 5, 2019

10.48~††	Collaboration and License Agreement, dated November 8, 2021, by and between the Registrant and Zai Lab (Shanghai) Co. Ltd	10-K	001-37359	10.54	February 17, 2021
10.49	Form of Indemnification Agreement entered into between the Registrant and its directors	S-1	333-202938	10.11	March 23, 2015
10.50	Form of Indemnification Agreement entered into between the Registrant and its officers	S-1	333-202938	10.12	March 23, 2015
10.51#	Senior Executive Cash Incentive Bonus Plan	10-K	001-37359	10.15	March 11, 2016
10.52	Purchase and Sale Agreement, dated as of June 30, 2022, by and among the Registrant Garnich Adjacent Investments S.a.r.l. the various other purchasers from time to time party thereto and Garnish Adjacent Investments S.a.r.l, as Purchaser's Representative	10-Q	001-37359	10.2	August 2, 2022
10.53	Financing Agreement, dated as of June 30, 2022, by and among the Registrant, as Borrower, certain subsidiaries of the Registrant, as Guarantors, various lenders from time-to-time party thereto and Tao Talents, LLC, as Administrative Agent for the lenders	10-Q	001-37359	10.3	August 2, 2022
10.54	First Amendment to Financing Agreement dated as of May 22, 2023 by and among Blueprint Medicines Corporation, the lenders party thereto, and TAO Talents LLC, as Administrative Agent for the lenders	8-K	001-37359	10.1	May 25, 2023
10.55#	Amended and Restated 2020 Inducement Plan	8-K	001-37359	10.1	June 27, 2022

10.56#	Non-Qualified Stock Option for Employees under the 2015 Stock Option and Incentive Plan (annual award)	10-K	001-37359	10.76	February 16, 2023
10.57#	Non-Qualified Stock Option for Employees under the 2015 Stock Option and Incentive Plan (non-U.S. new hire award)	10-K	001-37359	10.77	February 16, 2023
10.58#	Non-Qualified Stock Option for Non-Employee Directors under the 2015 Stock Option and Incentive Plan (annual award)	10-K	001-37359	10.78	February 16, 2023
10.59#	Non-Qualified Stock Option for Non-Employee Directors under the 2015 Stock Option and Incentive Plan (new director award)	10-K	001-37359	10.79	February 16, 2023
10.60#	Non-Qualified Stock Option for Employees under the 2020 Inducement Plan	10-K	001-37359	10.80	February 16, 2023
10.61#	Performance-Based Restricted Stock Unit Award Agreement for Employees under the 2015 Stock Option and Incentive Plan	10-K	001-37359	10.81	February 16, 2023
10.62#	Restricted Stock Unit Award for Employees under the 2015 Stock Option and Incentive Plan	10-K	001-37359	10.82	February 16, 2023
10.63#	Restricted Stock Unit Award for Non-Employee Directors under the 2015 Stock Option and Incentive Plan (annual award)	10-K	001-37359	10.83	February 16, 2023
10.64#	Restricted Stock Unit Award for Non-Employee Directors under the 2015 Stock Option and Incentive Plan (new director award)	10-K	001-37359	10.84	February 16, 2023
10.65#	Restricted Stock Unit Award for Employees under the 2020 Incentive Plan	10-K	001-37359	10.85	February 16, 2023

10.66#	Blueprint Medicines Corporation 2024 Stock Incentive Plan	Form 8-K	001-37359	99.1	June 14, 2024
10.67#	Form of award agreements under the Blueprint Medicines Corporation 2024 Stock Incentive Plan	Form 8-K	001-37359	99.2	June 14, 2024
19.1	Blueprint Medicines Insider Trading Policy and Special Trading Procedures for Insiders	Form 10-K	001-37359	19.1	February 15, 2024
21.1	Subsidiaries of the Registrant				*
23.1	Consent of Ernst & Young LLP				*
31.1	Certification of Principal Executive Officer pursuant to Rule 13a-14(a) or Rule 15d-14(a) of the Exchange Act, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002				*
31.2	Certification of Principal Financial Officer pursuant to Rule 13a-14(a) or Rule 15d-14(a) of the Exchange Act, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002				*
32.1+	Certifications of Principal Executive Officer and Principal Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002				+
97.1#	Blueprint Medicines Corporation Policy for Recoupment of Erroneously Awarded Compensation	Form 10-K	001-37359	97.1	February 15, 2024

101.INS	XBRL Instance Document - the instance document does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL Document	*
101.SCH	XBRL Taxonomy Extension Schema Document	*
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document	*
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document	*
101.LAB	XBRL Taxonomy Extension Label Linkbase Document	*
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document	*
104	Cover Page Interactive Data File (formatted as inline XBRL with applicable taxonomy extension information contained in Exhibits 101.*)	*

# Indicates management contract or compensatory plan or arrangement.

~ Certain schedules and exhibits to the Agreement have been omitted pursuant to Item 601(a)(5) of Regulation S-K. A copy of any omitted schedule and/or exhibit will be furnished to the Securities and Exchange Commission upon request

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

††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) likely to cause competitive harm to the Company if publicly disclosed.

* Filed herewith.

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

Item 16. Form 10-K Summary.

Not applicable.

SIGNATURES

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

BLUEPRINT MEDICINES CORPORATION

Date: February 13, 2025

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

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

Signature	Title	Date
/s/ Kathryn Haviland Kathryn Haviland	President, Chief Executive Officer and Director *(Principal Executive Officer)*	February 13, 2025
/s/ Michael Landsittel Michael Landsittel	Chief Financial Officer *(Principal Financial Officer)*	February 13, 2025
/s/ Ariel Hurley Ariel Hurley	Senior Vice President, Finance *(Principal Accounting Officer)*	February 13, 2025
/s/ Jeffrey W. Albers Jeffrey W. Albers	Chairman of the Board of Directors	February 13, 2025
/s/ Daniella Beckman Daniella Beckman	Director	February 13, 2025
/s/ Alexis Borisy Alexis Borisy	Director	February 13, 2025
/s/ Lonnel Coats Lonnel Coats	Director	February 13, 2025
/s/ Habib Dable Habib Dable	Director	February 13, 2025
/s/ Mark Goldberg Mark Goldberg, M.D.	Director	February 13, 2025
/s/ Nicholas Lydon Nicholas Lydon, Ph.D.	Director	February 13, 2025
/s/ Lynn Seely Lynn Seely, M.D.	Director	February 13, 2025
/s/ John Tsai John Tsai, M.D.	Director	February 13, 2025

Blueprint Medicines Corporation

Index to Consolidated Financial Statements

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Blueprint Medicines Corporation

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Blueprint Medicines Corporation (the Company) as of December 31, 2024 and 2023, the related consolidated statements of operations and comprehensive loss, stockholders' equity and cash flows for each of the three years in the period ended December 31, 2024, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2024 and 2023, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2024, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the Company's internal control over financial reporting as of December 31, 2024, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework), and our report dated February 13, 2025 expressed an unqualified opinion thereon.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

Critical Audit Matters

The critical audit matter communicated below is a matter arising from the current period audit of the financial statements that was communicated or required to be communicated to the audit committee and that: (1) relates to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective or complex judgments. The communication of the critical audit matter does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing a separate opinion on the critical audit matter or on the accounts or disclosures to which it relates.

Accrued Clinical Trial Expenses

Description of the Matter	As discussed in Note 2 to the consolidated financial statements, the Company accrues costs for clinical trial activities based upon estimates of the services received and related expenses incurred through the balance sheet date that have yet to be invoiced by the contract research organizations or other clinical trial vendors that perform the activities. Auditing the Company's accruals for clinical trials is challenging due to the fact that information necessary to estimate the accruals is accumulated from multiple sources. In addition, in certain circumstances, the determination of the nature and level of services that have been received during the reporting period requires judgment because the timing and pattern of vendor invoicing does not correspond to the level of services provided and there

may be delays in invoicing from clinical study sites and other vendors.

How We Addressed the Matter in Our Audit

We obtained an understanding of, evaluated the design and tested the operating effectiveness of internal controls that addressed the identified risks related to the Company's process for recording accrued clinical expenses.

To evaluate the accrual for clinical expenses, our audit procedures included, among others, testing the completeness and accuracy of the underlying data used in the estimates and evaluating the significant assumptions including, but not limited to, expected patient enrollment, costs per patient, site activation and estimated project duration, that are used by management to estimate the recorded accruals. To assess the reasonableness of the significant assumptions, we corroborated the progress of clinical trials with the Company's clinical team and obtained information directly from third parties related to active patient sites and currently enrolled patients. We also tested subsequent invoicing received from such third parties and inspected the Company's contracts with third parties and any pending change orders to assess the impact to the accrual through the balance sheet date and compared that to the Company's estimates.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2011.

Boston, Massachusetts
February 13, 2025

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

	December 31, 2024	December 31, 2023
Assets		
Current assets:		
Cash and cash equivalents	$ 102,014	$ 71,286
Marketable securities	513,473	639,355
Accounts receivable	75,797	42,827
Unbilled accounts receivable	1,812	351
Inventory	13,611	21,223
Prepaid expenses and other current assets	35,971	33,351
Total current assets	742,678	808,393
Marketable securities	248,450	56,530
Property and equipment, net	36,593	41,959
Operating lease right-of-use assets, net	64,181	73,691
Restricted cash	11,625	10,238
Equity investment	28,699	27,789
Other assets	47,587	30,650
Total assets	$ 1,179,813	$ 1,049,250
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 6,790	$ 4,710
Accrued expenses	133,088	127,992
Current portion of operating lease liabilities	13,346	11,933
Current portion of deferred revenue	2,005	812
Current portion of liabilities related to the sale of future royalties and revenues	61,650	39,198
Current portion of term loan	43,917	30,278
Total current liabilities	260,796	214,923
Operating lease liabilities, net of current portion	68,790	81,751
Deferred revenue, net of current portion	8,193	4,792
Liabilities related to the sale of future royalties and revenues, net of current portion	193,524	402,427
Term loan, net of current portion	343,053	208,535
Other long-term liabilities	6,792	6,213
Total liabilities	881,148	918,641
Commitments and Contingencies (Note 19)		
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; 63,712,256 and 61,147,236 shares issued and outstanding at December 31, 2024 and December 31, 2023, respectively	64	61
Additional paid-in capital	2,709,183	2,473,985
Accumulated other comprehensive loss	(3,551)	(3,495)
Accumulated deficit	(2,407,031)	(2,339,942)
Total stockholders' equity	298,665	130,609
Total liabilities and stockholders' equity	$ 1,179,813	$ 1,049,250

The accompanying notes are an integral part of the consolidated financial statements.

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

	Year Ended December 31,		
	2024	2023	2022
Revenues:			
Product revenue, net	$ 478,950	$ 204,207	$ 110,993
Collaboration, license and other revenue	29,874	45,173	65,543
License revenue - related party	—	—	27,500
Total revenues	508,824	249,380	204,036
Cost and operating expenses:			
Cost of sales	20,163	8,540	17,813
Collaboration loss sharing	—	4,256	8,948
Research and development	341,433	427,720	477,419
Selling, general and administrative	359,272	295,141	237,374
Total cost and operating expenses	720,868	735,657	741,554
Other income (expense):			
Interest expense, net	(28,151)	(18,793)	(16,767)
Other income (expense), net	656	(946)	2,004
Debt extinguishment gain	173,676	—	—
Total other income (expense)	146,181	(19,739)	(14,763)
Loss before income taxes	(65,863)	(506,016)	(552,281)
Income tax expense	1,226	968	5,236
Net loss	$ (67,089)	$ (506,984)	$ (557,517)
Other comprehensive income (loss):			
Unrealized gain (loss) on pension benefit obligations	(761)	(2,781)	666
Unrealized gain (loss) on available-for-sale investments	702	9,759	(7,246)
Currency translation adjustments	3	(30)	270
Comprehensive loss	$ (67,145)	$ (500,036)	$ (563,827)
Net loss per share — basic and diluted	$ (1.07)	$ (8.37)	$ (9.35)
Weighted-average number of common shares used in net loss per share — basic and diluted	62,857	60,558	59,642

The accompanying notes are an integral part of the consolidated financial statements.

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

	Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Loss	Accumulated Deficit	Stockholders' Equity
	Shares	Amount				
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 and stock purchase plan	817,833	1	8,134	—	—	8,135
Stock-based compensation expense	—	—	99,634	—	—	99,634
Other comprehensive loss	—	—	—	(6,310)		(6,310)
Net loss	—	—	—	—	(557,517)	(557,517)
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 and stock purchase plan	1,188,317	1	22,711	—	—	22,712
Stock-based compensation expense	—	—	93,256	—	—	93,256
Other comprehensive income	—	—	—	6,948	—	6,948
Net loss	—	—	—	—	(506,984)	(506,984)
Balance at December 31, 2023	61,147,236	$ 61	$ 2,473,985	$ (3,495)	$ (2,339,942)	$ 130,609
Issuance of common stock under stock plan and stock purchase plan	2,020,301	2	76,365	—	—	76,367
Stock-based compensation expense	—	—	109,920	—	—	109,920
At-the-market offerings, net of issuance costs	544,719	1	48,935	—	—	48,936
Other comprehensive loss	—	—	—	(56)	—	(56)
Other	—	—	(22)	—	—	(22)
Net loss	—	—	—	—	(67,089)	(67,089)
Balance at December 31, 2024	63,712,256	$ 64	$ 2,709,183	$ (3,551)	$ (2,407,031)	$ 298,665

The accompanying notes are an integral part of the consolidated financial statements.

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

	Year Ended December 31,		
	2024	2023	2022
Cash flows from operating activities			
Net loss	$ (67,089)	$ (506,984)	$ (557,517)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	16,291	11,665	11,735
Non-cash lease expense	9,925	9,109	8,364
Stock-based compensation	108,911	92,672	98,971
Non-cash interest expense	1,184	14,138	15,799
Non-cash customer consideration	—	—	(27,500)
Non-cash debt extinguishment gain	(173,676)	—	—
Net (accretion of discount) amortization of premium on investments	(22,465)	(17,466)	(982)
Other	(982)	1,147	2,622
Changes in assets and liabilities:			
Accounts receivable	(32,845)	(20,715)	1,572
Unbilled accounts receivable	147	13,061	(3,804)
Inventory	(4,026)	(4,366)	(8,922)
Prepaid expenses and other current assets	(2,630)	3,206	(16,938)
Other assets	(11,130)	(4,711)	(16,320)
Accounts payable	2,197	1,880	(5,816)
Accrued expenses	8,207	1,075	9,368
Other long term liabilities	(12,233)	(7,240)	—
Deferred revenue	(409)	(12,687)	(4,813)
Operating lease liabilities	(11,963)	(10,631)	(8,096)
Net cash used in operating activities	(192,586)	(436,847)	(502,277)
Cash flows from investing activities			
Purchases of property and equipment	(4,630)	(16,062)	(8,919)
Purchases of investments	(966,431)	(766,363)	(489,705)
Maturities of investments	923,560	1,056,465	349,373
Other	—	—	(290)
Net cash provided by (used in) investing activities	(47,501)	274,040	(149,541)
Cash flows from financing activities			
Proceeds from at-the-market offerings, net of issuance costs	48,936	—	—
Net proceeds from stock option exercises and employee stock purchase plan	77,743	21,336	8,196
Net proceeds from term loan facility	146,973	97,933	137,786
Net proceeds from the sale of future royalties and revenues	—	—	415,828
Principle payments for financing arrangements	(541)	(44)	—
Net cash provided by financing activities	273,111	119,225	561,810
Net increase (decrease) in cash, cash equivalents, and restricted cash	33,024	(43,582)	(90,008)
Cash, cash equivalents and restricted cash at beginning of period	81,524	124,904	215,119
Effect of exchange rate changes on cash, cash equivalents and restricted cash	(909)	202	(207)
Cash, cash equivalents and restricted cash at end of period	$ 113,639	$ 81,524	$ 124,904
Supplemental cash flow information			
Cash paid for interest	$ 79,852	$ 38,467	$ 9,814
Property and equipment purchases unpaid at period end	$ 425	$ 556	$ 324
Cash paid (refunds received) for taxes, net	$ 1,104	$ (49)	$ 6,505

The accompanying notes are an integral part of the consolidated financial statements.

Blueprint Medicines Corporation
Notes to Consolidated Financial Statements

1. Nature of Business

Blueprint Medicines Corporation (the Company), a Delaware corporation incorporated on October 14, 2008, is a global fully-integrated biopharmaceutical company that invents life-changing medicines in two core focus areas: allergy/inflammation and oncology/hematology. The Company's approach targets the root causes of disease, using deep scientific knowledge in the Company's core focus areas and drug discovery expertise across multiple therapeutic modalities.

The Company has a track record of success with two approved medicines, including AYVAKIT®/AYVAKYT® (avapritinib), which the Company is bringing to patients living with systemic mastocytosis (SM) and PDGFRA Exon 18 mutant GIST in the U.S. and Europe. Leveraging the Company's established research, development, and commercial capability and infrastructure, the Company now aims to significantly scale its impact by advancing a broad pipeline of programs ranging from early science to advanced clinical trials in mast cell diseases including SM and chronic urticaria, breast cancer and other solid tumors.

The Company is subject to a number of risks similar to those of other commercial-stage companies, including but not limited to: successful commercialization of its current and future drugs, either by itself or through collaboration with third parties; establishing safety and efficacy in clinical trials and obtaining regulatory approvals for its drug candidates; competition from other companies; compliance with comprehensive and ongoing regulatory requirements and legislative changes; and the need to obtain adequate additional financing to fund the development of its drug candidates. If the Company is unable to raise capital when needed or on attractive terms, it may be forced to delay, reduce, eliminate or repartner certain of its research and development programs or future commercialization efforts.

As of December 31, 2024, the Company had cash, cash equivalents and marketable securities of $863.9 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 audited consolidated financial statements of the Company included herein have been prepared in accordance with accounting principles generally accepted in the U.S. (GAAP) as found in the Accounting Standards Codification (ASC) and Accounting Standards Updates (ASU) of the Financial Accounting Standards Board (FASB) and the rules and regulations of the Securities and Exchange Commission (SEC).

The accompanying 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, debt modification, and income taxes.

Significant Accounting Policies

Revenue Recognition

The Company accounts for contracts with customers in accordance with ASC Topic 606, *Revenue from Contracts with Customers* (ASC 606). The Company recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration which the Company expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that the Company determines are within the scope of ASC 606, the Company performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the Company satisfies a performance obligation. The Company only applies the five-step model to contracts when it is probable that the Company will collect the consideration it is entitled to in exchange for the goods or services it transfers to the customer. At contract inception, once the contract is determined to be within the scope of ASC 606, the Company assesses the goods or services promised within each contract and determines those that are performance obligations, and assesses whether each promised good or service is distinct. The Company then recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied.

Consideration received prior to revenue recognition is recorded as deferred revenue in the consolidated balance sheets. Amounts expected to be recognized as revenue within the 12 months following the balance sheet date are classified as current portion of deferred revenue in the accompanying consolidated balance sheets. Amounts not expected to be recognized as revenue within the 12 months following the balance sheet date are classified as deferred revenue, net of current portion. Amounts are recorded as accounts receivable if the Company transfer goods or services to a customer before the customer pays consideration and the Company's right to consideration is unconditional. The Company does not assess whether a contract has a significant financing component if the expectation at contract inception is that the period between payment by the customer and the transfer of the promised goods or services to the customer will be one year or less.

Product revenue

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

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

Chargebacks: Chargebacks for fees and discounts represent the estimated obligations resulting from contractual commitments to sell product to qualified healthcare providers and government agencies at prices lower than the list prices charged to the customers who directly purchase the product from the Company. The customers charge the Company for the difference between what they pay for the product and the ultimate contractually committed or

government required lower selling price to the qualified healthcare providers. These reserves are estimated using the expected value method based upon a range of possible outcomes and are established in the same period that the related revenue is recognized, resulting in a reduction of product revenue.

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

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

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

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

Collaboration, license and other revenue

At contract inception, the Company analyzes its collaboration and license arrangements to assess whether such arrangements involve joint operating activities performed by parties that are both active participants in the activities and exposed to significant risks and rewards dependent on the commercial success of such activities and therefore within the scope of ASC Topic 808, *Collaborative Arrangements* (ASC 808). This assessment is performed throughout the life of the arrangement based on changes in the responsibilities of all parties in the arrangement. For collaboration arrangements within the scope of ASC 808 that contain multiple elements, the Company first determines which elements of the collaboration are deemed to be within the scope of ASC 808 and which elements of the collaboration are more reflective of a vendor-customer relationship and therefore within the scope of ASC 606.

For elements of collaboration arrangements that are accounted for pursuant to ASC 808, an appropriate recognition method is determined and applied consistently, either by analogy to authoritative accounting literature or by applying a reasonable and rational policy election. The Company evaluates the income statement classification for presentation of amounts due from or owed to other participants associated with multiple activities in a collaboration arrangement based on the nature of each separate activity. For the co-commercialization and marketing activities of certain of the Company's products and product candidates in a collaboration arrangement, where the Company is the principal on sales transactions with third parties, the Company recognizes revenues, cost of sales and operating expenses on a gross basis in their respective lines in its consolidated statements of operations and comprehensive income (loss). Where the Company is not the principal on sales transactions with third parties, the Company records its share of the revenues, cost of sales and operating expenses on a net basis as revenue (expenses) from the collaboration arrangement in its consolidated statements of operations and comprehensive loss.

For elements accounted within scope of ASC 606, to determine the appropriate amount of revenue to be recognized for the arrangements, the Company performs the following steps: (i) identification of the promised goods or services in the contract; (ii) determination of whether the promised goods or services are performance obligations including whether they are distinct in the context of the contract; (iii) measurement of the transaction price, including the constraint on variable consideration; (iv) allocation of the transaction price to the performance obligations; and (v) recognition of revenue when (or as) the Company satisfies each performance obligation. As part of the accounting for these arrangements, the Company must use significant judgment to determine: (a) the performance obligations based on the determination under step (ii) above; (b) the transaction price under step (iii) above; and (c) the stand-alone selling price for each performance obligation identified in the contract for the allocation of transaction price in step (iv) above.

The Company uses judgment to determine whether milestones or other variable consideration, including royalties and sales-based milestones, should be included in the transaction price as described further below. The transaction price is allocated to each performance obligation on a relative stand-alone selling price basis, for which the Company recognizes revenue as or when the performance obligations under the contract are satisfied.

Exclusive Licenses. If the license to the Company's intellectual property is determined to be distinct from the other promises or performance obligations identified in the arrangement, the Company recognizes revenue from non-refundable, upfront fees allocated to the license when the license is transferred to the customer and the customer is able to use and benefit from the license. In assessing whether a promise or performance obligation is distinct from the other promises, the Company considers factors such as the research, development, manufacturing and commercialization capabilities of the collaboration partner and the availability of the associated expertise in the general marketplace. In addition, the Company considers whether the collaboration partner can benefit from a promise for its intended purpose without the receipt of the remaining promise, whether the value of the promise is dependent on the unsatisfied promise, whether there are other vendors that could provide the remaining promise, and whether it is separately identifiable from the remaining promise. For licenses that are combined with other promises, the Company utilizes judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue. The Company evaluates the measure of progress each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition. The measure of progress, and thereby periods over which revenue should be recognized, are subject to estimates by management and may change over the course of the research and development and licensing agreement. Such a change could have a material impact on the amount of revenue the Company records in future periods.

Research and Development Services. The promises under the Company's collaboration agreements may include research and development services to be performed by the Company on behalf of the partner. Payments or reimbursements resulting from the Company's research and development efforts are recognized as revenue when the services are performed and presented on a gross basis because the Company is the principal for such efforts. Payments or reimbursements from the partner that are the result of a collaborative relationship with the partner, instead of a customer relationship, such as co-development activities, are recorded as a reduction to research and development expense.

Customer Options. If an arrangement is determined to contain customer options that allow the customer to acquire additional goods or services, the goods and services underlying the customer options that are not determined to be material rights are not considered to be performance obligations at the outset of the arrangement, as they are contingent upon option exercise. The Company evaluates the customer options for material rights, or options to acquire additional goods or services for free or at a discount. If the customer options are determined to represent a material right, the material right is recognized as a separate performance obligation at the outset of the arrangement. The Company allocates the transaction price to material rights based on the relative standalone selling price, which is determined based on the identified discount and the probability that the customer will exercise the option. Amounts allocated to a material right are not recognized as revenue until, at the earliest, the option is exercised.

Milestone Payments. At the inception of each arrangement that includes research or development milestone payments, the Company evaluates whether the milestones are considered probable of being achieved and estimates the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within the control of the Company or the licensee, such as regulatory approvals, are not considered probable of being achieved until those approvals are received. The Company evaluates factors such as the scientific, clinical, regulatory, commercial, and other risks that must be overcome to achieve the particular milestone in making this assessment. There is considerable judgment involved in determining whether it is probable that a significant revenue reversal would not occur. At the end of each subsequent reporting period, the Company reevaluates the probability of achievement of all milestones subject to constraint and, if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect revenues and earnings in the period of adjustment.

Royalties. For license arrangements that include sales-based royalties, including milestone payments upon first commercial sales and milestone payments based on a level of sales, which are the result of a customer-vendor relationship and for which the license is deemed to be the predominant item to which the royalties relate, the Company recognizes revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some

or all of the royalty has been allocated has been satisfied or partially satisfied. For arrangements involving the sale of intellectual property to customers, the Company estimates and recognizes revenue upon satisfying the related performance obligation, including any royalty payments deemed probable of achievement and not subject to significant subsequent revenue reversal. At the end of each subsequent reporting period, the Company reevaluates the expected royalties and adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect revenues and earnings in the period of adjustment.

For a complete discussion of accounting for collaboration, license and other revenues, see Note 11, *Collaboration, License and Other Agreements*.

Accounts Receivable, net

Accounts receivable arise from product sales and amounts due from the Company's collaboration partners. The amount from product sales primarily represents amounts due from specialty distributors and specialty pharmacy providers in the U.S. The Company provides reserves against accounts receivable for current expected credit losses that are estimated based on the composition of its accounts receivable and the financial condition of the counterparty, considering past events, current economic conditions, and reasonable and supportable forecasts about the future economic conditions. The contractual life of our accounts receivable is generally short-term. Amounts determined to be uncollectible are charged or written off against the reserve. For the years ended December 31, 2024, 2023 and 2022, the Company did not record any significant expected credit losses related to outstanding accounts receivable.

Inventory

Inventories are stated at the lower of cost or estimated net realizable value with cost based on the first-in first-out method. Inventory that can be used in either the production of clinical or commercial products is expensed as research and development costs when identified for use in clinical trials. The Company classifies its inventory costs as long-term when it expects to utilize the inventory beyond its normal operating cycle and includes these costs in other assets in the consolidated balance sheets.

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

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

Fair Value Measurements

The Company has certain financial assets and liabilities recorded at fair value which have been classified as Level 1, 2 or 3 within the fair value hierarchy as described in the accounting standards for fair value measurements.

- Level 1 — Fair values are determined utilizing quoted prices (unadjusted) in active markets for identical assets or liabilities that the Company has the ability to access;
- Level 2 — Fair values are determined by utilizing quoted prices for identical or similar assets and liabilities in active markets or other market observable inputs such as interest rates, yield curves and foreign currency spot rates; and
- Level 3 — inputs are unobservable inputs that reflect the Company's own assumptions about the assumptions market participants would use in pricing the asset or liability. Financial assets and liabilities are classified in their entirety based on the lowest level of input that is significant to the fair value measurement.

The Company's financial assets, which include cash equivalents and marketable securities, have been initially valued at the transaction price, and subsequently revalued at the end of each reporting period, utilizing third-party pricing services. The pricing services utilize industry standard valuation models, including both income and market based approaches, to determine value.

There have been no changes to the valuation methods during the years ended December 31, 2024, 2023 and 2022.

Cash and cash equivalents

The Company considers all highly liquid investments purchased with original maturities of 90 days or less from the date of purchase to be cash equivalents. As of December 31, 2024 and 2023, the Company's cash equivalents comprised of money market funds with less than 90 days from the date of purchase. Cash equivalents are reported at fair value.

Marketable securities

The Company classifies its investments in marketable debt securities as available-for-sale when their original maturities, from the date of purchase, exceed three months. Available-for-sale debt securities with a remaining maturity date greater than one year are classified as non-current assets. Available-for-sale marketable debt securities are maintained by an investment manager and mainly consist of U.S. treasury securities and U.S. government agency securities. Available-for-sale marketable debt securities are carried at fair value with the unrealized gains and losses included in other comprehensive income (loss) as a component of stockholders' equity until realized. Any premium or discount arising at purchase is amortized and/or accreted to interest income and/or expense over the life of the instrument. Realized gains and losses are determined using the specific identification method and are included in other income (expense). Realized losses are recognized only if the Company has the intention to sell the security or it is expecting to be required to sell the security before recovery of its amortized cost basis. The Company also reviews its portfolio of available-for-sale debt securities, using both quantitative and qualitative factors, to determine if declines in fair value below cost have resulted from a credit-related loss. If the decline in fair value is due to credit-related factors, a loss is recognized in other income (expense).

Comprehensive Income (Loss)

Comprehensive income (loss) is defined as the change in equity of a business enterprise during a period from transactions and other events and circumstances from non-owner sources. Other comprehensive income (loss) consisted of foreign currency translation adjustments, unrealized gains and losses on available-for-sale investments and unrealized gains and losses on pension benefit obligations.

Research and Development Expenses

Expenditures relating to research and development are expensed in the period incurred. Research and development expenses consist of both internal and external costs associated with the development of the Company's selective therapies and building of its discovery platform. As part of the process of preparing the consolidated financial statements, the Company accrues costs for clinical trial activities based upon estimates of the services received and related expenses incurred that have yet to be invoiced by the contract research organizations or other clinical trial vendors that perform the activities.

In certain circumstances, the Company is required to make nonrefundable advance payments to vendors for goods or services that will be received in the future for use in research and development activities. In such circumstances, the nonrefundable advance payments are deferred and capitalized, even when there is no alternative future use for the research and development, until related goods or services are provided. In circumstances where amounts have been paid in excess of costs incurred, the Company records a prepaid expense.

Selling, General and Administrative Expenses

Selling, general and administrative expenses are primarily comprised of compensation and benefits associated with sales and marketing, finance, human resources, legal, information technology and other administrative personnel,

business development, advertising and legal expenses and other general and administrative costs. Advertising costs are expensed as incurred. For years ended December 31, 2024, 2023 and 2022, advertising costs totaled $31.1 million, $16.9 million and $18.1 million, respectively.

Property and Equipment, Net

Property and equipment consists of lab equipment, furniture and fixtures, computer equipment, software, and leasehold improvements, all of which is stated at cost. Expenditures for maintenance and repairs are recorded to expense as incurred, whereas major betterments are capitalized as additions to property and equipment. Depreciation is recognized over the estimated useful lives of the assets using the straight-line method.

Impairment of Long-Lived Assets

The Company continually evaluates whether events or circumstances have occurred that indicate that the carrying amount of any of its long-lived assets might not be recoverable and that impairment might exist. If indicators of impairment are present, the Company performs a test for recoverability. The Company has not recognized any significant impairment charges associated with long-lived assets for the years ended December 31, 2024, 2023 and 2022.

Leases

Leases are accounted for in accordance with ASC Topic 842, *Leases* (ASC 842). At the inception of a contract, the Company assesses whether the contract is, or contains, a lease. The assessment is based on: (1) whether the contract involves the use of a distinct identified asset, (2) whether the Company obtains the right to substantially all the economic benefit from the use of the asset throughout the period, and (3) whether the Company has the right to direct the use of the asset. At inception of a lease, the Company allocates the consideration in the contract to each lease component based on its relative stand-alone price to determine the lease payments.

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

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

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

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

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

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

Stock-Based Compensation Expense

Stock-based compensation awards are accounted for in accordance with ASC Topic 718, *Compensation –Stock Compensation* (ASC 718). The Company expenses the fair value of stock awards granted to employees and members of the board of directors over the requisite service period, which is typically the vesting period. Compensation cost for stock-based awards issued to employees is measured using the estimated fair value at the grant date and is adjusted to reflect actual forfeitures.

Fair value of restricted stock awards granted to employees is based upon the quoted closing market price per share on the date of grant. Fair value of options granted to employees at the date of grant are estimated using the Black-Scholes option-pricing model that requires management to apply judgment and make estimates, including:

- expected volatility, which was calculated using the historical volatility of the Company's publicly traded stock. The Company computed the historical volatility data using the daily closing prices during the equivalent period of the calculated expected term of its stock-based awards;

- risk-free interest rate, which is based on the U.S. Treasury yield curve in effect at the time of grant commensurate with the expected term assumption;

- expected term, which is calculated using the simplified method, as prescribed by the Securities and Exchange Commission Staff Accounting Bulletin No. 107, *Share-Based Payment,* as the Company has insufficient historical information regarding its stock options to provide a basis for an estimate. Under this approach, the weighted-average expected life is presumed to be the average of the contractual term of ten years and the weighted-average vesting term of the stock options, taking into consideration multiple vesting tranches; and

- dividend yield, which is zero based on the fact that the Company never paid cash dividends and does not expect to pay any cash dividends in the foreseeable future.

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.

Stock-based awards issued to non-employees, including directors for non-board-related services, are accounted for based on the fair value of such services received or the fair value of the awards granted on the grant date, whichever is more reliably measured. Stock-based awards subject to service-based vesting conditions are expensed on a straight-line basis over the vesting period.

The purchase price of common stock under the Company's 2015 employee stock purchase plan (as amended, the 2015 ESPP) is equal to 85% of the lesser of (i) the fair market value per share of the common stock on the first business day of an offering period and (ii) the fair market value per share of the common stock on the purchase date. The fair value of the discounted purchases made under 2015 ESPP is calculated using the Black-Scholes valuation model. The fair value of the look-back provision plus the 15% discount is recognized as compensation expense over the 180-day purchase period.

Equity Investment

Investments in non-marketable equity securities of privately-held companies that do not have readily determinable fair values are carried at cost, less any impairments, plus or minus changes resulting from observable price

changes in orderly transactions for the identical or a similar investment of the same issuer. Each period the Company assesses relevant transactions to identify observable price changes, and the Company regularly monitors these investments to evaluate whether there is an indication of impairment. The Company evaluates whether an investment's fair value is less than its carrying value using an estimate of fair value, if such an estimate is available. For periods in which there is no estimate of fair value, the Company evaluates whether an event or change in circumstances has occurred that may have a significant adverse effect on the value of the investment.

Liabilities related to the sale of future royalties and revenues

The Company accounts for net proceeds from sales of the Company's rights to receive future royalty payments and from sales of future revenues as liabilities if the Company has significant continuing involvement in the generation of the related future cash flows. Interest expenses on the liabilities related to the sale of future royalties and revenues are recognized using the effective interest rate method over the life of the related royalty or revenue stream. The liabilities related to the sale of future royalties and revenues and the related interest expenses are based on the Company's current estimates of future royalties or revenues as well as commercial milestones expected to be achieved and received over the life of the arrangement, which the Company determines by using forecasts of the underlying drug products of the underlying regions. The Company periodically assesses the expected payments and to the extent the amount or timing of the future estimated payments is materially different than previous estimates, the Company accounts for any such change by adjusting the carrying value of the liabilities related to the sale of future royalties and revenues, and prospectively recognizing the related interest expenses.

Modification of debt instruments

When the Company's debt instrument, where the Company is the debtor, is modified or exchanged, the Company analyzes whether the modification should be accounted for as a modification or an extinguishment. Modified terms are considered substantially different if, after an exchange or modification of debt instruments with the same creditor, the present value of cash flows under the terms of the new debt instrument differs by at least 10% from the present value of the remaining cash flows under the terms of the original debt instrument. If the modified instrument is considered substantially different from the original debt instrument, the modification or exchange is accounted for as an extinguishment. The new instrument is recorded at its fair value and that fair value is used to determine the extinguishment gain or loss.

Income Taxes

The Company recognizes deferred tax assets and liabilities for the expected future tax consequences of events that have been recognized in the Company's financial statements or tax returns. Under this method, deferred tax assets and liabilities are determined based on differences between the financial statement carrying amounts and the tax bases of the assets and liabilities using the enacted tax rates in effect in the years in which the differences are expected to reverse. A valuation allowance against deferred tax assets is recorded if, based on the weight of the available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized. The Company accounts for uncertain tax positions using a more-likely-than-not threshold for recognizing and resolving uncertain tax positions. The evaluation of uncertain tax positions is based on factors including, but not limited to, changes in the law, the measurement of tax positions taken or expected to be taken in tax returns, the effective settlement of matters subject to audit, new audit activity, and changes in facts or circumstances related to a tax position.

Foreign currency translation

The financial statements of each of the Company's subsidiaries with a functional currency other than the U.S. dollar are translated into U.S. dollars using period-end exchange rates for assets and liabilities, historical exchange rates for stockholders' equity and weighted average exchange rates for operating results. Translation gains and losses are included in accumulated other comprehensive income (loss) in stockholders' equity. Foreign currency transaction gains and losses are included in other (expense) income, net in the results of operations.

Concentrations of Credit Risk and of Significant Suppliers

The Company has no significant off-balance-sheet risk such as foreign exchange contracts, option contracts, or other foreign hedging arrangements. Financial instruments that potentially expose the Company to concentrations of

credit risk primarily consist of cash and cash equivalents, marketable securities, accounts receivable and unbilled account receivables.

The Company maintains its cash, cash equivalents and marketable securities in custodian accounts at high quality financial institutions, and as of December 31, 2024 and 2023, substantially all the Company's cash, cash equivalents and marketable securities were invested in money market funds and U.S. government agency securities and treasury obligations, and consequently, the Company believes that such funds are subject to minimal credit risk. The Company has adopted an investment policy that limits the amounts the Company may invest in any one type of investment. The Company has not experienced any significant credit losses and does not believe it is exposed to any significant credit risk on these funds.

Accounts receivables and unbilled accounts receivables represent amounts arising from product sales and amounts due from the Company's collaboration partners. The Company monitors economic conditions to identify facts or circumstances that may indicate that its receivables are at risk of collection. The Company has not experienced any credit losses and does not believe it is exposed to any significant credit risk on these funds.

The Company is dependent on third-party manufacturers to supply products for commercial and research and development activities associated with its drug and drug candidates, as applicable. In particular, the Company relies and expects to continue to rely on a small number of manufacturers to supply it with its requirements for the active pharmaceutical ingredients and formulated drugs related to the Company's drug and drug candidate activities. These activities, including the commercialization of AYVAKIT/AYVAKYT, could be adversely affected by a significant interruption in the supply of active pharmaceutical ingredients and formulated drugs.

Segment and Geographic Information

Operating segments are identified as components of an enterprise about which separate discrete financial information is available for evaluation by the chief operating decision maker in making decisions on how to allocate resources and assess performance. The Company's chief operating decision maker is the chief executive officer. The chief operating decision maker views the Company's operations and manage its business as one operating segment. The Company operates in the U.S. and Europe. All material long-lived assets of the Company reside in the U.S. For additional information, see Note 18, *Segment Information*.

New Accounting Pronouncements

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

In November 2023, the FASB issued *ASU 2023-07, Segment Reporting (Topic 280): Improvements to Reportable Segment Disclosures*, which is intended to improve reportable segment disclosure requirements, primarily through additional disclosures about significant segment expenses. The standard is effective for fiscal years beginning after December 15, 2023, and interim periods within fiscal years beginning after December 15, 2024, with early adoption permitted. The Company adopted the new standard in fiscal year 2024 for annual and retrospective reporting periods with all interim disclosures to begin in the first quarter of fiscal year 2025. For additional information, see Note 18, *Segment Information*.

In December 2023, the FASB issued *ASU 2023-09, Improvements to Income Tax Disclosures*, which requires entities to disclose disaggregated information about their effective tax rate reconciliation and income taxes paid. The disclosure requirements will be applied on a prospective basis, with the option to apply them retrospectively. The standard is effective for fiscal years beginning after December 15, 2024, with early adoption permitted. The Company is currently evaluating the disclosure requirements related to this new standard.

In November 2024, the FASB issued ASU 2024-03, *Income Statement—Reporting Comprehensive Income—Expense Disaggregation Disclosures*, which requires disclosure of additional information about specific expense categories in the notes to the financial statements on an interim and annual basis. The standard is effective for fiscal years beginning after December 15, 2026, and for interim periods beginning after December 15, 2027, with early adoption permitted. The Company is currently evaluating the disclosure requirements related to this new standard.

Reclassification

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

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 Investments 2019 ICAV (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 the U.S., under the terms of the Roche pralsetinib collaboration agreement.

Despite selling all rights to receive royalties on GAVRETO net sales of the underlying territories to Royalty Pharma, the Company maintained its involvement in the global co-development of pralsetinib with Roche and was therefore involved in the generation of these future royalties. Due to the Company's significant continued involvement, any royalties and development and commercialization milestones earned pertaining to the underlying territory under the Roche pralsetinib collaboration agreement were recognized as collaboration revenue on the consolidated statements of operations and comprehensive loss throughout the contract term of the Roche pralsetinib collaboration agreement. The net proceeds received from the transaction were recorded as a liability related to sale of future royalties and revenues on the consolidated balance sheet on June 30, 2022.

The Roche pralsetinib collaboration agreement was terminated in February 2024 and the Company regained commercialization and development rights to GAVRETO from Roche worldwide excluding the CStone Territory. In connection with and effective upon the termination of the Roche pralsetinib collaboration agreement, on February 22, 2024 (the Royalty Pharma Termination Date), Royalty Pharma and the Company agreed to terminate the Royalty Purchase Agreement (Royalty Pharma Termination Agreement). Following the termination of the Royalty Purchase Agreement, the Company has no outstanding obligations under the Royalty Purchase Agreement, other than the remaining royalty payment obligation related to GAVRETO net sales as of the termination effective date. As of December 31, 2024, the Company had no plan to enter into a new arrangement to commercialize GAVRETO outside of the U.S. and the CStone Territory.

The Company has no material outstanding obligations under the Royalty Pharma Termination Agreement and it was accounted for as a debt extinguishment under ASC 470-50 as the terms and conditions of the Royalty Purchase Agreement had undergone a substantial modification and the modified terms are considered substantially different. As a result, during the year ended December 31, 2024, the Company recorded a debt extinguishment gain of $173.7 million as other income in the consolidated statements of operations and comprehensive loss. As of December 31, 2024, the net carrying value of the Company's liability related to these agreements was $0.7 million, which was determined based on the fair value of the remaining cash flow associated with anticipated future payments outlined in the Royalty Pharma Termination Agreement. The Company subsequently paid the final $0.7 million amount in February 2025.

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 debt 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 December 31, 2024, the Company's estimate of this total interest expense resulted in an effective annual interest rate of 10.3%. These estimates contain assumptions that impact the amount recorded and the interest expense that will be recognized in future periods.

As of December 31, 2024, the net carrying value of the liability related to this arrangement was $254.4 million. The following table shows the activity within the liability account during the years ended December 31, 2024 and 2023 (in thousands):

	Year Ended December 31,	
	2024	2023
Beginning balance at January 1	$ 266,670	$ 254,328
Interest expense recognized	27,134	28,065
Payments	(39,368)	(15,723)
Carrying value at December 31	$ 254,436	$ 266,670

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.

The following table shows the proceeds the Company has received under the Financing Agreement with Sixth Street Partners (in thousands):

Term loan draw	Date	Gross proceeds	Debt discount/ Transaction cost	Net proceeds
Senior Secured Term Loan Facility	July 2022	$ 150,000	$ 12,214	$ 137,786
1st Senior Secured Delayed Draw Term Loan Facility	August 2023	100,000	2,067	97,933
2nd Senior Secured Delayed Draw Term Loan Facility	May 2024	150,000	3,027	146,973
		$ 400,000	$ 17,308	$ 382,692

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 December 31, 2024, the Company's estimate of the total interest expense resulted in an effective annual interest rate of 12.0%. The carrying amount of the debt as of December 31, 2024 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 during the years ended December 31, 2024 and 2023 (in thousands):

	Year Ended December 31,	
	2024	2023
Beginning balance at January 1	$ 238,813	$ 139,083
Net proceeds received	146,973	97,933
Interest expense recognized	41,668	23,540
Payments	(40,484)	(21,743)
Carrying value at December 31	$ 386,970	$ 238,813

The total estimated total gross payments due under the term loan are as follows as of December 31, 2024 (in thousands):

	As of December 31, 2024
2025	$ 43,917
2026	43,917
2027	43,917
2028	421,897
Total	$ 553,648

The Company's obligations under the Financing Agreement are secured, subject to certain exceptions, by security interests in substantially all assets of the Company and certain of its 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 $80.0 million. As of December 31, 2024, the Company was in compliance with the applicable terms and conditions of the covenants under the Financing Agreement.

4. Marketable Securities

Marketable securities consisted of the following at December 31, 2024 and 2023 (in thousands):

December 31, 2024	Amortized Cost	Unrealized Gain	Unrealized Losses	Fair Value
Marketable securities, available-for-sale:				
U.S. government agency securities	$ 129,897	$ 118	$ (230)	$ 129,785
U.S. treasury obligations	631,514	1,025	(401)	632,138
Total	$ 761,411	$ 1,143	$ (631)	$ 761,923

December 31, 2023	Amortized Cost	Unrealized Gain	Unrealized Losses	Fair Value
Marketable securities, available-for-sale:				
U.S. government agency securities	$ 170,194	$ 27	$ (418)	$ 169,803
U.S. treasury obligations	525,880	588	(386)	526,082
Total	$ 696,074	$ 615	$ (804)	$ 695,885

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 December 31, 2024 and 2023 (in thousands):

	As of December 31,			
	2024		2023	
	Amortized Cost	Fair value	Amortized Cost	Fair value
Within one year	$ 512,515	$ 513,473	$ 639,881	$ 639,355
After one through five years	248,896	248,450	56,193	56,530
Total	$ 761,411	$ 761,923	$ 696,074	$ 695,885

As of December 31, 2024 and 2023, the Company held 32 and 62 debt securities, respectively, that were in an unrealized loss position. The following table summarizes the estimated fair value and the aggregate unrealized loss of the Company's available-for-sale securities that are in loss position as of December 31, 2024 and 2023 by the length of time the security has been in loss position (in thousands):

	As of December 31,			
	2024		2023	
	Fair value	Unrealized losses	Fair value	Unrealized losses
Debt securities in unrealized loss position for 12 months or less	$ 205,910	$ (631)	$ 267,917	$ (550)
Debt securities in unrealized loss position for more than 12 months	—	—	64,659	(254)
Total debt securities in unrealized loss position	$ 205,910	$ (631)	$ 332,576	$ (804)

The Company has the intent and ability to hold its debt securities until recovery of amortized cost basis. As a result, the Company did not recognize any differences between the fair value and amortized cost basis as a loss in its consolidated statements of operations and comprehensive loss for the years ended December 31, 2024, 2023 and 2022. The Company did not record any credit-related impairments for its available-for-sale securities for the years ended December 31, 2024, 2023 and 2022.

The following table summarizes the proceeds from maturities of debt securities during the years ended December 31, 2024, 2023 and 2022 (in thousands):

	Year ended December 31,		
	2024	2023	2022
Proceeds from maturities of debt securities	$ 923,560	$ 1,056,465	$ 349,373

The Company did not realize any gains or losses from maturities of debt securities for the years ended December 31, 2024, 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 December 31, 2024 (in thousands):

Description	December 31, 2024	Active Markets (Level 1)	Observable Inputs (Level 2)	Unobservable Inputs (Level 3)
Cash equivalents:				
Money market funds	$ 69,729	$ 69,729	$ —	$ —
Marketable securities, available-for-sale:				
U.S. government agency securities	129,785	—	129,785	—
U.S. treasury obligations	632,138	632,138	—	—
Total	$ 831,652	$ 701,867	$ 129,785	$ —

The following table summarizes the Company's cash equivalents and marketable securities measured at fair value on a recurring basis as of December 31, 2023 (in thousands):

Description	December 31, 2023	Active Markets (Level 1)	Observable Inputs (Level 2)	Unobservable Inputs (Level 3)
Cash equivalents:				
Money market funds	$ 55,412	$ 55,412	$ —	$ —
Marketable securities, available-for-sale:				
U.S. government agency securities	169,803		169,803	—
U.S. treasury obligations	526,082	526,082	—	—
Total	$ 751,297	$ 581,494	$ 169,803	$ —

6. Product Revenue and Related Reserves

The following table summarizes revenue recognized from the sales of AYVAKIT/AYVAKYT for the years ended December 31, 2024, 2023 and 2022 (in thousands):

	Year Ended December 31,		
	2024	2023	2022
United States	$ 421,837	$ 181,971	$ 97,226
Rest of World	57,113	22,236	13,767
Total product revenue, net	$ 478,950	$ 204,207	$ 110,993

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 years ended December 31, 2024, 2023, and 2022:

	Year ended December 31,		
	2024	2023	2022
Customer 1	39 %	43 %	45 %
Customer 2	12 %	* %	* %
Customer 3	* %	10 %	11 %

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

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 December 31, 2024 and 2023:

	As of December 31,	
	2024	2023
Customer 1	31 %	34 %
Customer 2	14 %	* %
Customer 3	11 %	11 %
Customer 4	* %	10 %
Customer 5	* %	10 %

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

The following table summarizes activity in the product revenue allowance and reserve for the years ended December 31, 2024 and 2023 (in thousands):

	Year Ended December 31,	
	2024	2023
Beginning balance at January 1	$ 19,274	$ 9,788
Provision related to sales in the current period	80,847	37,281
Adjustment related to prior periods sales	(566)	(700)
Credits and payments made	(65,776)	(27,095)
Ending balance at December 31	$ 33,779	$ 19,274

The total reserves that are included in the Company's consolidated balance sheets as of December 31, 2024 and 2023, are summarized as follows (in thousands):

	As of December 31,	
	2024	2023
Reduction of accounts receivable, net	$ 2,963	$ 1,809
Component of accrued expenses	30,816	17,465
Total revenue-related reserves	$ 33,779	$ 19,274

7. Inventory

Capitalized inventory consists of the following as of December 31, 2024 and 2023 (in thousands):

	As of December 31,	
	2024	2023
Raw materials	$ —	$ 3,147
Work in process	30,300	29,132
Finished goods	8,975	4,823
Total	$ 39,275	$ 37,102

Balance sheet classification

	As of December 31,	
	2024	2023
Inventory	$ 13,611	$ 21,223
Other assets	25,664	15,879
Total	$ 39,275	$ 37,102

Inventory amounts written down as a result of excess, obsolescence, unmarketability or other reasons are charged to cost of sales. For the years ended December 31, 2024, 2023 and 2022, the Company recognized write-downs of $0.4 million, $0.7 million and $2.1 million, respectively. Long-term inventory, which primarily consists of work in process is included in other assets in the consolidated balance sheets.

8. Restricted Cash

The following table provides a reconciliation of cash, cash equivalents, and restricted cash reported within the Company's consolidated balance sheets that sum to the total of the same such amounts shown in the consolidated statements of cash flows for the years ended December 31, 2024, 2023 and 2022 (in thousands):

	December 31,		
	2024	2023	2022
Cash and cash equivalents	$ 102,014	$ 71,286	$ 119,709
Restricted cash	11,625	10,238	5,195
Total cash, cash equivalents, and restricted cash shown in consolidated statements of cash flows	$ 113,639	$ 81,524	$ 124,904

At December 31, 2024 and 2023, $11.6 million and $10.2 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. For additional information, see Note 16, *Leases*.

9. Property and Equipment, Net

Property and equipment and related accumulated depreciation as of December 31, 2024 and 2023 are as follows (in thousands):

	Estimated Useful Life (Years)	As of December 31, 2024	As of December 31, 2023
Lab equipment	5	$ 25,720	$ 21,311
Furniture and fixtures	4	4,642	4,644
Computer equipment	3	2,062	2,028
Leasehold improvements	Term of lease	50,787	42,301
Software	3	902	657
Construction-in-progress		235	9,512
Total cost		84,348	80,453
Less: accumulated depreciation and amortization		(47,755)	(38,494)
Total		$ 36,593	$ 41,959

Property, plant and equipment are recorded at historical cost, net of accumulated depreciation. Depreciation expense for the years ended December 31, 2024, 2023 and 2022 was $9.7 million, $7.7 million and $6.5 million, respectively.

10. Accrued Expenses

Accrued expenses as of December 31, 2024 and 2023 consist of the following (in thousands):

	As of December 31, 2024	As of December 31, 2023
Research, development and commercial contract costs	$ 33,957	$ 49,354
Employee compensation	48,725	43,434
Accrued professional fees	14,134	12,522
Revenue-related reserves	30,816	17,465
Other	5,456	5,217
Total	$ 133,088	$ 127,992

11. Collaboration, License and Other Agreements

Rigel

On February 22, 2024, the Company entered into an Asset Purchase Agreement with Rigel Pharmaceuticals, Inc. (“Rigel”) for Rigel to purchase certain assets from the Company comprising the U.S. rights to research, develop, manufacture and commercialize GAVRETO (pralsetinib). Such assets include, among other things, applicable intellectual property related to pralsetinib in the U.S, including patents, copyrights and trademarks, as well as clinical regulatory and commercial data and records. Simultaneously and in connection with entering into the Asset Purchase Agreement, the parties also entered into certain supporting agreements, including a customary transition agreement, (such agreements collectively, the Rigel Agreement), pursuant to which, the Company transitioned certain inventory and regulatory and distribution responsibilities for pralsetinib to Rigel.

Under the terms of the Rigel Agreement, the Company has the right to receive a purchase price of $15.0 million, with $10.0 million paid upon first commercial sale of GAVRETO by Rigel and an additional $5.0 million as a delayed purchase price payable on the later of (i) the first anniversary of the closing date of the transaction, or (ii) the completion of certain transition activities. The Company is also eligible to receive up to $102.5 million in contingent specified regulatory and commercial milestone payments, in addition to tiered percentage royalties ranging from 10 percent to 30 percent on annual net sales of GAVRETO in the U.S. The royalties will be payable until the later of (i) the expiration of the royalty term, as defined in the agreement, which begins on the date of the first commercial sale of

GAVRETO in the U.S., (ii) the date of expiration of the last valid patent claim within the Company's IP that covers GAVRETO in the U.S., and (iii) the expiration of the last regulatory exclusivity for GAVRETO in the U.S.

The Company determined that the Rigel Agreement is a transaction with a customer and therefore accounted for the transaction in accordance with ASC 606. As of the effective date, the Company determined that the agreement includes three performance obligations: the delivery of (1) the U.S. rights to GAVRETO; (2) additional pralsetinib clinical data; and (3) GAVRETO product to be purchased from Genentech.

The transaction price under ASC 606 was fully constrained at the inception of the Rigel Agreement due to the pending completion of key transition activities stipulated in the agreement, including the transfer of the new drug application (NDA). These key transition activities, including the transfer of the NDA, related patents, and GAVRETO product, were completed in the second quarter of 2024. The performance obligations related to the U.S. rights to GAVRETO and the delivery of GAVRETO product were satisfied at a point in time upon the completion of these key transition activities. The transaction price was determined to be $27.7 million, which consisted of $6.5 million consideration for the GAVRETO product, $10.0 million upfront purchase price payment, and $11.2 million in the milestone and royalty payments that were considered probable of achievement and not subject to significant subsequent reversal of revenue. The transaction price was allocated to the three performance obligations on a relative stand-alone selling price basis.

During the year ended December 31, 2024, the Company recognized total revenue of $24.3 million which is primarily comprised of GAVRETO product consideration of $6.5 million and the transaction price allocated to the U.S. rights to GAVRETO performance obligation of $17.6 million. The additional clinical data performance obligation will be satisfied at a point in time once the transfer of such data to Rigel is completed, and the allocated transaction price of $3.6 million was recorded as deferred revenue on the consolidated financial statements as of December 31, 2024.

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.

The following table summarizes the assets and liabilities under the Rigel agreements as of December 31, 2024 (in thousands):

	As of December 31, 2024		
	Current	Noncurrent	Total
Contract assets	$ 2,939	$ 7,380	$ 10,319
Contract liabilities	$ —	$ 3,562	$ 3,562

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 a member 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 shares are restricted from reselling unless IDRx subsequently proposes a resale registered under the Securities Act or if an exemption from registration is otherwise available.

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 in 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 preferred stock investment was accounted for under the measurement alternative for equity investments that do not have a readily determinable fair value, at cost of $27.8 million including transaction costs of $0.3 million. If observable price changes in orderly transactions for the identical or similar investment are identified, the Company will adjust the carrying value of the investment to its fair value as of the transaction date. During the year ended December 31, 2024, IDRx completed a Series B preferred stock financing and accordingly, the Company adjusted the carrying value of its investment in IDRx to $28.7 million. The $0.9 million investment gain was recorded as other income on the Company's consolidated

statements of operations and comprehensive loss. No revenue was recorded under the IDRx License Agreement during the years ended December 31, 2024 and 2023.

In January 2025, IDRx announced that they had entered into an agreement under which GSK plc will acquire IDRx for $1.0 billion upfront with an additional $150.0 million regulatory approval-based milestone payment. The transaction is expected to close in the first quarter 2025.

VantAI

In February 2022, the Company entered into an exclusive collaboration agreement with Oncopia Therapeutics, Inc. d/b/a Proteovant Therapeutics, Inc. ("Proteovant") (the 2022 Agreement) to jointly research and advance certain protein degrader therapies into development candidates, with VantAI, Inc. ("VantAI") performing computational chemistry services on behalf of Proteovant under the agreement. In December 2023, the Company entered into an Amended and Restated Collaboration and License Agreement (the "A&R Agreement") with VantAI and Proteovant, which amended and restated and replaced in its entirety the 2022 Agreement. Under the A&R Agreement, Proteovant ceased its role under the 2022 Agreement and VantAI provides expanded computational support directly to the Company, including computational biology and expanded computational chemistry to advance three novel protein degrader programs, and the Company has the option, at its sole discretion, to expand the collaboration to include a fourth target program.

Under the A&R Agreement, VantAI is eligible to receive up to $1.67 billion in contingent payments including specified research, development, regulatory and commercialization milestones for all the target programs. The Company will be obligated to pay VantAI tiered percentage royalties on a licensed product-by-licensed product basis ranging from the mid-single digits on annual net sales of each licensed product in the applicable territory, subject to adjustment in specified circumstances.

Under the 2022 Agreement, the Company paid Proteovant an upfront payment of $20.0 million in connection with the execution of the 2022 Agreement. This upfront payment was recorded as a prepaid asset on the Company's consolidated balance sheet and was amortized as research and development expense over the expected research period because the Company concluded that Proteovant was providing the Company with research services throughout such period. The Company determined to continue to amortize the remaining prepaid asset balance as research and development expense over the expected research period of the A&R Agreement as VantAI continued to provide such research and development services. During the year ended December 31, 2024, the Company recorded research and development expense of $7.5 million under the A&R Agreement. During the years ended December 31, 2023 and 2022, research and development expense recorded under the 2022 Agreement was $4.0 million and $4.4 million, respectively. The following table summarizes the prepaid assets associated with the A&R Agreement as of December 31, 2024 and 2023 (in thousands):

	December 31, 2024			December 31, 2023		
	Current	Noncurrent	Total	Current	Noncurrent	Total
Prepaid assets	$ 4,971	$ 2,666	$ 7,637	$ 6,581	$ 6,581	$ 13,162

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.

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), which currently include BLU-945 and BLU-525. In January 2024, the Company decided to discontinue further investment in the early clinical-stage therapies for EGFR-mutant NSCLC globally. Zai Lab retains its rights to BLU-945 and BLU-525 under the agreement. The Company retains exclusive rights to the licensed products outside the

Zai Lab Territory. The decision to deprioritize the licensed products does not have an impact on the Company's accounting treatment related to the Zai Lab agreement.

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. Zai Lab is responsible for conducting all development and commercialization activities in the Zai Lab Territory related to the licensed drug candidates.

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 (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 concluded that the Zai Lab agreement is a collaborative agreement under ASC 808. 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) global development of the licensed products. The Company concluded that Zai Lab is the Company's customer for the licenses and related activities in the Zai Lab Territory under ASC 606, whereas payments received by the Company for global development activities, including manufacturing, are accounted for as a reduction of related expenses. The Company did not record significant net reductions of expenses under the Zai Lab agreement during the years ended December 31, 2024, 2023 and 2022.

The Company evaluated the Zai Lab Territory specific licenses and related activities under ASC 606 and identified one performance obligation, which consists of the licenses and their initial know-how transfer at the outset of the arrangement. The manufacturing activities were excluded as performance obligation at the outset of the arrangement because it represented a customer option that was not a material right.

The Company determined that the license is a functional intellectual property license as 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. The transaction price of the Zai Lab agreement at the outset of the arrangement was determined to be $25.0 million and the Company satisfied the performance obligation upon delivery of the licenses and initial know-how transfer and accordingly, the upfront payment of $25.0 million was recognized as revenue in 2021. All milestone and royalty payments that the Company is eligible to receive were excluded from the transaction price, as all 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. Costs that are incurred associated with Zai Lab Territory specific activities are reimbursable from Zai Lab and are recognized as revenue. The Company did not record any revenue under the Zai Lab agreement during the year ended December 31, 2024 and the revenue recorded during the years ended December 31, 2023 and 2022 was not significant.

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. The Roche pralsetinib collaboration agreement was terminated on February 22, 2024 (the collaboration termination effective date), at which time the Company regained commercialization

and development rights to GAVRETO from Roche worldwide excluding the CStone Territory. The Company and Roche continued to perform their respective obligations under the Roche pralsetinib collaboration agreement through the collaboration termination effective date. On February 22, 2024, the Company and Roche entered into a transition agreement (the Roche transition agreement) in connection with the termination of the Roche pralsetinib collaboration agreement.

Under the Roche pralsetinib collaboration agreement, the Company received an upfront cash payment of $675.0 million and Roche Holdings, Inc. (Roche Holdings) purchased 1,035,519 shares of the Company's common stock at a purchase price of $96.57 per share for consideration of $100.0 million under a stock purchase agreement entered into in July 2020 in connection with the agreement. The fair market value of the common stock issued to Roche Holdings was $79.3 million on the date of issuance and the premium of $20.7 million was attributed to the transaction price of the Roche pralsetinib collaboration agreement.

In the U.S., the Company and Roche co-commercialized pralsetinib and shared profits and losses equally. In addition, the Company received tiered royalties on annual net sales of pralsetinib outside the U.S., excluding the CStone Territory (the Roche Territory). The Company and Roche shared global development costs for pralsetinib at a rate of 45 percent for the Company and 55 percent for Roche.

The Company concluded that the Roche pralsetinib collaboration agreement contained two material promises within the scope of ASC 606, pralsetinib license and the Roche Territory activities. The Company evaluated the Roche pralsetinib license under ASC 606 and concluded that the pralsetinib license was a functional intellectual property license and 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 was satisfied at a point in time.

The transaction price of the Roche pralsetinib 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 the collaboration termination effective date, the Company 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 collaboration agreement and recorded as revenue in the respective periods when they were achieved.

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 were within the scope of ASC 808, as both parties were 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 were accounted for either as an increase or reduction of research and development expenses.

No operating expenses were recorded under the Roche pralsetinib collaboration since June 30, 2024. 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 reductions to (increases in) research and development expenses related to global development activities for pralsetinib under the Roche pralsetinib collaboration during the years ended December 31, 2024, 2023 and 2022 (in thousands):

	Year Ended December 31,		
	2024	2023	2022
Reductions to selling, general and administrative expenses	$ 980	$ 10,982	$ 16,600
Increases in research and development expenses	$ 1,103	$ 24,915	$ 19,297

Roche was the principal for recording product sales to customers in the U.S., and the Company recognized a portion of the profit as revenue and losses as collaboration loss sharing in its consolidated statements of operations and comprehensive loss. During the year ended December 31, 2024, the Company recorded revenue of $1.4 million derived from profit sharing on Roche sales of GAVRETO in the U.S. During the years ended December 31, 2023 and 2022, the Company recorded a collaboration loss sharing expense of $4.3 million and $8.9 million on Roche's sales of GAVRETO in the U.S., respectively. Costs incurred associated with the Roche Territory activities were reimbursable from Roche and were recognized as revenue

The following table summarizes revenue recognized under the Roche pralsetinib collaboration during the years ended December 31, 2024, 2023 and 2022 (in thousands):

	Year Ended December 31,		
	2024	2023	2022
Manufacturing and research and development services related to Roche Territory-specific activities	$ 324	$ 679	$ 6,710
Royalty revenue	180	1,464	848
Profit sharing revenue	1,416	—	—
Total Roche pralsetinib collaboration revenue	$ 1,920	$ 2,143	$ 7,558

Upon termination of the Roche pralsetinib collaboration agreement, the Company chose not to assume responsibility for any ongoing pralsetinib clinical trials, and under the terms of the Roche pralsetinib collaboration agreement, Roche bears sole responsibility for all costs associated with the wind-down of these trials.

Pursuant to the Roche transition agreement, the Company is obligated to reimburse Roche for wind-down costs associated with the marketing and commercialization activities occurred for Roche Territory until December 31, 2026. Additionally, the Company is obligated to reimburse Roche for any U.S. transition related costs that exceeds GAVRETO's net sales in the U.S., and any remaining net profit are shared equally between the Company and Roche until December 31, 2025. The Company has concluded that such activities and associated payments to Roche are not within the scope of ASC 808 as only the Company is exposed to significant risks and awards associated with those activities. The Company records those wind-down costs and the net amount of U.S. transition costs reimbursable to Roche as selling, general, and administrative expenses when they are incurred. During the year ended December 31, 2024, the Company recorded a total of $5.7 million in such costs.

The following table summarizes the assets and liabilities associated with the Roche pralsetinib agreements as of December 31, 2024 and 2023 (in thousands):

	December 31, 2024	December 31, 2023
Unbilled accounts receivable	$ —	$ 361
Accrued expenses	$ 1,712	$ 7,388

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 clinical development for the treatment of fibrodysplasia ossificans progressiva (FOP), now referred to as fidrisertib, 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 December 31, 2024, 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 December 31, 2024, 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 in prior years.

The Company did not recognize revenue under the Clementia agreement during the years ended December 31, 2024 and 2023. During the year ended December 31, 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. All 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 December 31, 2024 and 2023.

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 and 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 December 31, 2024, 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 December 31, 2024, 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 years ended December 31, 2024 and 2023. During the year ended December 31, 2022, the Company recorded $1.7 million in reduction of related expenses from manufacturing and research and development services related to global 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 year ended December 31, 2024. During the years ended December 31, 2023, and 2022, cash consideration associated with achieved development and sales-based milestones of $9.0 million and $6.5 million, respectively, were added to the estimated transaction price for the CStone agreement and recognized as revenue in such periods. 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 active pharmaceutical ingredient (API), 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 supply to CStone. Considerations payable to CStone related to the Company's obligations in connection with commercial supply of pralsetinib for the CStone Territory was recognized as a reduction of collaboration revenue.

A summary of revenue recognized under the CStone agreement during the years ended December 31, 2024, 2023 and 2022 is as follows (in thousands):

	Year Ended December 31,		
	2024	2023	2022
License milestone revenue	$ —	$ 9,000	$ 6,500
Manufacturing services and royalty revenue related to CStone Territory-specific activities	3,304	8,312	17,794
Total CStone collaboration revenue	$ 3,304	$ 17,312	$ 24,294

The Company did not have any contract assets related to the CStone collaboration as of December 31, 2024 and 2023. The following table presents the contract liabilities associated with the CStone collaboration as of December 31, 2024 and 2023 (in thousands):

	As of December 31,	
	2024	2023
Contract liabilities	$ —	$ 604
Accrued expenses	$ 2,027	$ 1,863

The Company's liabilities associated with the CStone collaboration as of December 31, 2024 and 2023 resulted primarily from the Company's obligations 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.

On April 30, 2023, the Company and Roche entered into a mutual termination agreement to terminate the Roche immunotherapy agreement. Certain licenses granted by Roche to the Company survived and became exclusive, worldwide, perpetual, royalty-free and irrevocable and the Company retained ownership of all the 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 consisted 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. The Company recognized revenue associated with the performance obligation using an input method, based on the costs incurred for 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 and no revenue was recognized thereafter for this agreement. During the years ended December 31, 2023 and 2022, the Company recognized research and development services revenue of $25.7 million and $2.3 million, respectively, under the Roche immunotherapy agreement, of which $16.0 million and $4.4 million, respectively, resulted from changes in contract liability balances at the beginning of the period. There was no revenue deferred as a contract liability associated with the Roche immunotherapy agreement as of December 31, 2024 and 2023.

12. Stockholders' Equity

In February 2022, the Company entered into an at-the-market (ATM) Facility with Cowen and Company, LLC (Cowen), pursuant to which the Company may offer and sell, from time to time at its sole discretion, shares of its common stock having an aggregate offering price of up to $300.0 million through Cowen as sales agent. During the year ended December 31, 2024, the Company issued and sold 544,719 shares of its common stock under the ATM Facility and received net proceeds of $48.9 million. The Company did not issue any shares under the ATM Facility during the years ended December 31, 2023 and 2022.

13. Stock-based Compensation

Stock Plans

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 provided that the number of shares reserved and available for issuance under the 2015 Plan would 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, 2024, the number of shares reserved for issuance under the 2015 Plan was increased by 2,445,889 shares.

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 and 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.

At the Company's annual meeting of stockholders held on June 12, 2024, the Company's stockholders approved the 2024 Stock Incentive Plan (the 2024 Plan), which replaced the Company's 2015 Plan and the Inducement Plan. As of December 31, 2024, there were 7,832,847 and 724,176 shares underlying awards outstanding under the 2015 Plan and the Inducement Plan, respectively. No further shares will be granted under the 2015 Plan and the Inducement Plan after the effective date of the 2024 Plan. The 2024 Plan provides for the granting of incentive stock options, nonstatutory stock options, stock appreciation rights, restricted stock, restricted stock units, performance-based restricted stock units, unrestricted stock and cash-based awards. The 2024 Plan provides for the issuance of up to 9,200,000 shares. Any shares of common stock underlying any awards that are forfeited, canceled, held back upon exercise or settlement of an award to satisfy the exercise price or tax withholding, repurchased, expire or are otherwise terminated by the Company under the 2024 Plan and the 2015 Plan will be added back to the shares of common stock available for issuance under the 2024 Plan. As of December 31, 2024, there were 9,116,614 shares available for future grant under the 2024 Plan.

On November 22, 2024, the Company learned that the record date for its 2024 annual meeting was 61 days prior to the meeting, exceeding the 60-day limit under Section 213(a) of the Delaware General Corporation Law (DGCL). On December 2, 2024, the Company petitioned the Delaware Court of Chancery under Section 205 of the DGCL to validate the actions taken at the 2024 annual meeting, including the adoption of the 2024 Plan. The Court granted the Company's petition on January 23, 2025, ratifying these actions as of the meeting date. During the year ended December 31, 2024, the Company granted 247,987 shares under the 2024 Plan. For more information, see "*Legal Proceedings*" in Note 19, *Commitments and Contingencies*.

2015 Employee Stock Purchase Plan

In 2015, the Company's board of directors and stockholders approved the 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 years beginning January 1, 2024 and 2025, the number of shares reserved for issuance under the 2015 ESPP was increased by 611,472 and 637,122 shares, respectively. As of December 31, 2024, there were 4,196,701 shares available for issuance under the 2015 ESPP. The Company issued 65,813, 96,290, and 80,717 shares under the ESPP during the years ended December 31, 2024, 2023, and 2022 respectively.

Stock-based Compensation Expense

The Company recognized stock-based compensation expense totaling $108.9 million, $92.7 million and $99.0 million for the years ended December 31, 2024, 2023 and 2022, respectively. Stock-based compensation expense by award type included within the consolidated statements of operations and comprehensive loss is as follows (in thousands):

	Year Ended December 31,		
	2024	2023	2022
Stock options	$ 42,031	$ 40,560	$ 52,931
Restricted stock units	61,722	50,095	45,285
Performance-based restricted stock units	4,445	867	—
Employee stock purchase plan	1,722	1,734	1,418
Subtotal	109,920	93,256	99,634
Capitalized stock-based compensation costs	(1,009)	(584)	(663)
Stock-based compensation expense included in total cost and operating expenses	$ 108,911	$ 92,672	$ 98,971

The following table presents stock-based compensation expense that is included in operating expenses by classification within the consolidated statements of operations and comprehensive loss (in thousands):

	Year Ended December 31,		
	2024	2023	2022
Research and development	$ 47,455	$ 41,534	$ 40,302
Selling, general and administrative	61,456	51,138	58,669
Total stock-based compensation expense included in operating expenses	$ 108,911	$ 92,672	$ 98,971

At December 31, 2024, there was $207.6 million of total unrecognized compensation cost related to non-vested stock awards, which is expected to be recognized over a weighted-average period of 2.4 years.

Stock Options

Stock options granted by the Company generally vest ratably over four years, with a one-year cliff for new employee awards and are exercisable from the date of grant for a period of ten years. The fair value of each option issued to employees was estimated at the date of grant using the Black-Scholes option pricing model with the following weighted-average assumptions:

	Year Ended December 31,		
	2024	2023	2022
Risk-free interest rate	4.26 %	4.13 %	2.27 %
Expected dividend yield	—	—	—
Expected term (years)	6.0	6.0	6.0
Expected stock price volatility	55.54 %	56.01 %	55.15 %

The following table summarizes the stock option activity for the year ended December 31, 2024:

	Shares	Weighted-Average Exercise Price	Remaining Contractual Life (in Years)	Aggregate Intrinsic Value(1) (in thousands)
Outstanding at December 31, 2023	6,658,444	$ 66.48	6.39	$ 178,581
Granted [2]	1,075,799	95.77		
Exercised	(1,159,269)	61.96		
Canceled	(205,250)	75.42		
Outstanding at December 31, 2024	6,369,724	$ 72.09	6.14	$ 115,874
Exercisable at December 31, 2024	4,514,741	$ 71.51	5.20	$ 82,016

(1) Intrinsic value represents the amount by which the fair market value as of December 31, 2024 of the underlying common stock exceeds the exercise price of the option.

(2) Out of stock options granted in 2024, 55,119 stock options were granted under the 2024 Plan.

The weighted average grant date fair value of options granted in the years ended December 31, 2024, 2023 and 2022 was $54.15, $25.81 and $32.30, respectively. The total intrinsic value of options exercised in the years ended December 31, 2024, 2023, and 2022 was $45.1 million, $11.6 million, and $11.8 million, respectively.

At December 31, 2024, the total unrecognized compensation expense related to unvested stock option awards was $71.4 million, which is expected to be recognized over a weighted-average period of approximately 2.4 years.

Restricted stock units

Restricted stock units granted by the Company generally vest ratably over four years. The following table summarizes the restricted stock units activity for the year ended December 31, 2024:

	Shares	Weighted-Average Grant Date Fair Value
Unvested shares at December 31, 2023	2,107,026	$ 60.33
Granted [1]	1,130,316	95.24
Vested	(795,219)	64.77
Forfeited	(151,192)	70.34
Unvested shares at December 31, 2024	2,290,931	$ 75.36

(1) Out of restricted stock units granted in 2024, 192,868 restricted stock units were granted under the 2024 Plan.

The total fair value of restricted stock units vested during the years ended December 31, 2024, 2023 and 2022 was $75.8 million, $31.6 million and $29.4 million, respectively. As of December 31, 2024, the total unrecognized compensation expense related to unvested restricted stock units was $126.2 million, which is expected to be recognized over a weighted-average period of approximately 2.4 years.

Performance-based restricted stock units

In 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 which is measured 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 year ended December 31, 2024:

	Shares	Weighted-Average Grant Date Fair Value
Unvested shares at December 31, 2023	52,500	$ 59.32
Granted	90,000	135.84
Vested	—	—
Forfeited	—	—
Unvested shares at December 31, 2024	142,500	$ 107.65

As of December 31, 2024, the total unrecognized compensation expense related to unvested PSUs was $10.0 million, which is expected to be recognized over a weighted-average period of approximately 1.8 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.

14. Net Loss per Share

Basic net loss per share is calculated by dividing net loss by the weighted average shares of common stock 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 diluted 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 years ended December 31, 2024, 2023 and 2022 because including them would have had an anti-dilutive effect (in thousands):

	Year Ended December 31,		
	2024	2023	2022
Stock options	6,370	6,658	6,233
Restricted stock units	2,291	2,107	1,894
Performance-based restricted stock units	143	53	—
ESPP shares	28	39	55
Total	8,832	8,857	8,182

15. Income Taxes

The Company recorded an income tax provision of $1.2 million for the year ended December 31, 2024 due to state income taxes and taxable income from the jurisdictions in which the Company is subject to tax.

A reconciliation of the U.S. statutory income tax rate to the Company's effective tax rate is as follows for the years ended December 31, 2024, 2023 and 2022:

	Year Ended December 31,		
	2024	2023	2022
Federal income tax (benefit) at statutory rate	21.00 %	21.00 %	21.00 %
Permanent differences	0.82	(0.42)	(0.38)
U.S. Tax on foreign earnings	—	—	2.52
Federal research and development credits	14.43	2.50	1.39
Federal orphan drug credits	18.41	1.63	(0.42)
State income tax, net of federal benefit	7.91	3.41	2.92
Foreign rate differential	(13.47)	(0.41)	(0.13)
Deferred rate change	(9.21)	2.53	0.52
Foreign tax credit	—	—	0.03
Stock Based Compensation	(5.33)	(0.76)	(1.03)
Other	(0.27)	(0.02)	0.39
Change in valuation allowance	(36.17)	(29.65)	(27.76)
Effective income tax rate	(1.88)%	(0.19)%	(0.95)%

The Company's deferred tax assets and liabilities consist of the following (in thousands) as of December 31, 2024 and 2023:

	As of December 31,	
	2024	2023
Deferred tax assets:		
Net operating loss carryforwards	$ 244,189	$ 232,624
Research and development credit carryforwards	67,592	53,329
Orphan drug credit carryforwards	168,799	156,816
Accrued expenses and other	62,187	60,350
Royalty Pharma milestones	—	12,024
R&D capitalization	190,040	153,836
Financing arrangements	63,424	107,693
Deferred rent	19,040	22,204
Other	3,785	1,488
Total gross deferred tax asset	819,056	800,364
Deferred tax liability		
Depreciation	(6,123)	(6,107)
Right of use assets	(14,837)	(17,423)
Other	—	(2,068)
Valuation allowance	(798,096)	(774,766)
Net deferred tax asset	$ —	$ —

Management has evaluated the positive and negative evidence bearing upon the realizability of its deferred tax assets and has determined that it is more likely than not that the Company will not recognize the benefits of its net federal, foreign and state deferred tax assets, and as a result, a valuation allowance of $798.1 million and $774.8 million has been established at December 31, 2024 and 2023, respectively. The change in the valuation allowance was $23.3 million and $149.7 million for the years ended December 31, 2024 and 2023, respectively. The increase of deferred tax asset between December 31, 2024 and 2023 is primarily driven by the generation of federal and state net operating losses and the generation of research and development and orphan drug credits, as well as the capitalization and amortization of all Sec. 174 costs associated with research and development costs.

The Company has incurred net operating losses (NOL) since inception with the exception of years 2020 and 2022. As of December 31, 2024, the Company had federal and state NOL carryforwards of $859.2 million and $1,077.3 million, respectively, which begin to expire in 2030, and of which $843.3 million of the Company's federal NOL is post 2017 NOL that will be carried forward indefinitely. As of December 31, 2024, the Company had federal and state research and development tax credit carryforwards of $39.9 million and $31.0 million, respectively, which begin to expire in 2039 and 2028 respectively. As of December 31, 2024, the Company had federal orphan drug credits of $168.8 million, which begin to expire in 2035 and state investment tax credits of $0.9 million, which have begun to expire in 2024. As of December 31, 2024, the Company has foreign tax credits of $2.5 million which will expire in 2031.

The Company has analyzed and validated its research and development tax credits as well as its orphan drug credits for 2011-2023. The Company generated research credits in 2024 but has not conducted a formal study to document its qualified activities. This study may result in an adjustment to the Company's research and development credit carryforwards. No amounts are being presented as an uncertain tax position as of December 31, 2024 until such study is completed and the adjustment is known. A valuation allowance has been provided against the Company's research and development credits and, if an adjustment is required, this adjustment would be offset by an adjustment to the deferred tax asset established for the research and development credit carry-forwards and the valuation allowance.

The Internal Revenue Code of 1986, as amended (the Code), provides for a limitation of the annual use of NOL and other tax attributes (such as research and development tax credit carryforwards) following certain ownership changes (as defined by the Code) that could limit the Company's ability to utilize these carryforwards. The Company may have experienced such ownership changes in the past, and may experience ownership changes in the future as a result of shifts in its stock ownership, some of which are outside the Company's control. Approximately $2.0 million of the Company's NOL carryforwards may not be available for utilization within their applicable carryforward periods based on the Section 382 study in 2021. In addition, U.S. tax laws limit the time during which these carryforwards may be applied against future taxes. Therefore, the Company may not be able to take full advantage of these carryforwards for federal or state income tax purposes.

Interest and penalty charges, if any, related to unrecognized tax benefits would be classified as income tax expense in the accompanying statements of operations and comprehensive income (loss). As of December 31, 2024, the Company did not have any gross unrecognized tax benefit, excluding interest and penalties. As of December 31, 2024, the Company was open to examination in the U.S. federal and certain state jurisdictions for all of the Company's tax years since the net operating losses may potentially be utilized in future years to reduce taxable income. Since the Company is in a loss carryforward position, it is generally subject to examination by the U.S. federal, state, and local income tax authorities for all tax years in which a loss carryforward is available.

Effective January 1, 2022, a provision of the Tax Cuts and Jobs Act (TCJA) took effect creating a significant change to the treatment of research and experimental (R&E) expenditures under Section 174 of the Code (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 TCJA provision, however, eliminates this option and requires 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 are 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 calendar year ended December 31, 2024.

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. In connection with and effective upon the termination of the Roche collaboration agreement, on February 22, 2024, Royalty Pharma and the Company entered into the Royalty Pharma Termination Agreement to terminate the Royalty Purchase Agreement. The Company accounted for the Royalty Pharma Termination Agreement as a debt extinguishment. As a result, during the year ended December 31, 2024 the Company recorded $173.7 million as a debt extinguishment gain in its consolidated financial statements. For additional information, see Note 3, *Financing Arrangements*. For tax purposes, the debt extinguishment gain was excluded from the December 31, 2024 estimated taxable income calculation since it was previously included in taxable income during the year ended December 31, 2022.

On August 1, 2022, the Company entered into the IDRx License Agreement and IDRx Stock Purchase Agreement. Pursuant to these agreements, the Company licensed its internally discovered KIT exon 13 inhibitor to IDRx in exchange for a 4,509,105 shares of IDRx's Series A preferred stock and the eligibility to receive future milestones and tiered royalty payments. For book and tax purposes, the value of the equity totaling $27.5 million was included in the taxable income for the year ended December 31, 2022.

As of December 31, 2024, the Company did not have any gross unrecognized tax benefits, excluding interest and penalties due to an audit settlement. The following table provides the reconciliation of the total amounts of the Company's unrecognized tax benefits for the years ended December 31, 2024 and 2023 (in thousands):

	Year ended December 31,	
	2024	2023
Beginning balance at January 1	$ 211	$ —
Gross Increases - tax positions in prior periods	—	211
Gross Increases - current period tax positions	—	—
Settlements	(211)	—
Lapse of statutes	—	—
Ending balance at December 31	$ —	$ 211

16. 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 December 31, 2024.

38 Sidney Street

In February 2015, the Company entered into a lease for approximately 39,000 rentable square feet of office and laboratory space at 38 Sidney Street in Cambridge, Massachusetts, which was extended in December 2021. The extended lease term will expire on November 30, 2029. The Company agreed to pay an initial annual base rent of approximately $4.5 million, which rises annually until it reaches approximately $5.5 million. The lease extension provided the Company with an allowance for leasehold improvements of $0.8 million improvements to be made to the premises. A security deposit of $0.9 million was recorded as restricted cash on the Company's consolidated balance sheet as of December 31, 2024. The Company's sublease agreements for the 38 Sidney Street property expired in 2022.

45 Sidney Street

In April 2017, the Company entered into a lease agreement for approximately 99,833 rentable square feet of office and laboratory space located at 45 Sidney Street in Cambridge, Massachusetts. In September 2018, the Company entered into an amendment to the lease agreement to expand the rentable square footage to approximately 139,216 square feet. The initial term of the lease agreement will expire on November 30, 2029, unless terminated sooner. The lease agreement also provides the Company with an option to extend the lease agreement for two consecutive five-year periods at the then fair market annual rent, as defined in the lease agreement.

The Company has agreed to pay for the 99,833 rentable square feet an initial annual base rent of approximately $7.7 million, which increases annually until it reaches approximately $10.6 million in the last year of the initial term. The Company has also agreed to pay an initial annual base rent of approximately $3.2 million for the expansion premises, which increases annually until it reaches approximately $4.2 million in the last year of the initial term for the expansion premises. The amended lease provided the Company with a total tenant improvement allowance of approximately $17.4 million for improvements to be made to the premises. A security deposit of $3.3 million was recorded as restricted cash on the Company's consolidated balance sheet as of December 31, 2024.

The lease agreements do not contain residual value guarantees and the components of lease cost for the years ended December 31, 2024, 2023 and 2022 were as follows (in thousands):

	Year Ended December 31,		
Operating leases:	2024	2023	2022
Lease cost	$ 23,238	$ 23,190	$ 21,830
Sublease income	-	-	(2,132)
Net lease cost	$ 23,238	$ 23,190	$ 19,698

The Company has not entered into any material short-term leases or financing leases as of December 31, 2024.

Supplemental cash flow information related to leases for the years ended December 31, 2024, 2023 and 2022 was as follows (in thousands):

	Year Ended December 31,		
	2024	2023	2022
Cash paid for amounts included in the measurement of lease liabilities	$ 18,284	$ 17,741	$ 15,891
Lease liabilities arising from obtaining right-of-use assets:			
Operating leases	$ 556	$ 915	$ 72

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	4.8
Weighted average discount rate	7.3%

Future minimum lease payments under non-cancellable leases as of December 31, 2024 were as follows (in thousands):

2025	$ 18,757
2026	19,318
2027	19,876
2028	20,451
2029	19,268
Thereafter	84
Total future minimum lease payments	97,754
Less imputed interest	(15,618)
Total	$ 82,136

17. Employee Benefit Plans

The Company sponsors various retirement and pension plans. The estimates of liabilities and expenses for these plans incorporate a number of assumptions, including expected rates of return on plan assets and interest rates used to discount future benefits.

401(k) Savings Plan

The Company maintains a 401(k) plan for employees (the 401(k) Plan). The 401(k) Plan is intended to qualify under Section 401(k) of the Code, so that contributions to the 401(k) Plan by the Company, and the investment earnings on contributions, are not taxable to the employees until withdrawn from the 401(k) Plan, and so that contributions by the Company, if any, will be deductible by the Company when made. Under the 401(k) Plan, employees may elect to reduce their current compensation by up to the statutorily prescribed annual limit and to have the amount of such reduction

contributed to the 401(k) Plan. The 401(k) Plan permits the Company to make contributions up to the limits allowed by law on behalf of all eligible employees. The expense related to the 401(k) Plan primarily consists of the Company's matching contributions. The expenses related to the 401(k) Plan for the years ended December 31, 2024, 2023 and 2022 were $4.7 million, $4.6 million and $3.7 million, respectively.

Switzerland Defined Benefit Plan

The Company maintains a pension plan covering employees of its Swiss subsidiary, Blueprint Medicines (Switzerland) GmbH (the "Swiss Plan"). The Swiss Plan is a government-mandated retirement fund that provides employees with a minimum benefit. Employer and employee contributions are made to the Swiss Plan based on various percentages of salary and wages that vary according to employee age and other factors. As is customary with Swiss pension plans, the assets of the Swiss Plan are invested in a collective fund with multiple employers. The Company has no investment authority over the assets of the Swiss Plan, which are held and invested by a Swiss insurance company. The investment strategy of the Swiss Plan is managed by an independent asset manager with the objective of achieving a consistent long-term return which will provide sufficient funding for future pension obligations while limiting risk.

The following table summarizes the plan balances as of December 31, 2024 and 2023 (in thousands):

	December 31, 2024	December 31, 2023
Fair value of plan assets	$ 9,241	$ 8,416
Projected benefit obligation	(16,065)	(14,632)
Unfunded status recorded as other long-term liabilities	(6,824)	(6,216)
Accumulated benefit obligation	$ 12,071	$ 10,984

The Company's net periodic benefit cost for the years ended December 31, 2024, 2023 and 2022 was $1.4 million, $1.0 million and $1.2 million, respectively. The contributions to the Swiss Plan for the years ended December 31, 2024, 2023 and 2022 were $1.1 million, $1.0 million, and $0.8 million.

The following table summarizes the benefits expected to be paid by the Company in each of the next five years and in aggregate for the five years thereafter as of December 31, 2024 (in thousands):

	As of December 31 2024
2025	$ 466
2026	599
2027	546
2028	582
2029	623
2030 to 2034	4,028

18. Segment Information

The Company operates as one operating segment, focused on discovering, developing and delivering therapies for allergy/immunology and oncology/hematology. The determination of a single business segment is consistent with the consolidated financial information regularly provided to the Company's chief operating decision maker ("CODM"). The Company's CEO, as the chief operating decision maker (CODM), uses consolidated, single-segment financial information for purposes of evaluating performance, making operating decisions, allocating resources, and planning and forecasting for future periods.

The CODM assesses performance and decides how to allocate resources based on consolidated net income (loss). This measure is used to monitor budget versus actual results to evaluate the performance of the segment.

The CODM reviews cash, cash equivalents and marketable securities as a measure of segment assets. As of December 31, 2024 and 2023, the Company's cash, cash equivalents and marketable securities were $863.9 million and $767.2 million, respectively.

The following tables illustrates information about segment revenue, significant segment expenses and segment operating loss for the years ended December 31, 2024, 2023 and 2022 (in thousands):

	Year Ended December 31,		
	2024	2023	2022
Revenue	$ 508,824	$ 249,380	$ 204,036
Less[1]:			
Cost of sales	20,163	8,540	17,813
Research and development expense[2]:			
Compensation and related expenses	114,861	110,740	96,625
Early drug discovery and platform	76,970	70,383	75,542
Clinical and manufacturing related activities	38,889	138,801	198,317
Facilities and IT	35,589	33,783	28,917
Consulting and professional services	24,182	29,189	33,033
Other research and development	3,487	3,290	4,683
Total research and development expense[2]	293,978	386,186	437,117
Selling, general and administrative expense[3]:			
Compensation and related expenses	127,286	120,756	84,324
Commercial and related expenses	96,604	53,579	33,334
Consulting and professional services	49,575	41,876	36,264
Facilities and IT	12,214	13,126	11,431
Other selling, general and administrative	12,137	14,666	13,352
Total selling, general and administrative expense[3]	297,816	244,003	178,705
Collaboration loss sharing	—	4,256	8,948
Stock-based compensation	108,911	92,672	98,971
Other segment items[4]	144,955	(20,707)	(19,999)
Net loss	$ (67,089)	$ (506,984)	$ (557,517)

1) The significant expense categories and amounts align with the segment-level information that is regularly provided to the chief operating decision maker.
2) Research and development expense for the years ended December 31, 2024, 2023 and 2022 exclude $47.5 million, $41.5 million, and $40.3 million of stock-based compensation expense, respectively.
3) Selling, general and administrative expense for the years ended December 31, 2024, 2023 and 2022 exclude $61.5 million, $51.1 million, and $58.7 million of stock-based compensation expense, respectively.
4) Other segment items include interest expense, net, other income (expense), net, debt extinguishment gain, and income tax expense.

The Company operates in the U.S. and Europe. All material long-lived assets of the Company reside in the U.S. For geographic information about the Company's product revenues, see Note 6, *Product Revenue and Related Reserves*.

19. Commitments and Contingencies

Purchase Commitments Associated with Clinical and 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. The aggregate amount of future unconditional purchase obligations under these manufacturing agreements over the period of next five years is approximately $2.0 million as of December 31, 2024.

Legal Proceedings

In the normal course of business, the Company from time to time is named as a party to various legal claims, actions and complaints, which have included and may include matters involving securities, employment, intellectual property, arising from the use of therapeutics utilizing its technology, or others. The Company records a loss contingency reserve for a legal proceeding when it considers the potential loss probable and it can reasonably estimate the amount of the loss or determine a probable range of loss. The Company provides disclosure when it considers a loss reasonably possible or when it determines that a loss in excess of a reserve is reasonably possible. The Company provides an estimate of such reasonably possible losses or an aggregate range of such reasonably possible losses, unless the Company believes that such an estimate cannot be made. The Company expenses the costs related to its legal proceedings as they are incurred. As of December 31, 2024, the Company has not recorded any significant accruals for loss contingencies.

On June 7, 2024, a purported stockholder filed a putative class action lawsuit against the Company in the Court of Chancery of the State of Delaware, with the caption Johnson v. Blueprint Medicines Corporation, Case No. 2024-0625. Plaintiff claims in the complaint that a "Proxy Access" provision in the Company's Amended and Restated Bylaws, effective November 30, 2022, is invalid under Delaware law because it allegedly usurps the right of stockholders to select the members of the board of directors, and plaintiff seeks declaratory relief invalidating that provision, as well as attorneys' fees and costs. On October 7, 2024, the lawsuit was consolidated with twelve other lawsuits against companies with similar bylaw provisions under the caption In re Irrevocable Resignation Bylaw Litigation, Consolidated C.A. No. 2024-0538-JTL. On October 11, 2024, the Company, together with the other companies in the consolidated action, filed an opening brief in support of a motion to dismiss the complaint. Plaintiff filed an answering brief on November 25, 2024, and the Company filed a reply brief on December 20, 2024. The Company does not believe the outcome of this matter will have a material effect on its financial position, results of operations, or liquidity.

On November 22, 2024, a purported stockholder filed a putative class action against the Company, the members of the board of directors and certain executive officers of the Company, as well as a derivative action against the members of the board of directors and certain executive officers of the Company, in the Court of Chancery of the State of Delaware in an action captioned *Taylor v. Haviland, et al.*, C.A. No. 2024-1203-JTL (the "*Taylor* Action"). Plaintiff in the *Taylor* Action claims that the record date for the Company's 2024 annual meeting of stockholders, which was the close of business on Friday, April 12, 2024, did not comply with the 60-day maximum under Section 213(a) of the DGCL, because it was 61 days before the date of the 2024 annual meeting. Plaintiff brings direct claims for violation of Section 213(a) of the DGCL and breach of fiduciary duty, and derivative claims for breach of fiduciary duty and unjust enrichment, and seeks a declaration that certain actions taken in connection with the Company's annual meeting of stockholders are void, as well as attorneys' fees and costs.

On December 2, 2024, the Company filed a petition pursuant to Section 205 of the DGCL seeking the validation of the certain actions taken in connection with the Company's 2024 annual meeting of stockholders, retroactive to the date of the 2024 annual meeting, in the Court of Chancery of the State of Delaware in an action captioned In re Blueprint Medicines Corporation, C.A. No. 2024-1234-JTL (the "Section 205 Action"). On December 4, 2024, plaintiff in the *Taylor* Action agreed to hold the defendants' answer in abeyance pending resolution of the Section 205 Action. Following the Company's brief in support of its petition in the Section 205 Action on December 20, 2024, and the lack of any objection, the Court granted the petition on January 23, 2025, such that the stockholder proposals that were presented to and approved by the Company's stockholders at the 2024 annual meeting, and all actions taken in reliance on the stockholder votes at the annual meeting, were hereby declared valid and effective as of the date of the 2024 annual meeting.

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 material claims under indemnification arrangements, and it has not accrued any liabilities related to such obligations in its consolidated financial statements as of December 31, 2024 or 2023.

20. Subsequent Events

In January 2025, IDRx announced that they had entered into an agreement under which GSK plc will acquire IDRx for $1.0 billion upfront with an additional $150.0 million regulatory approval-based milestone payment. The transaction is expected to close in the first quarter 2025. Consequently, the Company will recognize an investment gain based on its ownership in IDRx.

Exhibit 21.1

Subsidiaries of the Registrant

Entity	State/Jurisdiction of Incorporation or Organization
Blueprint Medicines Security Corporation	Massachusetts
Blueprint Medicines (Switzerland) GmbH	Switzerland
Blueprint Medicines (Netherlands) B.V.	Netherlands
Blueprint Medicines (UK) Ltd.	United Kingdom
Blueprint Medicines (Germany) GmbH	Germany
Blueprint Medicines Spain, S.L.	Spain
Blueprint Medicines (France) SAS	France
Blueprint Medicines (Italy) S.r.L.	Italy

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

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

(1) Registration Statement (Form S-3ASR No. 333-236424) of Blueprint Medicines Corporation,
(2) Registration Statement (Form S-8 No. 333-203749) pertaining to the 2011 Stock Option and Grant Plan, 2015 Stock Option and Incentive Plan, and 2015 Employee Stock Purchase Plan of Blueprint Medicines Corporation,
(3) Registration Statements (Form S-8 Nos. 333-210125, 333-216575, 333-223131, 333-229885, 333-236421, 333-253215,333-262800, 333-269844, and 333-277149) pertaining to the 2015 Stock Option and Incentive Plan and 2015 Employee Stock Purchase Plan of Blueprint Medicines Corporation,
(4) Registration Statement (Form S-8 No. 333-238039 and 333-266469) pertaining to the 2020 Inducement Plan of Blueprint Medicines Corporation, and
(5) Registration Statement (Form S-8, No. 333-280405) pertaining to the 2024 Stock Incentive Plan of Blueprint Medicines.

of our reports dated February 13, 2025, with respect to the consolidated financial statements of Blueprint Medicines Corporation and the effectiveness of internal control over financial reporting of Blueprint Medicines Corporation included in this Annual Report (Form 10-K) of Blueprint Medicines Corporation for the year ended December 31, 2024.

/s/ Ernst & Young

Boston, Massachusetts
February 13, 2025

Exhibit 31.1

CERTIFICATIONS

I, Kathryn Haviland, certify that:

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

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

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

4. The registrant's other certifying officer(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 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: February 13, 2025

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

Exhibit 31.2

CERTIFICATIONS

I, Michael Landsittel, certify that:

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

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

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

4. The registrant's other certifying officer(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 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: February 13, 2025

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 Annual Report on Form 10-K of Blueprint Medicines Corporation (the "Company") for the year ended December 31, 2024 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 (15 U.S.C. 78m or 78o(d)); 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: February 13, 2025

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

Date: February 13, 2025

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